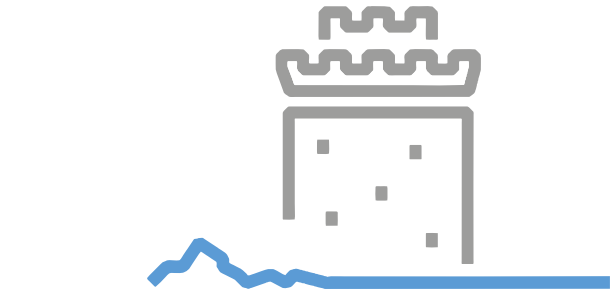

EERVC 4

EASTERN EUROPEAN REGIONAL VETERINARY CONFERENCE

Grand Hotel Palace, Thessaloniki, Greece
October 3-5, 2019

In collaboration with
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PROCEEDINGS

Advancing the veterinary profession
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EERVC

EASTERN EUROPEAN REGIONAL VETERINARY CONFERENCE

Advancing the veterinary profession in Eastern Europe

EERVC is a not-for-profit organization that will reinvest all conference profits into the annual event and improving professional standards in the region. EERVC is managed by a Project Board joined together under a European Economic Interest Group partnership. The founding partners in this Board are the Small Animal Veterinary Associations of Croatia and Serbia, working together with the British Small Animal Veterinary Association (BSAVA). BSAVA has invested in EERVC as part of its remit as a registered charity and is offering its expertise gained from 60 years of BSAVA Congress.

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Welcome

Dear EERVC delegate,

Welcome to Thessaloniki, the second largest city in Greece and the capital of the geographic region of Macedonia, for the 4th Eastern European Regional Veterinary Conference (EERVC).

The conference will offer cutting-edge international speakers, the largest regional and international trade exhibition in the region and unparalleled opportunities for professional networking during an affordable, high-quality, 3 -day annual meeting.

EERVC speakers have been selected by recommendation and their expertise. Over the last 3 years we have received fantastic feedback from delegates and we continue to follow your suggestions when considering the speakers and their topics. Lectures cover all aspects of small animal medicine and surgery, as well as topics of current interest for the profession.

The trade exhibition at EERVC 2019 is a fantastic place to discover the newest products from industry, including the very latest innovations and services focused on the needs of the small animal veterinarian. We recommend that you plan a trip to explore the trade exhibition and make the most of the veterinary industry expertise and their products.

The EERVC Organising Team have prepared lots of great opportunities for networking including the Greek Night on Thursday evening, Welcome Reception on Friday and the famously known EERVC Party on Saturday Night with the Perpetuum Mobile Band and top-class DJ – we hope you can join us and dance until the very late hours!

On behalf of the EERVC Board, I would like to thank our exhibitors and sponsors, whose support ensures we can continue to deliver high quality and affordable CPD in this region.

My personal thanks go to the EERVC Project Board and the founding partners from the Small Animal Veterinary Associations of Croatia, Serbia and the British Small Animal Veterinary Association. The team all work in a voluntary capacity and have worked extremely hard to continue this ambitious mission of advancing the veterinary profession in Eastern Europe.

The EERVC Board thank every individual delegate, coming from more than 40 countries across the globe and we hope to see you again at EERVC 2020 and beyond!

Denis Novak DVM MRCVS

EERVC Chairman

Table of contents

Keynote Lecture

Anastasios & Theodoros Koumartzis

A vet reviving Ancient Greek music instruments and culture

The «heart» of Luthieros Musical Instruments is the father of the family, Anastasios, an amateur musician (for more than 40 years), a best-selling author of luthiers' how-to guides in Greek and a luthier for more than two decades. Working as a vet for than 30 years, he started to make music instruments 15 years ago at his workshop, at a small village named Europos at the north of Thessaloniki. Along with his three sons and his wife, Eleni, have managed to create a product line of top quality musical instruments such as Ancient Greek Lyres, complicated ancient musical instruments (Kithara, Lyre of Ur etc.), Ancient Egyptian Drums (Bendir) etc. Even if our musical instruments travel literally around the globe (Luthieros is a niche brand with a great reputation worldwide), our family-based company's vision is to provide employment to our small community, especially during the harsh years of Greek financial recession.

We strongly believe that music is the intermediate for people to communicate, and so we focus on providing the right "tools" to make that happen (i.e. musical instruments that can be seen as unique artifacts). In collaboration with world-renowned musicians, topnotch music instructors, academics, tour guides and performers we brought a unique ancient Greek experience to both expert and not-expert audiences all over the world.

We have great experience working with museums, as Luthieros team in collaboration with SEIKILO Cultural Centre organize for five consecutive years the ancient music festival "The Gift of Gods" that took place in Byzantine Museum (Thessaloniki, Greece), Archaeological Museum (Nicosia, Cyprus), Museum of Ancient Greek Technology (Athens, Greece), and Villa Kerylos (Beaulieu-sur-Mer, France). Interactive exhibition of ancient music instruments, breathtaking live performances, inspirational speeches, and well-thought teaching workshops were part of phenomenal events in Singapore, Hong Kong, Germany, UK, France, Spain, Greece and Cyprus so far.

Anesthesia and Analgesia

Paulo V. Stegall (CAN)

DVM, Ms, PhD, Diplomate ACVAA (Anesthesiology)

An associate professor of Veterinary Anesthesiology and Pain Management at the Université de Montréal. He is the head of a research laboratory dedicated to improving the standards in pain management in companion animals. He earned his DVM and completed a residency at Sao Paulo State University, then earned his MS and PhD with emphasis in feline analgesia at the same institution. He is a member of the Journal of Feline Medicine and Surgery editorial board, the WSAVA Global Pain Council, the WSAVA Dental Guidelines Committee and he has been recently appointed the co-chair of the WSAVA Therapeutic Guidelines group. Dr. Steagall has published more than 80 articles on pain management in small animals. He has recently published the book entitled 'Feline Anesthesia and Pain Management'.

The secrets of dental pain: current knowledge

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The pain experience is a combination of sensory and emotional components. Pain causes fear, stress and anxiety, negatively impacting quality of life. It also delays recovery and induces behavioral changes that affect the owner-companion animal bond.[1] Dental and oral diseases are by far the most common conditions seen in small animal practice. They can produce significant pain, as well as localized and potentially systemic infection.[2] Indeed, severe pain and inflammation might further impact nutrition and feeding behavior. Treatment of periodontal disease often involves general anesthesia and dental extractions.[3]

Recently, extensive guidelines on the management of dental disease in dogs and cats have been reported.[2,3] These documents highlight the importance of adequate pain management and the mandatory use of general anesthesia for appropriate dental treatment.

The literature specific to dental pain is quite limited in veterinary medicine. Nevertheless, recent studies have shed some light into the subject. For example, in a study involving cats with minimal or severe periodontal disease, several parameters were evaluated including pain scores, analgesic requirements and food intake before and after dental treatment. Cats were evaluated under general anesthesia and treatment was performed according to what was clinically recommended; they were evaluated for up to 6 days. Pain scores were significantly increased in cats with severe disease when compared with baseline and with cats with minimal disease. Prevalence of rescue analgesia was significantly higher in severe (91.7%) than minimal disease (0%). Pain scores and frequency of rescue analgesia were significantly correlated with the number of tooth extractions, gingival and calculus index. Finally, food intake was significantly lower in cats with severe dental disease.[4] Those authors highlighted the need for long-term analgesia after dental extractions in cats with severe oral disease.

Furthermore, when the behaviors of cats with minimal and severe dental disease were compared using video-analysis before and after treatment, cats with severe disease showed particular behaviors when compared with those with minimal disease. They spent significantly less time sitting and paying attention to surroundings, and significantly more time laying down, at the back of the cage or curling the tail.[5]

Pain scales such as the Glasgow feline composite measure pain scale can be used to help in the assessment of postoperative pain after dental treatment and extractions in cats. Detailed information of the use of these scales is available elsewhere.[6] The prevalence of chronic pain in cats due to periodontal disease is unknown, but it is believed to be quite prevalent if one considers the frequency at which these are diagnosed in practice. It can involve periodontal disease, but also tumors affecting the oral cavity, for example.[7]

In dogs, a few studies are also available. For example, a study designed to evaluate the analgesic efficacy of local anesthetic techniques in models of oral pain in dogs revealed that the addition of buprenorphine to bupivacaine may extend the duration of analgesia during regional anesthetic blocks.[8] In another study, the efficacy and safety of deracoxib administered for 3 days was compared with placebo for the control of postoperative pain and inflammation associated with dental surgery in dogs. Dogs were evaluated prior to and after surgery using a modified Glasgow Composite Pain Scale (mGCPS). Pain scores were lower in dogs treated with deracoxib than placebo. Four out of 27 deracoxib-treated dogs (14.8%) were rescued compared to 20 out of 30 placebo-treated dogs (66.7%).[9] This study highlights the importance of long-term analgesic requirements in dogs undergoing dental treatment. When it comes to chronic pain, a recent survey involving veterinarians from the UK revealed that dental pain is considered an important cause of chronic pain in dogs.[10] They can also be affected by malignant and non-malignant diseases of the oral cavity causing chronic pain.

The treatment of dental pain is multimodal and involves pharmacological and non-pharmacological techniques. In the pharmacological treatment of acute pain, local anesthetic techniques, non-steroidal anti-inflammatory drugs and opioids should always be considered. In the pharmacological treatment of chronic pain, non-steroidal anti-inflammatory drugs as well as centrally acting analgesics such as gabapentin, amitriptyline and tramadol (cats only) might be considered.

This lecture will improve your knowledge on dental pain and will ultimately impact how you manage these patients in the clinic to provide them with better hospital experiences and better outcomes.

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Ketamine: anesthesia or analgesia?

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THE NMDA RECEPTOR

A noxious stimulus (i.e. surgical trauma) is translated into electrical impulses that are transmitted to the dorsal horn of the spinal cord. During this process, there is the release of glutamate which is an important excitatory neurotransmitter that activates N-Methyl D-Aspartate (NMDA) receptors. There is now evidence that long-term changes in the central nervous system following peripheral tissue or nerve injury are dependent on the activation of NMDA receptors.[1] The role of the NMDA receptor in the processing of nociceptive input has led to renewed interest in NMDA receptor antagonists such as ketamine.[2] These drugs may provide useful insight in the treatment of different painful conditions.

Ketamine is a popular dissociative anesthetic that acts as NMDA receptor antagonist. This drug may prevent central sensitization and cumulative depolarization ("wind-up") from occurring. Doses of ketamine associated with NMDA antagonism are considered sub-anesthetic and lower than dosage regiments required for induction of anesthesia.

CLINICAL USE

Doses

Sub-anesthetic doses of ketamine have been used as an adjunctive analgesic agent in dogs undergoing surgery.[3–5] In this species, dosage regimens usually consist of administering a loading dose (0.15-0.7 mg kg^{-1}) followed by a constant rate infusion (CRI) (2-10 µg kg^{-1} $minute^{-1}$).[4,5] As an alternative option for the loading dose, anesthesia can be induced with a combination of ketamine and diazepam.

Studies in dogs

Ketamine improved feeding behavior when administered as a CRI in dogs after mastectomy[5] but did not provide an opioid-sparing effect. In a recent study, pain scores after ketamine were not significantly different than a group receiving butorphanol, and the drug did not provide adequate analgesia in 37.5% of dogs undergoing ovariohysterectomy.[6] Ketamine should be used as part of a multimodal analgesic approach and not as a sole method of providing pain relief in dogs after surgery.[4,5]

Indeed, when combined with opioids and other analgesic techniques, a CRI after a loading dose has been associated with analgesia of longer duration in dogs undergoing limb amputation[4] and with an anesthetic-sparing effect in dogs.[7,8] It seems to be advantageous to combine opioids, loco-regional blocks, NSAID therapy and NMDA antagonists in the treatment of acute and chronic pain if one considers the concept of multimodal analgesia.

Studies in cats

The administration of ketamine has reduced the minimum alveolar concentration of isoflurane in cats.[9] At high doses or after prolonged administration, ketamine may impair anesthetic recovery in feline patients. In a recent case report, a combination of an NSAID and fentanyl-ketamine CRI was administered to cats, and ketamine was used as an adjunctive analgesic agent in order to minimize the risk of central sensitization, potentially decreasing opioid requirements.[10] In the clinical setting, ketamine may be used as an additional tool for decreasing inhalant anesthetic requirements and to provide analgesia in cats that are poorly responsive to opioid analgesics.

Practical tip

If one wants to administer a ketamine CRI intraoperatively at 10 µg kg^{-1} $minute^{-1}$, one can add 60 mg of ketamine into a 1L bag of a crystalloid solution and set the fluid rate at 10 mL kg^{-1} $hour^{-1}$. A fluid pump is recommended for volume accuracy. A bolus of 0.5 mg kg^{-1} has been used by the author

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Local anesthetics: simple and practical

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GENERAL CONSIDERATIONS

Local anesthetics are low-cost, non-controlled drugs that are readily available world-wide. They are administered routinely for the prevention and treatment of intraoperative and early postoperative pain.[1] These drugs are key players in multimodal analgesia especially when they are administered in combination with NSAIDs and opioid analgesics.

Other advantages may include:

- Blunting of stress response to surgery
- Reduction of intravenous and inhalant anesthetic requirements
- Reduction of analgesic requirements. For example, opioids are not required intraoperatively if an anesthetic block is successful

Local anesthetics block the generation and propagation of nociceptive input by blocking Na+ channels in a reversible manner resulting in transient loss of sensory, motor and autonomic function. Local anesthetics block small unmyelinated C-fibres and myelinated Aδ fibers before other sensory and motor fibers (unmyelinated Ay, Aβ and Aα). In a neuraxial blockade (epidural, intrathecal) from least to most sensitive to local anesthetics are: autonomic, pain, proprioception, and motor fibers. Knowledge of canine/feline anatomy and clinical pharmacology of local anesthetics are paramount for the application of loco-regional anesthetic techniques. On the other hand, it is important to appreciate possible complications associated with these techniques and the use of local anesthetics in practice.

PHYSICOCHEMICAL PROPERTIES AND PHARMACODYNAMICS

Most of these drugs are formulated as a racemic mixture (1:1). Ropivacaine and levobupivacaine are the exceptions. Local anesthetics have a non-ionized lipid-soluble form (base) and an ionized water-soluble form (conjugated acid). The dissociation constant (pKa) corresponds to the value of pH at which the acid and base forms exist in equal amount (Henderson-Hasselbalch equation).

Local anesthetics have a pKa between 7.5 and 9 and are formulated as acid solutions of hydrochloride salts (pH 3.5 – 5.0). This formulation gives a net prevalence of the ionized form and thus a water-soluble solution. Once the local anesthetic solution is injected into the body, the non-ionized lipid-soluble form will prevail. This is important for the drug effect since the non-ionized form crosses the biological membranes. In inflamed tissues, the ionized form prevails, and this explains why local anesthetics do not usually "work" in inflammation (acidic pH).

Protein binding influences the activity of the drug since only the unbounded free fraction is pharmacologically active. Higher protein binding of a local anesthetic is associated with a longer duration but slow onset of action. Lipid solubility promotes sequestration of the local anesthetic into lipophilic compartments (e.g. myelin) from where the drug is slowly released. Lipid solubility is directly correlated with potency. It also contributes to the slower onset and longer duration of action of these drugs. Therefore, increased protein binding, potency and the activity of the local anesthetic on vascular tone correlate with increased duration of action.

The following factors influence the onset and duration of action of a local block: site of injection, dose, volume and concentration of local anesthetic, physical and chemical characteristics (potency, lipid solubility, protein binding), and metabolism.

ADVERSE EFFECTS

Neurotrauma can occur with intraneural injection. For this reason, the lack of resistance to injection is important before the administration of local anesthetics. In addition, maximum doses should always be calculated based on lean body weight before administration. There should be always negative aspiration of blood before injection. This is particularly important with bupivacaine because of its cardiotoxic profile.

Local anesthetic toxicity occurs when doses and concentrations are not respected, or with accidental intravascular administration. Adverse effects with neurological (nystagmus, muscle tremors, seizures, stupor and coma) and cardiovascular (bradycardia, hypotension and ventricular tachycardia) signs may occur. This lecture will discuss how to treat these adverse effects.

Suggested maximum doses* are presented below:

Local anesthetic	Canine	Feline
Bupivacaine 0.5%*	4 mg/kg	2 mg/kg
Ropivacaine 0.5%	0.22 mg/kg	0.22 mg/kg
Lidocaine 2%	10 mg/kg	5 mg/kg

*These doses of bupivacaine are also suggested for intraperitoneal analgesia

- Doses for intratesticular anesthesia or dental blocks: 0.25-1 mL

FIVE BLOCKS EVERY PRACTITIONER SHOULD KNOW

1. Topical anesthesia

Local anesthetics can be used as topical anesthetics for desensitization of the skin when using a eutectic mixture of local anesthetics (EMLA cream). This cream is used for venipuncture and venous catheterization. Systemic absorption is minimal and analgesia occurs at a local level.

2. Intratesticular anesthesia

This block blunts stress response to castration, decreases intra- and post-operative pain and prevalence of rescue analgesia.[2] It decreases inhalant anesthetic requirements during surgery. Under general anesthesia and aseptic conditions, a 23-G or 25-G needle is inserted into the testicular parenchyma and approximately 0.25-0.5 mL per testis is injected.

3 and 4. Intraperitoneal and incisional analgesia

Incisional anesthesia is accomplished by infiltrating the skin in the surroundings of the surgical field with local anesthetics. For laparotomy, local anesthetics are injected into the subcutaneous tissues along the linea alba, just before final aseptic preparation.

Intraperitoneal anesthesia with bupivacaine produces postoperative analgesia in cats undergoing an ovariohysterectomy;[1] plasma concentrations of bupivacaine were below toxic levels. For ovariohysterectomy, the solution of bupivacaine 0.5% (2 mg/kg) is diluted with an equal volume of saline 0.9% resulting in a final concentration of 0.25%. The final solution is equally divided in three parts and instilled into the peritoneal space, specifically over the right and left ovarian pedicles, and caudal uterus using a 3 ml syringe attached to a 22-G X 1.16'' catheter.

5. Oral cavity (dental blocks)

Dental cleaning/procedures should always be performed under general anesthesia and proper intubation. *Mouth-gags are no longer applied for surgical procedures involving the head and oral cavity in cats because they are associated with post-anesthetic blindness.*[3] These techniques require simple and low-cost material such as disposable 1 mL syringes and 25-mm to 30-mm needles. Stainless steel needles can be used but they are relatively costly. Larger needles may cause nerve and vascular damage.

These following blocks can be used for dental procedures including extractions or surgery of the oral cavity such as maxillectomy, mandibulectomy, among others: infraorbital, mental, inferior alveolar (mandibular) and maxillary nerve block.[4]

A small amount of local anesthetic (lidocaine or bupivacaine) is required. In general, volumes may vary between 0.2-0.5 mL unless otherwise indicated. These blocks will reduce intraoperative heart rate and blood pressure, anesthetic requirements and postoperative pain. Importantly, a technique used in dogs cannot be extrapolated to the cat due to some anatomical differences between species.[5] This lecture discusses these blocks using videos and case examples.

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Pain assessment in cats: introducing the Feline Grimace Scale

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Pain assessment is fundamental for appropriate analgesic treatment. It should be part of every physical examination in addition to temperature, pulse, respiration (TPR) and nutritional assessment. The knowledge on feline acute pain assessment has improved over the years with the development and validation of different pain scoring systems.[1,2] Additionally, some studies have reported some factors and limitations of using these tools in clinical practice.[3–5] Indeed, a review article has been recently published with updates and clinical advances in the subject.[6] This review article presents a step-wise approach to feline pain assessment and recognition, and discusses the advantages and challenges in practice.

Facial expressions of pain have been identified and validated in numerous species through the development of "grimace scales". Changes in ear and muzzle position have been identified in painful versus non-painful cats,[7] and evaluation of these features have been incorporated into the Glasgow rCMPS-F.[2] However, other facial features could also be important in painful states.

This lecture will discuss the results of the development and validation of the Feline Grimace Scale (FGS), a novel facial-expression-based pain scoring system to recognize and guide the treatment of pain in this species.[8,9] The audience will go through the process of construction and creation of the FGS.

Briefly, a prospective, observational, case-control study involving client-owned painful and non-painful cats presented to the intensive care unit of the Université de Montréal was performed. Cats were video-recorded in their cages after a physical examination and pain assessment using the rCMPS-F. Facial expressions were studied via screenshots obtained from video files. Five different action units were different between painful and pain-free cats. They included ear position, orbital tightening, muzzle tension, whiskers position and lowering of the head.[8] Then, 180 images were scored by four raters independently, twice, and 30-days apart. For each action unit, a score from 0-2 was given. The study found that FGS scores were higher in painful versus pain-free cats. The correlation between the Glasgow composite pain scale and the FGS was very strong. The FGS showed good inter- and excellent intra-rater reliability in general.[9] Additionally, the FGS has excellent internal consistency (i.e. the action units are all important for the final score). It also showed good response to analgesic treatment (scores after analgesia were lower than before). Finally, the tool has a cut-off score of 0.39 out of 1.0.

The FGS is a valid tool for acute pain assessment in cats. Current studies are investigating the effects of sedation, surgery, different painful conditions (i.e. dental pain) and real-time versus image assessment.

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Ten tips on small animal anesthesia and pain management in practice

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1) Intraperitoneal and incisional anesthesia

Intraperitoneal anesthesia with bupivacaine produces postoperative analgesia in cats undergoing an ovariohysterectomy;[1] plasma concentrations of bupivacaine were below toxic levels.[2] For ovariohysterectomy, the solution of bupivacaine 0.5% (2 mg/kg) is diluted with an equal volume of saline 0.9% resulting in a final concentration of 0.25%. Otherwise, commercial formulations of bupivacaine 0.25% are available. The final solution is equally divided in three parts and instilled into the peritoneal space over the ovarian pedicles and caudal uterus using a 3 ml syringe. The solution is prepared sterilely.

Incisional anesthesia is accomplished by infiltrating the skin in the surroundings of the surgical field with local anesthetics. For laparotomy, local anesthetics are injected into the subcutaneous tissues along the linea alba before celiotomy. Videos will be presented to describe these techniques.

2) Supraglottic airway devices

Supraglottic airway devices are good options for airway management in cats. The device comprises a tube with a distal elliptical component that has an inflatable bladder on the dorsal aspect that is used when needed to create a better seal. Intubation is easy and well performed by individuals with little experience in feline airway management. A lower incidence of upper airway discomfort after extubation when compared with an endotracheal tube. They can be inserted at a more superficial depth of anesthesia than an endotracheal tube and used for mechanical ventilation.[3] However, the author does not use in dental procedures due to the excessive movement of the head and the risk of accidental extubation. A capnograph is recommended to avoid complications. These devices are more expensive than endotracheal tubes.

3) Pulse oximetry

Pulse oximeters are insensitive monitors but they give rapid and continuous assessment of the pulse rate. SpO2 (i.e. measurement of hemoglobin saturation) values correlate with PaO2 (i.e. partial pressure of oxygen). Values that are lower than 90% indicate hypoxemia which will have deleterious effects in the body with potential cardiovascular collapse.

4) Capnography

Capnographs are devices used to measure the end-tidal volume of carbon dioxide during anesthesia and it is an indirect representation of partial pressure of carbon dioxide (PaCO2) and represents the ventilatory status of the patient with some information on the cardiorespiratory function. The use of pulse oximeters and capnography decrease the risk of anesthetic-induced death dramatically.[4]

5) Dexmedetomidine

Dexmedetomidine is an agonist of alpha-2 adrenergic receptors that produce sedation, muscle relaxation and chemical restraint. Lower doses are used for premedication especially in combination with opioid analgesics. Higher doses are used for sedation and chemical restraint especially in fractious animals or when immobility is required for radiographs and lancing of abscesses. The drug has also been administered in the early postoperative period to control dysphoria. It smooths anesthetic recovery in healthy patients when administered at 0.5-1 mcg/kg IV. In cats, dexmedetomidine can be given by the buccal route of administration (oral transmucosal) for hands-off, off-label sedation.

6) Gabapentin

Gabapentin is a lipophilic structural analogue of the inhibitory neurotransmitter GABA. The mechanism of action of gabapentin remains to be elucidated but the drug acts on voltage-gated calcium channels. This lecture will introduce some new insights in the administration of gabapentin for the treatment of acute pain and for transportation to veterinary visits in cats.[5]

7) Alfaxalone

Alfaxalone is a neurosteroid with a similar mechanism of action to propofol and barbiturates via modulation of the $GABA_A$ receptor, producing anesthesia and muscle relaxation. The drug produce dose-dependent cardiovascular and respiratory depression. As with propofol, apnea may be observed but is less common that after propofol. Slow administration reduces the prevalence of apnea. Alfaxalone is approved for IV administration but it is often used for chemical restraint after IM administration in cats.[6]

8) Ketofol or Propoket

The combination of propofol and ketamine has been used with the goal of maximizing the benefits while minimizing the adverse effects of each drug alone.[7] A smooth recovery is generally observed after the administration of propofol, but not ketamine. Sympathetic stimulation and minimal respiratory depression is produced by ketamine. The latter effects can override the cardiorespiratory depression produced by propofol alone. Propofol (2 mg/kg) is usually administered before ketamine (2 mg/kg) to avoid muscle rigidity and anesthetic induction is completed with "top-ups" of ketamine at 0.5 or 1 mg/kg IV.

9) The basic four questions in the treatment of acute pain

Veterinarians may find difficult to address a therapeutic plan for acute pain management that is tailored to the patient. The author uses the following four questions to help:

a. What is the most appropriate opioid for this case?
b. Are there any contra-indications to the administration of NSAIDs? Since surgery will induce some degree of inflammation, NSAIDs are important in providing pain relief; the likely duration of treatment should be considered.
c. Are there any local anesthetic techniques that could be applied to this case?
d. Is there a need to administer adjuvant analgesics? (e.g. ketamine, agonists of α2-adrenoreceptors, tramadol).

10) TLC

Tender, loving and care are pillars of a compassionate profession that is always aiming for better patient care and animal welfare. Canine and feline friendly handling techniques in a "fear-free" model should be common sense in clinical practice.

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Protocols for feline sedation: when, why and how

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Sedation is often required in cats for diagnostic procedures or as part of premedication. Sedatives can produce profound cardiorespiratory changes. Procedural sedation is not necessarily safer than general anesthesia. It can often be challenging in cats due to their natural demeanor and behavior as well as concomitant conditions and diseases.[1]

What drugs should be used for sedation, what doses? Should drugs be always antagonized when possible especially considering the basic pharmacology and physiological changes associated with their administration? What are the concerns and the "knows" of feline sedation in clinical practice?

This lecture will revisit drug protocols for sedation in cats with a quick overview of advantages and disadvantages for each one. It will discuss the use of alfaxalone or ketamine for chemical restraint and sedation, oral dexmedetomidine for hands-off sedation, among other practical protocols in the context of friendly handling techniques.[2]

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Canine Leishmaniosis

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Geographical distriburion of canine leishmaniosis in Europe: how exotic is it really?

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Canine leishmaniosis due to *L. infantum* (syn: *L. chagasi*) has traditionally been considered endemic in the Mediterranean area, Middle East, Asia and Latin America. The dog is the primary reservoir host, while in Europe, certain species of the genus *Phlebotomus (P. perniciosus, P. ariasi, P. perfiliewi, P. neglectus,* and *P. tobbi)* are the vectors of the parasite. During the last years, there has been an increase of reported cases of the disease in areas previously considered non endemic and the suspicion of a wider geographical distribution than previously considered was raised (1).

As a vector borne disease, the geographical distribution of leishmaniosis is predominantly influenced by the living habits of the sand fly vector. Indeed, favoured by temperatures of 15 – 28º C, high humidity and absence of rain or strong winds, the sandflies are abundant in the temperate region of Europe and in the adjoining parts of it (2).

Competent sand fly vectors have, however, been identified in regions not typically considered temperate, where canine leishmaniosis is not endemic, like Germany, Switzerland and Belgium. Climatic changes may have contributed to the sand flies expansion towards northern latitudes and higher altitudes (3).

Increased dog travelling and growing pet adoption services have contributed to the numerous imported cases in traditionally non endemic countries (4, 5).

Autochthonous cases have also been increasingly reported even in the absence of a competent sand fly vector. Alternative ways of transmission (venereal, transplacental, through bite wounds, and via blood transfusions) are frequently recorded and although of minimal importance in endemic countries, they can play a significant role in non-endemic regions. The disease was even able to pass on through two consecutive generations via transplacental transmission during an overall course of 7-year progression in a recorded case in Czech Republic (6-9).

Transmission via other hematophagous ectoparasites such as ticks and fleas has not been proven under natural conditions (10,11). Furthermore, the role of additional hosts as possible secondary reservoirs has been investigated using xenodiagnosis. Cats, hares and black rats demonstrated infectiousness to competent vectors, but their role in the epidemiology of canine leishmaniosis has yet to be determined (12-14).

Interestingly, apart from dogs with severe disease, oligosymptomatic or even asymptomatic dogs can transmit the parasite to the natural vector too (15). This is of great importance given that only a small part of the infected dogs will eventually develop severe symptoms of the disease (16).

Conclusively, canine leishmaniosis in Europe should be considered an emerging disease, which during the last years has expanded its geographical distribution towards the north, via various mechanisms. The increasing numbers of dogs travelling to previously non endemic regions, where competent vectors may now be present, should raise alertness, as the disease is known to spread rapidly under optimal conditions (17).

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Typical and atypical clinical manifestations of canine leishmaniosis

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Canine leishmaniosis due to *L. infantum* is a disease with great clinical polymorphism, as any tissue, biological fluid or organ can potentially be involved. Furthermore, individual hosts act with different immune response and given the long-time course of the disease, any dog may present with a single or multiple clinical manifestation. Furthermore, the pathomechanisms of systemic clinical signs include both the granulomatous inflammation caused by the parasite itself and the immune complexes formation and deposition by the host (1).

The most common clinical manifestation of canine leishmaniosis is cutaneous lesions, present in 80-90% of cases. Exfoliative dermatitis is the most common lesion, present in 53-73% of the cases and can be accompanied by erythema, scales, xerosis, hypotrichosis-alopecia and hyperpigmentation. Ulcerative lesions (15-40% of the cases) can be found over the ear pinnae, pressure points and mucocutaneous junctions of nostril and paws. The nodular form is less frequent (2-9% of the cases) and should be differentiated from the sites of parasite inoculation (1,2,3).

Peripheral lymphadenomegaly, present in 62-90% of the cases is one of the most typical signs of the disease. It is caused by the increased number and size of lymphoid follicles and the marked hypertrophy and hyperplasia of medullary macrophages (2,3,4).

Ocular lesions are present in 26-81% of the cases and consist of blepharitis, conjunctivitis, keratitis, keratoconjunctivitis sicca, anterior uveitis, retinal detachment or combination of those (2,3,5).

Epistaxis (6-19% of the cases) is associated with tissue ulceration, thrombocytopenia, vasculitis and most importantly, thrombocytopathy and rhinitis (3,4,6,7).

Nonspecific clinical signs such as cachexia, body weight loss, decreased appetite, polyuria – polydipsia, vomiting, lethargy, and fever can also be present, in varying frequency and depend on the stage of the disease and the presence of complications, such as renal damage, polyarthritis, secondary bacterial infections and coexisting disease (2,3,4,8).

Onychogryposis (20-31%), splenomegaly (10-53%) and pale mucous membranes (58%) are also often described in canine leishmaniosis cases (2,3,4).

Muscle inflammation resulting in muscle atrophy is common among affected dogs. Bone and joint lesions are common findings as well, however, gait abnormalities are described much less frequently and usually associated with immune-mediated polyarthritis (9,10,11,12).

Similarly, although microscopic intestinal and hepatic lesions are common, they rarely lead to noteworthy symptomatology. Lung involvement has also been described in naturally infected dogs, however, respiratory-associated symptoms are rarely described and attributed mostly to secondary infections (13,14,15,16,17).

Central nervous system involvement is a rare entity too, however granulomatous inflammation, vasculitis and immune-complex deposition in meninges could explain the symptoms of the cases reported (18,19,20,21).

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Diagnosis of canine leishmaniosis: the science behind differentiation of infection from disease

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The term canine leishmaniosis (CanL) is used to describe the dog that has been infected with the causative parasite (namely, in Europe, *L. infantum*) and expresses compatible clinical signs and/or clinicopathological abnormalities. However, only a small number of the infected dogs will develop the disease, which is why the terms infection and disease should be clearly differentiated (1,2).

The parasite is transmitted from biting female sandflies that inject metacyclic promastigotes into the skin of the dog. What happens after this point will depend on various factors such as the intensity of infectious bites, the virulence of the parasite, the genetic background and type of immune response of the host.

Possible scenarios after the infection include: local elimination of the parasite (self-limited infection), isolation of the parasite in the skin and lymph nodes (nondisseminated, asymptomatic infection), dissemination through the body without clinical signs or clinicopathological abnormalities (disseminated asymptomatic infection) and finally dissemination with clinical signs and/or clinicopathological abnormalities (CanL) (3).

The type of immune response the dog will develop defines in a great extent the outcome of the infection. Strong cell-mediated immune response in which Th1 response dominates is corelated with intracellular eradication of the parasite and resistance to disease. Humoral response on the contrary, with overproduction of immunoglobulins is related with increased parasitic multiplication and severe manifestations of CanL. Any dog can, however, move from susceptibility to resistance and all the stages between, at any point of the infection (3,4,5).

Molecular methods aiming to the parasite's DNA are highly sensitive and specific, however can only prove infection. A variety of different tissues and methods can be used, but none can differentiate infection from disease. Their value is limited to epidemiological studies, blood donors and imported dogs (6).

Serological methods (IFAT, ELISA) are gaining ground in the diagnostic field, as depending on the cut-off point, they can be relatively sensitive and specific. Furthermore, they can be quantitative and since the concentration of *Leishmania* specific antibodies is generally lower in asymptomatic infected dogs than those with CanL, differentiating infection from disease is one of their indications. Attention should be paid due to low sensitivity in asymptomatic infected dogs (7,8).

Cytological examination of smears from lymph nodes, spleen and bone marrow can be of great usefulness as they provide direct visualisation of the parasite and the associated inflammation and an indirect estimation of the parasitic load. However, it is time consuming and is usually negative in asymptomatic infected dogs (5,9,10).

Conclusively, in the absence of a single gold standard examination for differentiating infection from disease, serology in combination with cytology in the presence or absence of compatible physical examination findings is the best first choice in the clinical setting. Additional molecular techniques may be used while acknowledging that a positive result only proves infection and not the disease (1,2).

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Treatment of canine leishmaniosis and the development of drug resistance

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Treatment is indicated for the majority of dogs with leishmaniosis due to *L. infantum* (syn: *L. chagasi*). The alternative approach, namely, euthanasia of dogs with the disease and of healthy seropositive dogs, although still practiced in some areas, is ineffective to block the transmission cycle of the parasite (1). This lack of efficacy has multiple explanations: dogs are not the only reservoir of *L. infantum*, the number of seropositive dogs can be very high (up to 10-30% of the total canine population, depending on the cut-off value of serology), some seronegative dogs may be able to transmit the parasite to sandflies and an effective program for mass screening and elimination of seropositive dogs is hard to implement. Another argument in favor of euthanasia is that dogs under treatment may transmit resistant parasites that eventually will infect other dogs and especially humans. To minimize this risk, dogs should be treated with effective drugs that minimize their infectiousness to sandflies, insect repellents should be applied on these dogs on a permanent basis and amphotericin-B, which is the most effective drug for the treatment of human visceral leishmaniosis, should not be used for the treatment of canine leishmaniosis. Therefore, euthanasia may be indicated only in specific circumstances, such as in dogs with advanced kidney disease or in stray dogs where long-term treatment administration and application of transmission-blocking measures may not be feasible.

Seropositive dogs without clinical signs and laboratory abnormalities of leishmaniosis may or may not develop the disease in the future and the chances for disease development are greater if they have a high antibody titer. The administration of leishmanicidal (meglumine antimonate, miltefosine) or leishmaniostatic (allopurinol) drugs will be useless if they are not going to develop the disease and it will promote the development of drug-resistant parasites. However, these dogs are infectious to sandflies. For these reasons, the only interventions that are recommended for seropositive dogs without leishmaniosis are the permanent use of insect repellents, the periodic administration of domperidone and the regular (e.g. every 2-3 months) monitoring for the appearance of the disease. The same applies for dogs with mild leishmaniosis (LeishVet Stage I) because they usually self-cure.

Dogs with moderate, severe or very severe disease (LeishVet Stages II, III and IV) should be treated in order to control their clinical signs, laboratory abnormalities and organ pathology. Also, treatment should be effective to prevent relapses, to minimize infectivity to sandflies and to avoid the induction of drug-resistant parasites (2). The aim of the treatment is not to achieve parasitological cure (which is usually non feasible), but to decrease the parasitic load and to induce an effective *Leishmania*-specific cell-mediated immune response. For dogs with stage II disease, treatment includes the administration of meglumine antimonate or miltefosine for 4 weeks plus allopurinol for at least 6-12 months. For dogs with stage III disease, the treatment is the same with the additional implementation of symptomatic therapy for chronic kidney disease, according to the guidelines of the International Renal Interest Society (IRIS). For dogs with stage IV leishmaniosis, in addition to the symptomatic treatment for the kidney disease, we typically administer allopurinol; the safety and efficacy of leishmanicidal drugs (meglumine antimonate, miltefosine) in these dogs remains unknown and their use is equivocal (3). Finally, in all dogs with leishmaniosis, a thorough search for concurrent diseases is indicated and their treatment is strongly advised.

Treatment monitoring includes thorough physical examination, hematology, serum biochemistry, urinalysis (including measurement of urine protein-to-creatinine ratio), lymph node cytology and quantitative serology (indirect immunofluorescence antibody test or ELISA). These examinations are usually performed at 2 and 4 weeks after the beginning of the treatment (with the exception of serology) and then every 6 months or earlier if there is indication of relapse. Treatment is discontinued after at least 6-12 months of allopurinol administration if the dog is clinically healthy, there are no abnormalities on hematology, serum biochemistry and urinalysis (with the possible exception of proteinuria that may persist or even deteriorate despite effective treatment), there are no parasites in lymph node cytology and there is a significant reduction of antibody titer (or ELISA optical density).

The development of drug-resistant parasites during treatment of dogs with meglumine antimonate was first recorded more than 25 years ago (4) and currently there is evidence that *L. inafntum* can develop resistance to every leishmanicidal or leishmaniostatic drug (5-8). In order to avoid or at least to delay the development of drug resistance, it is recommended to avoid underdosing, shorter or longer than necessary courses of allopurinol treatment, monotherapy and repeated administration of the same leishmanicidal medication.

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Prevention strategies for canine leishmaniosis

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Currently, there are three approaches for the prevention of canine leishmaniosis due to *Leishmania infantum*: insect repellents, vaccination and periodic administration of domperidone. Insect repellents prevent the infection, whereas vaccination and periodic administration of domperidone prevent the disease in infected dogs (1, 2).

Available insect repellents that effectively prevent sandfly bites include deltamethrin and flumethrin collars and spot-on formulations containing permethrin. Depending on the specific product, they can reduce the chances of permanent infection, of seropositivity and of development of the disease in dogs and they may also help in the prevention of human infection by *L. infantum* (3-10).

Two different vaccines against canine leishmaniosis are available in Europe. One of them contains excreted-secreted proteins from the supernatants of *L. infantum* amastigote cultures plus saponin as adjuvant (CaniLeish, Virbac), whereas, the second one contains a chimeric recombinant protein, called protein Q, that has been formed by the genetic fusion of five fragments from the acidic ribosomal proteins Lip2a, Lip2b, LiP0 and the histone H2A protein of the parasite without adjuvant (LetiFend, Leti). Both vaccines are reasonably safe and their efficacy for the prevention of the disease (calculated as the percentage of dogs that would have developed leishmaniosis if they had not been vaccinated) is around 70%, which is a level of efficacy that is considered adequate for a protozoan disease (11).

Domperidone is a prokinetic drug that blocks D2 dopamine receptors, leading to increased serotonin and blood prolactin concentrations. It augments cell-mediated immune responses and this action is not specific for *L. infantum*. The effect of domeridone on cell-mediated immunity is illustrated by the induction of increased leishmanin skin test reactions, the increased lymphocyte proliferation and interferon-gamma production and the increased production of reactive oxygen species by neutrophils. It is administered orally at 0.5 mg/kg body weight, once daily, for one month every 3 to 6 months (usually 3 times/months per year) and it is reasonably safe (side effects include lactation, pseudo-pregnancy and diarrhea and are usually mild). In a randomized, controlled clinical trial, of 21 month duration, it was administered every 4 months and demonstrated significant efficacy over placebo for the prevention of the disease (12). Furthermore, when seropositive dogs without leishmaniosis and dogs with mild disease were given domperidone for one month, all of them were clinically healthy and their antibody titers decreased after 3 months (13).

Since none of the above strategies will prevent the disease in all dogs, their combination is desirable (14). On the other hand, the recommendation to apply all three of them to all dogs that live or visit endemic areas is unrealistic and probably unjustified. Therefore, this author recommends the use of insect repellents, throughout the sandfly period, for all dogs that live or visit endemic areas and the addition of one or both of the remaining prevention measures (vaccination, domperidone) for dogs at increased risk for the disease, like dogs of predisposed breeds, spending the night outdoors and living in rural areas.

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Diagnostic approach of anemia in the dog and cat

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Anemia is one of the commonest abnormalities detected during clinicopathological testing of dogs and cats and the most common erythrocyte disorder. The identification of the responsible pathophysiologic mechanism relies on a systematic interpretation of historical information, clinical findings indicating the presence of anemia (mucosal pallor, tachycardia, tachypnea, exercise intolerance) or even its initiating cause (jaundice, hemoglobinuria, bleeding diathesis, fever) and the results of laboratory testing (complete blood counts, serum biochemistry and urinalysis). This review presents a step-by-step diagnostic approach to canine and feline anemia in an attempt to help practitioners choose the most appropriate therapy and prevention measures.

By definition anemia is characterized by a low number of circulating red blood cells (RBC), resulting in a decreased packed cell volume (PCV) or hematocrit (Hct) and hemoglobin (Hgb) concentration. Interpretation of these findings should be done with caution and bearing in mind that they may be influenced by other factors such as total plasma volume (hydration status), signalment of the animal (breed and age) and examination stress-induced splenic contraction with subsequent pseudopolycythemia. Errors that may lead to misinterpretation of erythron values include the presence of lipemia that may artifactually increase Hgb concentration, the aging of samples that may induce RBC swelling and increased mean corpuscular volume (MCV) and the presence of certain RBC morphological abnormalities that facilitate erythrolysis during centrifugation of samples with subsequent PCV decrease.

Breed and age should be taken into consideration when evaluating anemia. For example, greyhounds have increased PCV values (50-65%) compared to other breeds, which means that anemia may not be diagnosed if standard reference ranges are used. Similarly, puppies cannot be evaluated according to adult reference ranges as they have lower PCV and plasma protein concentration, but higher reticulocyte counts.

Intense stress during clinical examination and collection of blood samples may promote splenic contraction and artifactual PCV increase (pseudo-polycythemia). Alternatively, a dehydrated anemic animal may appear normal as contracted plasma volume may mask laboratory evidence of anemia.

Detection of anemia should be followed by assessment of the regenerative response (reticulocyte count), the RBC indices (mean corpuscular volume-MCV, mean corpuscular haemoglobin concentration-MCHC). The regenerative response will determine whether anemia is regenerative or non-regenerative. Regenerative anemia indicates bone marrow response to its primary cause by increasing RBC production. The main types of regenerative anemia are hemorrhagic (blood loss) anemia, characterized by a moderate regenerative response and hemolytic anemia where regenerative response is very intense and may reach up to a six-fold increase in red cell production.

Classification of anemia by the regeneration response

Classification of anemia as regenerative or non-regenerative should be done with caution and taking into consideration that the regenerative response becomes evident after an initial lag phase of 3-5 days with the appearance of reticulocytes in the circulation. The presence of polychromasia in peripheral blood smear is an indication of regenerative response, however its objective verification necessitates the enumeration of reticulocytes by manual or automated methods. In cats the regenerative response is more complex as two types of reticulocytes are encountered, aggregate (0.5% of RBC) and punctate (1-10% of RBC). This reflects different stages in feline bone marrow stimulation, as the predominance of aggregate reticulocytes indicates recent response. Aggregate reticulocytes quickly mature to the punctate type, which persist for 3-4 weeks, thus indicating chronic bone marrow stimulation.

Reticulocytes may be reported as absolute numbers/μl, percentage (%) or corrected reticulocyte percentage (CRP). In dogs an estimation of this response may be done with the inspection of a stained peripheral blood smear for the presence of polychromasia, as polychromatophils correspond to reticulocytes. In the cat only aggregate reticulocytes appear as polychromatophils in stained smears. The manual counting method is the only way of detecting both types of reticulocytes in cats, and therefore it must be included in the evaluation of the feline regenerative response. The estimation of absolute reticulocyte count (% reticulocytes X number of RBC) is a more reliable indicator of erythropoiesis and avoids its overestimation that often happens with calculation of reticulocyte percentage in anemic animals.

Alternatively, the CRP and the reticulocyte production index (RPI) may be estimated, although their use in anemia investigation is discouraged. The CRP is adjusted for the severity of anemia and the RPI (in dogs only) for the life span of reticulocytes in peripheral blood.

Classification of anemia by erythrocyte indices

Morphologic classification of anemia is based on erythrocyte indices, RBC volume and Hgb content, represented by MCV and MCHC, respectively. Using these criteria anemia is classified into three patterns, normochromic normocytic (non-regenerative with residual normal erythrocytes), macrocytic hypochromic (regenerative with large immature erythrocytes) and microcytic hypochromic (most commonly iron deficiency anemias). However, the attempt to classify anemia by relying solely on these indices is often misleading as they are too insensitive. The study of graphic charts and histograms provided by modern automated hematology analyzers is a more reliable and sensitive way of describing morphologic classification of anemia in current clinical practice. Red cell distribution width (RDW), an indice provided by hematology analyzers, offers additional information by numerically representing the variability of RBC in size, although values may differ depending on apparatus type. An increased RDW and MCV usually indicate regenerative anemia.

Peripheral blood smear evaluation is an essential part of anemia classification because it may reveal information directly related to its etiology (hemoparasites, spherocytes, Heinz bodies). Apart from significant diagnostic information, blood smear evaluation may serve as a means for internal quality control of automated hematology analyzers and reveal abnormalities that may have led to analytical errors (falsely increased MCHC in Heinz body anemias). It is a tedious and time consuming technique, directly depending on the examiner's experience and blood smear quality. Morphologic abnormalities of RBC are classified according to changes in shape, size, colour or presence of intracellular structures. Commonly reported changes include polychromasia (reticulocytosis), hypochromasia, micro- or macrocytosis, presence of spherocytes, echinocytes, acanthocytes, schistocytes or Heiz bodies, basophilic stippling, Howell-Jolly bodies, blood parasites (*Mycoplasma* spp*, Babesia* spp*, Cytauxzoon* spp) or viral inclusions (canine distemper virus). Autoagglutination and rouleaux formation represent cell arrangement changes evident in blood smear examination that suggest autoimmune disorders (immune mediated hemolytic anemia-IMHA).

Etiologic diagnosis of anemia

The diagnostic approach of each anemia case requires an integration of information obtained by history, clinical examination and basic hematological evaluation described above. Any additional special testing will be dictated by this initial workup.

Blood loss (hemorrhagic) anemia is usually accompanied by a decrease in plasma proteins that are lost together with RBC mass. An exception to this is internal bleeding where RBC loss is not combined with hypoproteinemia. Other parameters affecting findings in blood loss anemia include duration and severity of hemorrhage.

Acute hemorrhage (trauma, surgery, gastrointestinal ulceration, bleeding highly vascular neoplasms, coagulopathies) is accompanied by systemic signs of hypovolemia (mucosal pallor, tachycardia, weak pulses). Blood volume expansion with subsequent decrease in PCV and plasma proteins is evident after 3-4 hours. The decrease of PCV may lag behind hypoproteinemia due to compensatory splenic contraction and release of RBC into circulation and may not reflect the actual severity of anemia for the first 1-2 days. Blood loss anemia is regenerative however its chronic forms may become less responsive or even non-regenerative with time, due to depletion of nutrients such as iron and proteins. Reticulocyte numbers increase after the first 3-4 and peak at 5-8 days while PCV returns to nearly normal values within the first 2 weeks. Plasma protein replacement by increased liver and lymphoid tissue synthesis occurs more progressively and thus is less indicative of anemia severity than PCV. In cats the estimation of predominating reticulocyte type may help in determining anemia duration, as aggregate reticulocytosis reflects recent onset while punctate reticulocytosis is more consistent with chronic (1-3 week) duration. In internal hemorrhage the majority of RBC and plasma proteins are reabsorbed from the hemorrhage site within the first days, followed by an increase in relevant values. Specific morphological RBC abnormalities (acanthocytosis) may be observed as erythrocytes are damaged in this process. Other hematological findings seen in acute blood loss anemia include a neutrophilic leucocytosis with a left shift and thrombocytopenia followed by thrombocytosis.

Chronic blood loss anemia is better tolerated as there is more time for the adaptation, however its persistence will ultimately lead to iron store depletion, iron deficiency, defective erythrocyte hemoglobinization, hypoproteinemia and loss of regenerative response (microcytic normochromic anemia).

Hemolytic anemia is most commonly associated with immune mediated disorders (primary or secondary IMHA), Heinz body anemia, blood parasites (*Mycoplasma hemofelis, Babesia canis*), malignant neoplasia or inherited disorders of erythrocytes. RBC destruction may be intravascular or extravascular. The former is acute in onset and often accompanied by hemoglobinemia, hemoglobinuria or jaundice. Extravascular hemolysis is more progressive and characterized by removal of damaged RBC by macrophages in the spleen, liver and bone marrow. Splenomegaly, hepatomegaly and jaundice are common accompanying clinical manifestations. Additional blood smear examination findings in IMHA include the presence of spherocytes and ghost RBC, while autoagglutination may be evident in the sample tube or with the saline dilution test. Hemoparasitoses are important causes of hemolytic anemia and causative organisms may be detected in blood smear examination along with other morphological RBC changes, however verification of diagnosis should be done with more sensitive methods (serology, PCR testing) because parasitemia may be transient. Oxidative damage leading to hemolysis may be accompanied by the formation of Heinz bodies (hemoglobin precipitates) in RBC membrane and other morphological erythrocytic abnormalites such as eccentrocytosis.

Common causes of non regenerative anemia include primary bone marrow disorders (aplastic anemia, leukemia, myelofibrosis, myelodysplastic syndrome), anemia of chronic disease (chronic renal or hepatic disease, chronic inflammatory diseases, endocrinopathies, neoplasia).

In summary, etiologic diagnosis of anemia is based on the findings of clinical examination and an extended clinicopathological testing (CBC, serum biochemistry, urinalysis, special endocrine function tests) including (when indicated) bone marrow examination.

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The diagnostic significance and interpretation of serum protein changes

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Plasma proteins are the most abundant molecules circulating in blood, responsible for carrying over 95% of its nitrogenous substances. Blood serum contains albumin and globulins but not fibrinogen, which is converted to fibrin during the clotting process, thus its protein content is approximately 5% less than plasma. Over 1000 plasma proteins have been identified and several of them are not pure proteins but more complex chemical combinations, as for example the glucoproteins (containing saccharides) and the lipoproteins (containing cholesterol and triglycerides).

In veterinary medicine considerable advances have been established regarding analysis and interpretation of plasma protein changes over the last 20 years. The evolution of sophisticated analytical techniques and the extensive clinical research in several animal species have showed the medical significance of these biochemical analyses in practice. For example, it has been recognized that the measurement of a selected group of proteins, called the acute phase proteins (APP), can be a useful diagnostic tool in the clinical assessment, prognosis and follow up of systemic inflammation, infection and trauma in several domestic animal species.

The majority of plasma proteins (albumin, α and β globulins) is produced in the liver by the hepatocytes. An exception to that are the immunoglobulins (γ globulins), which are synthesized following an antigenic stimulation of B lymphocytes in lymphoid tissue and plasma cells. The most common plasma protein abnormalities are the dysproteinemias, protein dyscrasias or paraproteinemias and APP changes. A dysproteinemia is the presence of a normal plasma protein in abnormal concentrations, whereas a protein dyscrasia is the presence of a plasma protein with an abnormal structure.

The non-selective hyperproteinemia is characterized by the simultaneous increase of all protein fractions (albumin and globulins) in plasma (panhyperproteinemia) or the selective increase of a particular protein type (hyperglobulinemia). Non-selective hyperproteinemia is usually attributed to the clinical manifestations of systemic illness resulting in dehydration and hemoconcentration (vomiting, diarrhea, polyuria) and is commonly accompanied by other clinicopathological abnormalities such as prerenal azotemia and increased packed cell volume.

A selective hyperproteinemia is seen in systemic inflammatory diseases (infection, autoimmune diseases, malignant neoplasia). This hyperproteinemia is attributed to the increased synthesis of immunoglobulins (IgG, IgA, IgE, IgM) from B lymphocytes, globulins from the hepatocytes and selected APP (fibrinogen, haptoglobin). Most systemic infections (viral, bacterial, protozoal, fungal infections, parasitic skin disease, pyometra) are characterized by a polyclonal or oligoclonal gammopathy. On the contrary, monoclonal gammopathies are usually attributed to the increased synthesis of a single immunoglobulin type from neoplastic cells (as in multiple myeloma), that sometimes is intense and may lead to the hyperviscosity syndrome and its complications.

Panhypoproteinemia is the concurrent decrease of all plasma proteins and is commonly caused by the decreased synthesis (liver disease) or the increased loss (blood loss, protein-losing nephropathy or enteropathy, vasculitis, peritonitis) of plasma proteins. In chronic liver disease hypoproteinemia is attributed to hypoalbuminemia and develops in the terminal stage, while globulin concentration may be either normal or even increased if there is local inflammatory reaction. In chronic nephropathies hypoproteinemia is mainly the result of albumin loss, while globulins are not affected due to their large molecular size that prevents their leakage from the damaged glomerulus. In generalized protein-losing dermatopathies (extensive skin burns, deep pyoderma) the hypoproteinemia is caused by the excessive and protein-rich exudate formation. It should however be emphasized that in some of the aforementioned conditions there is a concurrent hyperglobulinemia and an increase in APP synthesis, that may mask hypoproteinemia and delay its diagnosis. In chronic enteropathies the continuous and non-selective protein loss from the damaged intestinal mucosa leads to panhypoproteinemia.

The APP is a special protein group whose plasma concentration changes in response to infection, inflammation and trauma. APP are classified as *positive* or *negative* depending on the type of change (increase or decrease, respectively) in plasma secondary to an inflammatory process. Fibrinogen, haptoglobin, C-reactive protein (CRP), A-amyloid (SAA), α_1-acid glucoprotein (AGP), ceruloplasmin and ferritin are the major positive APP and albumin and transferrin the major negative ones. Usually the increase in plasma APP is not of a magnitude capable to influence total protein concentration, with the exception of fibrinogen and haptoglobin, which may increase it up to 0.5 g/dl. Similarly, negative APP changes become evident several days after the disease onset and do not affect plasma total protein content. The most sensitive APP in dogs is CRP that has been shown to increase up to 100 times within 24-48 hours. Immunoglobulins and complement proteins are considered as "delayed response" APP, as their plasma concentration increases 1 to 3 weeks after the onset of inflammation.

The evaluation of plasma or serum proteins includes the measurement of total protein and albumin. Serum electrophoresis is used to differentiate protein fractions by placing the sample on cellulose acetate gel in an electrical field. Individual protein fractions migrate towards the anode at different speeds, depending on their molecular size

and electrical charge, are stained and scanned by a densitometer. The fractions separated in dogs and cats include albumin, α_1, α_2, β_1, β_2 and γ globulins. Although the diagnostic significance of electrophoresis is limited, it may contribute in the investigation of dysproteinemias or the screening for monoclonal gammopathies. Novel and more sophisticated techniques, such as immunoelectrophoresis, have further facilitated the characterization of dysproteinemias.

Plasma protein changes should be interpreted in combination with other useful information obtained from the patient's history, clinical examination and basic clinicopathological investigation (complete blood counts, serum biochemistry, urinalysis). There are also normal variations depending on the species, age, reproductive status and nutrition, which should also be accounted for. The basic diagnostic workup may provide evidence for underlying conditions (liver, kidney or gastrointestinal disease) that could be the cause of dysproteinemia, so that further more specific laboratory test may be pursued.

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Dentistry

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Ana Nemec graduated from the Veterinary Faculty University of Ljubljana, Slovenia in 2004 and continued with a multi-disciplinary PhD program in Biomedicine at the University of Ljubljana. She was awarded her PhD in 2009. Ana wanted to complement research with in-depth clinical knowledge and applied for a 3-year residency training in Dentistry and Oral Surgery at the University of California-Davis, USA.

Upon completion of the residency programme in 2012, Ana returned home to the Small Animal Clinic of the Veterinary Faculty in Ljubljana. She passed her board examination and became a Diplomate of the American Veterinary Dental College (AVDC) in 2013 and has also been accepted to the European Veterinary Dental College (EVDC). Ana joined the team at Animal Hospital Postojna, Slovenia in April 2018. She is a guest lecturer at the postgraduate study programme in surgery, anaesthesiology, ophthalmology, and veterinary dentistry at the Veterinary Faculty, University of Zagreb, Croatia, a member and past-treasurer of the European Veterinary Dental Society, Secretary of the EVDC, Credential Committee member of AVDC, recipient of several national and international awards in veterinary medicine, an Associate Editor of 'Veterinary Dentistry and Oromaxillofacial Surgery' journal, a reviewer in several international journals and author of research and professional papers, but her greatest passion remains the teaching of veterinary dentistry.

Feline and canine tooth resorption – should I treat it?

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Tooth resorption is defined as a loss of tooth substance due to odontoclastic activity and it is considered physiologic during the process of exfoliation of deciduous teeth. However, when tooth resorption (either internal, i.e. within the root canal, or external, i.e. on the root surface) affects permanent dentition, it is considered pathologic.

Tooth resorption in cats

Tooth resorption affects 32%–70% of domestic cats (depending on the study) and the prevalence is higher in older cats and pure-breed cats. The etiology and pathophysiology is still unclear; several possible reasons have been investigated, including the role of active vitamin D signaling pathway, mast cells and inherited flaws in the protective properties of periodontal ligament and cementoblast layer, but none has been elucidated. Most commonly affected teeth are mandibular third premolar and first molar teeth, and the lesions are many times bilaterally symmetrical.

Lesions can start anywhere on the root and gradually progress to involve also the pulp, which is considered very painful. Interestingly, pulpal involvement associated with tooth resorption is not associated with the development of radiographically detectable periapical disease. The resorption process leads to tooth loss.

Dental charting and dental radiographs are of utmost importance to diagnose the stage and type of tooth resorption and plan an appropriate treatment. When deciding on the best treatment approach, the type of the tooth resorption lesion is important. Type 1 lesion indicates presence of periodontal ligament (as visible on dental radiographs). There is strong association between type 1 tooth resorption and periodontal diseases. Any tooth in a cat affected by type 1 tooth resorption should be extracted. Type 2 tooth resorption indicates that there is bone replacing the resorbing tooth (as determined by dental radiographs). Generally, type 2 tooth resorption is slightly more common than type 1 tooth resorption. Teeth with type 2 tooth resorption may be treated by crown amputation with intentional root retention, if there are no signs of stomatitis and endodontic pathology. In these cases, radiographic re-check is recommended in 12 months. The only stage that may not require treatment in cats is stage 5, type 2 tooth resorption (there are only resorbing root remnants visible radiographically while the gingiva covering them is intact). In cases, where lesions are not exposed to the oral cavity, monitoring may be elected, although the lesions will likely progress.

Currently there is no known treatment that would prevent the disease from progression. Restoration of the early external lesions is possible, but not recommended as it is usually only a short-term solution, because the tooth resorption process continues despite the restoration.

Tooth resorption in dogs

Tooth resorption is also very common in dogs (53,6% of dogs are affected). Increased occurrence was found in older and heavier neutered male dogs, but the reason is unknown. Tooth resorption in dogs is classified differently than in cats, namely as external tooth resorption (external surface resorption, external replacement resorption, external inflammatory resroption, external cervical root surface resorption) and internal tooth resorption (internal inflammatory resorption, internal surface resorption, internal replacement resorption). Several types of tooth resorption may be found in the same dog. The most commonly affected is maxillary first premolar tooth.

As in cats, dental charting and dental radiographs are needed to diagnose the disease and plan the treatment; in general, lesions, that are exposed to the oral cavity and/or associated with inflammation, require treatment, which is in most cases extraction or endodontic treatment.

References available upon request

How to avoid failures in oral and maxillofacial patients?

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Complications related to surgical procedure

Root fracture

The most common complications are related to dental extractions, with root fracture probably being the most common complication, especially when extracting feline teeth. A retained root tip may cause persistent infection, draining tract formation and/or chronic nasal discharge. Therefore, a root tip is carefully inspected following the extraction and a post-extraction dental radiograph should be obtained. If a retained root fragment is noted, it needs to be carefully removed. Blind attempts to remove the root tip and "pulverisation" of the root tip are strongly discouraged, as this may result in an incomplete removal of dental tissues, significant trauma to the surrounding tissues and/or dislodgement of the root tip into the mandibular or infraorbital canal, nasal cavity, or maxillary recess, the structures located in the immediate vicinity of the root tips. Rather, upon careful examination, supported by dental radiography, surgical extraction of the root tip is planned (mucoperiosteal flap is created if it has not been performed previously), with following gentle alveolectomy and special root tip elevators/root tip teasers and root tip forceps are used to remove the root tip remnants. Upon removal of the retained root tips, another dental radiograph should be obtained to confirm vacated alveoli. If a root tip is accidentally displaced into the mandibular canal, infraorbital canal or nasal cavity, removal should be carefully planned to avoid further significant trauma, or the client informed about the complication and the surgical site monitored periodically (clinically and radiographically), or the animal referred to a specialist.

Hemorrhage

Hemorrhage may be a problem in patients with impaired hemostasis or where significant blood loss is expected. Therefore, before any procedure, where severe bleeding is expected (e.g. maxillecytomy/mandibulectomy, palatal surgery, full-mouth extractions), appropriate pre-operative laboratory tests should be performed and blood (products) readily available. Most of mucosal bleeding can be well-controlled with a digital pressure over a wet gauze. If severe bleeding is encountered due to the damage of the infraorbital, major palatine or inferior alveolar artery, the vessel(s) should be identified and ligated and blood loss estimated in order to act further appropriately. Iatrogenic damage to blood vessel(s) is avoidable with careful extraction techniques and the knowledge of anatomy.

Soft tissue trauma

Orbital penetration with a dental elevator with subsequent ocular and/or brain trauma during dental extractions has been reported for cats and dogs. The consequences may be fatal. The complication can be avoided with proper and gentle extraction technique. Nasolacrimal duct, which in cats runs just dorsal or dorsomedial to the maxillary canine tooth root (and is separated from it only by the thin alveolar bone), may be obstructed as a result of an aggressive extraction of the maxillary canine tooth or as a result of a fractured maxillary canine tooth with periapical disease.

Other soft tissue injuries are related to flap tear during flap elevation, lip and cheek trauma, or trauma to the salivary ducts with rotary instruments, and puncture wounds due to instrument slippage. Soft tissue injuries to the floor of the mouth may result in significant sublingual edema, that would require medical treatment if interfering with breathing, or sublingual sialocele, if salivary ducts are damaged.

Jaw fracture

Fracture of the alveolar process may occur with an aggressive extraction technique. This is mostly a minor complication, unless the alveolar fracture extends to a jaw fracture (e.g., during extraction of a mandibular canine tooth). In cats and small dogs, use of small instruments (e.g., 1 mm luxators) or a piezotome and gentle extraction technique can prevent this complication.

Blindness

Central neurological deficits, including temporary or permanent blindness, may be a sequel of keeping the mouth of a cat open widely with a mouth gag for extended periods of time, which reduces the maxillary artery blood flow. It is therefore recommended to avoid especially spring-loaded mouth gags and use smaller (up to 30 mm) plastic mouth gags, or try to avoid using mouth gags at all. Post-anaesthetic blindness may also be related to anaesthesia procedure (e.g., hypotension, hypoxemia).

Air embolism and emphysema

Air-powered systems (e.g., high-speed handpiece) are commonly used in dental extractions (sectioning of multi-rooted teeth, alveolectomy, alveoloplasty) and associated complications are rare. However, fatal venous air embolism was reported in a cat following such a procedure, but the case raised some concerns as to what the real cause of the cardiac arrest was and the case remains debatable. Emphysema is also possible, mostly related to the use of the three-way syringe. Although emphysema usually resolves spontaneously in a few days, the use of a three-way syringe in open wounds is discouraged.

Postoperative complications related to surgical technique

Inappropriate/aggressive surgical technique is also the most common reason for postoperative complications. Poor surgical planning (e.g. not performing a CT prior to palatal defect repair), aggressive extraction technique, absence of aseptic technique and poor pain management are related to postoperative swelling, pain, infection, delayed wound healing or wound dehiscence, systemic complications, occlusal trauma (e.g., maxillary lip entrapment following extraction of maxillary canine teeth, mandibular drift post segmental or total mandibulectomy), glossoptosis (e.g., following extraction of mandibular canine tooth), oronasal fistula formation (especially if pre-existing), alveolar margin recession and weakening of the mandible. Dental extractions were also reported to be associated with post-operative development of endophtalmitis caused by *Actinomyces* species in a cat.

Complications related to local anaesthesia

Nerve blocks are commonly used in animals undergoing oral/dental procedures as a part of multimodal approach to analgesia/anaesthesia. Administration of nerve blocks has been shown to help reduce the amount of general anaesthetic used and the postoperative pain. Careful (aseptic) technique and appropriate maximum dosage/volume of the local anaesthetic used are of the utmost importance to avoid complications.

Nerve blocks may be associated with systemic toxicity of the local anaesthetic, including life-threatening neurotoxicity and cardiotoxicity. Accidental direct intravascular injection and/or excessive dose of local anaesthetic is the most common mechanism for production of excess plasma concentrations of local anaesthetics and their adverse effects. Hence maximum total dose (in milligrams) must be calculated and aspiration must be performed prior to injection. Local anaesthetics can also be locally toxic causing nerve damage if injected intrafascicularly or deposited within the nerve as the needle is withdrawn. Application of local anaesthetics can affect mechanoreception, thermoreception and nociception, taste sensation may also be altered long-term or irreversibly in humans, but the exact mechanism of injury is still a subject of debate (e.g., neurotoxicity, direct trauma from the injection needle, intraneural hematoma formation) and little is known about these adverse effects in veterinary medicine.

As nerve damage may possibly be related to mechanical trauma of the needle, gentle technique and use of fine needles (27G) with short bevel, which is oriented in the same direction as the nerve fibers, is recommended. Local anaesthetic should not be injected if resistance to injection is encountered, which likely indicates nerve penetration– in such case, gentle repositioning of the needle, aspiration and application should be performed. If hematoma occurs at the site of injection, it usually resolves without complications.

Infections associated with nerve blocks appear to be extremely rare, however, aseptic technique is recommended especially when using extraoral approaches, and disinfection of the oral cavity (with e.g., 0.12 % chlorhexidine) is recommended prior to any oral/dental procedure.

With inferior alveolar nerve block one needs to be aware of the possibility to block the lingual and mylohyoid nerves, if the local anaesthetic is deposited too far away from the mandibular foramen, which may result in (temporary) desensitization of the tongue and related tongue chewing post-operatively.

Maxillary nerve block was associated with a globe penetration and subsequent need for eye enucleation in cats, hence the knowledge of the anatomy of the feline maxilla and careful nerve block technique (infraorbital nerve block is considered preferable) are of an utmost importance.

Complications related to general anaesthesia

General anaesthesia is required for all dental procedures. It has been reported, that, overall, cats have a higher risk of complications from anaesthesia compared to dogs. Reported risk factors included higher ASA grade, old age, extremes of body weight, urgency of procedure, endotracheal intubation and intravenous fluid therapy. The risks can be significantly reduced with meticulous pre-anaesthetic examination and preparation of the patient, good anaesthesia planning, aggressive monitoring of the life functions during anaesthesia (ideally with an experienced anaesthetist and involving monitoring of at least body temperature, blood pressure, capnography, pulse oximetry), and close observation of the patient during the recovery period.

Hypothermia

Hypothermia is a common problem during anaesthesia of cats, especially with long dental procedures. It is expected even more so in geriatric patients with underlying diseases. Hypothermia can affect function of several body systems and hence impair anaesthesia and general recovery, or even lead to peri- and post-operative complications. In dental

patients, body heat is dissipated with evaporation, conduction, convection and radiation – most important ways are through the anaesthetic system (especially non-rebreathing systems) and cold anaesthetic gases, by large amounts of water used in the oral cavity and cool surgical tables/rooms. Therefore, it is very important to prevent hypothermia from occurring as much as possible by close monitoring of the patient's body temperature throughout the procedure (every 5 minutes) and after the procedure until the patient is normothermic, and provide adequate thermoregulatory support. To avoid any long-term detrimental effects, body temperature should be maintained above 35.5°C.

Aspiration

Aspiration of liquids from the oral cavity is possible, especially if animals are placed in dorsal recumbency. Hence, airway protection is needed and the animals should be endotracheally intubated, pharynx gently packed with absorbent pack (e.g., gauzes) that is changed during the procedure when saturated with fluid (and removed at the end of the procedure!), and aspiration used at all times. Note that sublingual edema may result from pharyngeal pack packed too tightly.

Tracheal rupture

Tracheal rupture has been reported to occur in cats during anaesthesia, commonly related to dental procedures, although the cause has remained undetermined. To prevent tracheal damage, head and neck should be carefully manipulated during dental procedure and endotracheal tube disconnected from the breathing system any time when changing patient's or tube's position. If using the stylet during intubation, special care should be employed. Endotracheal tube cuff must be carefully inflated, as its' overinflation has been considered the most likely cause of tracheal rupture with ruptures being of a greater length when high-volume low-pressure cuff was used. The cuff should be carefully inflated also to avoid pressure on the mucosal blood flow in the trachea, and always deflated before extubation.

Corneal damage

Eyes should be lubricated every 30 minutes in all patients undergoing general anaesthesia and the eyes protected from the physical trauma in order to avoid corneal damage and ulceration.

References available upon request

Non-periodontal inflammatory oral lesions in cats

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Feline chronic gingivostomatitis

Severe inflammation of the oral cavity in feline patients can be found in the literature under different names, but the term gingivostomatitis indicates general inflammation of the gingiva and non-gingival oral mucosa. Although it seems relatively rare, the complexity of the syndrome and its painful nature make it one of the most challenging diagnostic and therapeutic problems in feline medicine. Evidence-based medicine approach to treatment is the goal, but sometimes difficult to achieve, hence discussion with the owner prior to any treatment is of utmost importance.

The etiology of feline chronic gingivostomatitis (FCGS) is still unknown and the disease likely has a multifactorial etiology. A likely cofactor in the induction or progression of the disease is calicivirus (FCV). An immune-mediated component is suspected to play a role in FCGS development, as diseased cats demonstrated generalized and progressive up-regulation of cytokine expression as the lesion severity increased. Also, increased expression of mRNA for toll-like receptors (TRL) was found in cats with FCGS and associated with FCV and *Tannerella forsythia* infection, suggestive of certain putative pathogens stimulating a host immune response. Furthermore, in cats with FCGS, a predominantly type 1 response switches to a mixed type 1 – type 2 response as the lesion progresses. Attempts to produce an experimental model for FCGS have so far been unsuccessful, presumably due to a multifactorial etiology.

FCGS is characterised by persistent severe very painful inflammation of the oral (sometimes including lingual) mucosa which may also extend into the pharyngeal mucosa and can be present in the absence of significant dental deposits. Clinically, lesions are described according to the location within the oral cavity, where two specific sites are the glossopalatine mucosa and the buccal mucosa overlying the premolar/molar teeth. Lesions are usually diffuse, bilaterally almost symmetrical, proliferative and bleed easily.

CBC and biochemistry as well as urinalysis should be performed in all cats to be treated for FCGS as a part of pre-anaesthetic exam and to rule-out any underlying systemic diseases that may result in stomatitis (e.g., uremia). Detailed oral exam and full-mouth dental radiographic survey performed under general anaesthesia are used to assess status of teeth and bone quality. Extensive and advanced periodontitis, presence of root remnants and tooth resorption are common findings. Biopsy of affected areas is always highly recommended to rule-out possibility of malignant neoplasms, and, less likely, eosinophilic granuloma complex or autoimmune diseases.

Since the cause of the disease remains unclear, a number of different combination treatments are currently in use, with no treatment regimen demonstrating clear superiority. As FCGS is a painful condition, it requires prompt treatment. The first line of treatment is still surgical elective extraction of all premolar and molar teeth (and canine and incisor teeth, if these are also associated with severe inflammation). Typically 60-80 % of cats are clinically cured or improved within a few weeks of such treatment.

Any medical treatment is reserved for those cases that are refractory to surgical treatment. Medical treatments aim at reduction of inflammation (e.g., corticosteroids, NSAIDs), immunomodulation/immunosuppression (e.g., recombinant feline interferon omega, cyclosporine, corticosteroids, stem cells, lactoferrin), inhibition of bacterial growth (e.g., lactoferrin), and interference with viral replication (e.g., recombinant feline interferon omega).

Pain medications are mandatory at any step of the treatment as severe pain associated with the stomatitis must be appropriatelly addressed, especially when oral medications are to be administered to patients. In the immediate post-operative period pain control is provided by a multimodal analgesia approach, combining local anaesthetics (regional nerve blocks given pre-operatively), NSAIDs (e.g., meloxicam), opioids (e.g., fentanyl, methadone, buprenorphine), ketamine and gabapentin. For longer-term pain control usually NSAIDs (e.g., meloxicam–be aware of the off-the-label use) are combined with opioids (e.g., buprenorphine or fentanyl patch).

Owners need to be informed that thorough oral homecare is an essential part of the treatment and that the need for homecare is not eliminated by full-mouth extractions.

If several treatments of FCGS have failed, or the client declines further attempts, it is necessary to address the issue of quality of life and possibly consider euthanasia.

Alveolar bone expansion

Alveolar bone expansion can be observed affecting especially maxillary canine teeth in domestic cats, but can affect other teeth as well (e.g., mandibular canine teeth, maxillary premolar teeth, mandibular molar tooth). Clinically, buccal expansion of alveolar bone, extrusion of the tooth or tooth loss, swelling and erythema of soft tissues and gingivomucosal ulcerations can be seen. This condition is associated with periodontitis and also tooth resorption, but

the causal relationship between the diseases remains unclear. Dental radiographs commonly reveal rarefying osseous proliferation of alveolar bone, radiologic features associated with periodontitis and external inflammatory resorption (type 1 tooth resorption). Histopathology is consistent with bone remodelling and proliferation associated with inflammation. Histologically, the pattern of inflammation in the premolar/molar regions is very similar to the pattern seen in feline chronic gingivostomatitis (intense inflammatory infiltrate rich in plasma cells), but the diseases represent different entities and should be differentiated as such based on clinical appearance (location of the lesions). Treatment usually requires extraction of the teeth involved and debridement of abnormal tissues.

Non-neoplastic lesions

Among neoplastic lesions, *odontogenic* and *non-odontogenic* oral tumors may affect cats, with non-odontogenic being much more common. Squamous cell carcinoma and fibrosarcoma are the most common and both carry guarded to poor prognosis in cats, also due to common presentation late in the course of the disease. Neoplastic lesions usually appear as a swelling, but especially squamous cell carcinoma can appear as a non-healing ulcerative lesion. Before any treatment is attempted, a diagnosis and extent of the primary lesion must be determined, together with staging of the disease. In addition to routine blood tests, biopsy of the primary tumour, fine needle aspiration of lymph nodes, CT of the head, neck and thorax (CT preferable over thoracic radiographs) before and after application of contrast, as well as abdominal ultrasound are recommended. Treatment is based on the type of the tumour and extent of the disease and currently mostly includes surgical and/or radiation therapy.

However, several tumor-like lesions may appear on the gingiva or elsewhere in the mouth (e.g., gingival hyperplasia, drug-induced gingival enlargement, peripheral giant cell granuloma, traumatic mucosal hyperplasia, traumatic caudal mucogingival lesions, proliferative caudal mucositis, cystic ectopic lingual thyroid tissue).

Eosinophilic granuloma complex can appear as an eosinophilic granuloma (raised, linear, well-circumscribed lesion), eosinophilic ulcer (well-circumscribed lesion with raised edges) and/or eosinophilic plaque with or without a systemic component. The etiology is in most cases unknown, and the disease is considered idiopathic. However, an extensive history is usually obtained and detailed physical examination performed to look for possible underlying causes (e.g., ectoparasite infestation). The lesions may or may not be painful. The clinical appearance is usually highly suggestive of a disease, but biopsy is always recommended. The disease can most commonly be treated with antibiotics and/or corticosteroids.

Viral diseases can also cause oral lesions. Particularly lingual ulcerations (limited to the dorsum of the tongue) can be observed in animals affected by calicivirus, or, more rarely, herpesvirus-1 (rhinotracheitis). Both infections usually cause moderate to severe upper respiratory signs (e.g., conjunctivitis, ocular discharge, nasal discharge, sneezing), but also (severe) systemic signs (e.g., fever, pneumonia). Clinical presentation is usually highly suggestive of the diagnosis, although further laboratory testing is recommended to assess general status of the patient (e.g., CBC, biochemistry) and possibly determine the virus (e.g., electron microscopy, molecular methods). Treatment is usually focused on supportive care. Vaccination as a preventative measure should be recommended. Papillomavirus has been described in cats, presented with oral lesions/small sessile lingual lesions (papillomas).

Similarly, immune-mediated diseases, uremia, chemical exposure or electrical injury can also cause oral soft tissue lesions.

History, general physical and oral examination, laboratory tests and histopathology are needed to determine the diagnosis and plan treatment. Biopsy is highly recommended, but the results may be non-specific (e.g., chronic lymphoplasmacytic mucositis) in many of these cases, hence correlation of clinical and pathologic features always needs to be considered prior to determining the diagnosis and accurately plan treatment.

Dental abscesses

Dental abscesses with or without a draining tract are possible, but seem to be less common in cats compared to dogs. Detailed oral and dental examination supported by dental radiography is usually diagnostic and the problem resolved with removal of the cause (extraction of the tooth or endodontic treatment; with antibiotic support as indicated). However, even if the swelling is highly suggestive of an abscess, biopsy is always a good option.

Osteomyelitis

Osteomyelitis (mostly bacterial or fungal) representing as a soft tissue or bony swelling is also possible as a sequel of dental or periodontal disease, foreign body, trauma, extension from soft tissues or hematogenous spread, or surgical intervention. By the time the animal is presented, the process is usually chronic and the diagnostic procedures should include oral/dental exam, imaging (CT recommended, especially for larger lesions), and biospy for histopathology and culture/sensitivity (aerobic, anaerobic, fungal) tests. Removal of the cause (e.g., compromised tooth) is mandatory, and prolonged antimicrobial treatment is needed based on culture/sensitivity testing. Several debridement procedures of the lesion may be required, and in extreme cases removal of the entire portion of the jaw may be indicated.

References available upon request

Non-periodontal inflammatory oral lesions in dogs

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Chronic ulcerative stomatitis

Chronic ulcerative stomatitis can be found in the literature under different names (e.g., chronic ulcerative paradental stomatitis (CUPS), contact mucositis, "kissing lesions", plaque-reactive stomatitis) and affects commonly neutered small male dogs (e.g., Maltese, Cavalier King Charles Spaniels, Labradors, Greyhound dogs). The most common clinical signs include oral pain, inappetence, halitosis, salivation and enlarged mandibular lymh nodes. Oral exam will reveal focal or diffuse erosions, and/or ulcers, typically opposite plaque on the teeth and commonly associated with teeth with early periodontitis. Lesions may involve lateral margins of the tongue, glossopalatine folds, mucocutaneous borders and are typically bilaterally symmetrical.

Dogs with chronic ulcerative stomatitis should be thoroughly examined (physical examination, CBC, biochemistry profile, urinalysis) before general anaesthesia and the complete oral examination with dental radiographs and biopsy of the lesions performed. Treatment aims at controlling plaque and includes periodontal treatment with (elective) extractions combined with oral homecare, pain medications and topical antiseptics. If antibiotics are needed, these should be used based on the culture and sensitivity results. Some cases may require immunosupressive medications (prednisolone, cyclosporine) and prognosis is guarded.

Erythema multiforme

Erythema multiforme is a rare immune-mediated mucocutaneous disease with oral involvement in 31.8% of cases. Triggers are mostly infectious agents. Clinical signs most commonly include severe oral pain, halitosis, hypersalivation and blistering/erosive/ulcerative stomatitis.

Diagnosis is made based on clinical signs, thorough oral/dental examination and biopsy of the lesions. Results of patohistological examination will reveal lymphocyte-rich inflammation that targets epidermal keratinocytes (satellitosis) and induces apoptosis at multiple epidermal levels. Sometimes additional tests need to be performed (e.g., immunohistochemistry and clonality assessment) to rule out epitheliotropic lymphoma. Mild cases are usually self-limiting with removal of the trigger; e.g., removal of the plaque bacteria with periodontal treatment and dental extractions as indicated combined with oral homecare, pain medications and topical antiseptics. Some cases may require elective dental extractions and/or immunosupressive medications (prednisolone, cyclosporine). Prognosis varies greatly and is usually excellent with plaque control in most dogs, questionable in ambigous EM/ETCL cases, and in some cases the disease may progress despite the treatment.

Eosinophilic granuloma complex

Eosinophilic granuloma complex is rare in dogs compared to cats and its' etiology is still unclear. The lesions are characterised by local accumulation of eosinophils indicating likely immune-mediated or hypersensitivity reaction, and are most commonly seen in Siberian Huskies, Malamutes and Cavalier King Charles Spaniels. The lesions usually appear as bilaterally symmetrical granulomas or plaque-like lesions and may or may not be painful.

Diagnosis is made based on clinical signs, FNA/FNI/IS or biopsy and a thourough dermatologic/allergy evaluation.

No treatment is indicated in mild cases, but medical management including corticosteroids, cyclosporine and/or antibiotics is needed, if animals are showing clinical signs. Some dogs do not respond to treatment and life-long treatment may be needed in others, so the prognosis may be guarded.

Other immune-mediated and autoimmune diseases

Oral cavity can be affected in dogs with mucocutaneous lupus erythematosus, toxic epidermal necrolysis, pemphigus foliaceus, pemphigus vulgaris, mucous membrane pemphigoid, epidermolysis bullosa acquisita and discoid and systemic lupus erythematosus. Treatment of the oral cavity lesions is symptomatic (topical antiseptics, pain medications) and these dogs should be thoroughly evaluated and treated by a dermatologist.

Osteomyelitis

Osteomyelitis is an inflammatory process of bone. Clinical signs most commonly include oral pain, swelling, draining tract, non-healing wounds, severe periodontitis, lymphadenopathy, fever, lethargy and inappetence.

Diagnosis is made based on clinical signs, diagnostic imaging (preferably CT) findings, biopsy and culture and sensitivity results.

Treatment and prognosis vary, depending on the extent of the lesion(s) and the cause (e.g., dental infection, trauma). Affected bone should be surgically debrided or »en block« removed via mandibulecotmy/maxillecotmy. Long-term (at least 4 weeks) antibiotic treatment as per culture and sensitivity results is indicated, combined with local antiseptics and pain medications. Prognosis is guarded, especially in extensive lesions.

Osteonecrosis of the jaw

Osteonecrosis of the jaw is a relatively rare problem and indicates chronically (> 6 wks) exposed necrotic bone. History and clinical findings include halitosis, enlarged mandibular lymph nodes, oral pain, ewelling, drooling, lethargy, inappetence and recent dental extractions.

Diagnosis is made based on clinical signs, diagnostic imaging (preferably CT) findings, biopsy and culture and sensitivity results.

Treatment depends on the extent of the lesion(s) and the cause, but is similar to that in dogs with osteomyelitis. Prognosis is mostly very good, but chronic stomatitis may persist (Scottish terriers) and new lesions may develop.

Radiotherapy-related inflammatory lesions

Radiation-related stomatitis is a common (expected) often dose-limiting early side-effect of radiotherapy of oral tumors as radiation disrupts superficial cells of the oral mucosa.

Radiation-related stomatitis resolves with supportive treatment (local antiseptics, pain medications), but siscontinuation of radiotherapy may be needed in rare cases. Radiation-related osteonecrosis of the jaw is an osteonecrosis lesion in a previously irradiated field. It is a rare devastating long-term complication of radiotherapy of oral tumors and a deterministic effect of radiotherapy. Diagnosis is made based on history of radiotherapy, clinical signs, diagnostic imaging (preferably CT) findings, biopsy and culture and sensitivity results. Previous surgery/dental extractions in the irradiated field are often reported. Treatment usually requires more aggressive approach and/or several debridement procedures than in osteonecrosis cases and there may be no response to treatment with progression of the lesion(s).

Other causes of stomatitis

S. canis necrotising stomatitis has recently been described as a case of extremely rapid progression of necrotising oral lesions despite aggressive medical and surgical therapy, resulting with euthanasia of the affected dog.

Uremic stomatitis describes oral ulcers secondary to renal disease, although not all renal patients with uremia are affected. Clinical signs include acute oral pain, inappetence, halitosis (uremic and necrotic odor), hypersalivation, ulcerative lesions, non-vital tissue (dark discolored sloughing necrotic tissue). Tongue is usually the most affected. Diagnosis is made based on history of renal disease and other clinical signs of renal disease, clinical signs, biochemistry results and biopsy (if the patient is stable). Treatment is focused on the treatment of renal disease and supportive care for oral leasions is included. Prognosis depends on the renal disease and extent of oral lesions. Caustic burns (acids and bases, phenols, turpentine, pine oil, essential oils, bleach), plants (causing chemical burns, photodermatitis, foreign-body reaction) and electrocution injuries can all lead to (severe) inflammation of the oral cavity. Treatment usually consists of conservative supportive care and debridement, once the full extent of the lesions has been determined and the patient is stable.

References available upon request

Interpretation of dental radiographs: normal finding or pathology?

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Full-mouth dental radiographs are still the golden standard of imaging in veterinary dentistry, especially if the animal is presented for the first time, or if the clinical condition has changed significantly since the previous visit. In cats, clinical examination without supporting dental radiographs could miss clinically important findings in 41.7% of the animals without clinical signs of dental disease. In dogs, this value is 27.8%. Dental radiographs are of utmost importance also during treatment (e.g., endodontic treatment, complicated extractions, crown amputation with intentional root retention procedure).

Technical quality and orientation of dental radiographs

Obtained full-mouth dental radiographs need first to be examined for their technical quality – check, if 1) the area of interest is on the image, 2) there is any elongation/foreshortening of the teeth radiographed, 3) the quality of exposure is appropriate, 4) there are any processing errors.

Radiographs should then be properly oriented using "labial mounting" – 1) if using conventional dental films assure that the embossed dot/orientation mark faces up for all radiographs, where intra-oral technique was used, 2) by knowing anatomical features, determine, what are maxillary and what mandibular views, 3) crowns of the maxillary teeth are to point down and crowns of the mandibular teeth up, 4) occlusal views are in the center, with first incisor teeth at the midline, 5) last molar teeth are on the periphery. This orientation results in the radiographs of the teeth from the patient's left side to be on the right side and vice-versa (note positioning of the extra-oral views with the dot facing down if using conventional dental films or flip the dental radiograph if using digital system).

Interpretation of dental radiographs

Systematical examination of diagnostic-quality dental radiographs is ideally performed on a tooth-by-tooth basis and findings directly compared to those found on the detailed dental examination (dental charting). Closely examine the crown, root (and apex), dentin, enamel, pulp cavity, alveolar margin, periodontal ligament space (lamina lucida), alveolar bone (with the cortical bone of the alveolus–lamina dura, and trabecular bone of the alveolus) and bone forming the jaw. Interpretation of dental radiographs requires knowledge of normal dental/oral radiographic anatomy in order to be able to diagnose any anatomical/developmental abnormalities, periodontal pathologies, endodontal pathologies and other abnormalities. It is also important to remember, that bone loss is only radiographically evident once 30-50% of mineralized component is lost, hence bone loss will be underestimated on the radiographs. Also, radiographs will only give a 2-dimensional view of a 3-dimensional structure, therefore sometimes several views may help to better visualize a specific structure.

The most common pathology

Periodontal disease is the most common oral/dental disease. The first radiographic signs of the disease are seen as rounding of the alveolar margin. Further, widening of the periodontal ligament space and the loss of integrity of the lamina dura are seen. Alveolar bone osteolysis can be further interpreted as horizontal bone loss, vertical bone loss or combined bone loss. Periodontitis may also present as alveolar bone expansion in cats. Severe cases with total loss of attachment may lead to "perio-endo" type lesions – when primary advanced periodontal disease causes endodontic infection. Vacated alveoli may be noted if periodontitis was so advanced that the tooth exfoliated. Pathologic jaw fractures are possible in chronic advanced periodontitis cases.

Tooth resorption (TR) commonly affects domestic cats, but also dogs. In cats, based on radiographic findings currently we diagnose two types of TR. Type 1 describes lack of any dental hard tissue replacement by bone (lamina lucida and lamina dura can be distinguished), while in cases, where type 2 tooth resorption is diagnosed, dental hard tissues are morphed with bone and lamina lucida and lamina dura cannot be distinguished. The radiodensity of the roots in the latter case is not homogenous. In dogs, the classification of TR types is based on human TR classification.

Dental trauma and associated endodontic disease is very common in dogs, but also in cats. Integrity of the crown is evaluated primarily clinically, and dental radiographs aid in evaluation of the pulp cavity width and shape (especially in comparison with the contralateral tooth), width of the periodontal ligament space (especially apically) and integrity of the periapical bone (presence of periapical lesion) and of the apex (inflammatory root resorption). Ill-defined moth-eaten bone resorption and periosteal reaction in chronic cases may be suggestive of osteomyelitis. "Endo-perio" lesions may develop, when primary endodontic infection spreads into the periodontal ligament and causes total loss of attachment. Sometimes there are no radiographic changes associated with a fractured tooth with exposed pulp as

some time is needed before radiographic changes are detected after pulp exposure, infection, inflammation and necrosis; such tooth still requires treatment.

However, the limitations of intraoral radiography must be considered, especially when dealing with e.g., palatal defects, maxillofacial trauma, TMJ disease or oral neoplasia, when advanced 3-dimensional imaging techniques (usually computed tomography or cone-beam computed tomography) are recommended.

References available upon request.

Periodontal diseases – etiology, diagnosis and optimal management

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Periodontal diseases

Oral microbiome is abundant with, as some studies suggest, over 400 bacterial species. Periodontal diseases are usually chronic inflammatory diseases induced by bacteria in the oral biofilm (i.e., dental plaque). Development of dental plaque is an orchestrated process, that starts with initial coating of the dental surface with a pellicle to which bacteria then adhere and start organizing into a biofilm. Mature biofilm is very resistant to host response and antimicrobials. Plaque formation always precedes calculus formation, with plaque serving as an organic matrix for the subsequent mineralization. The pathogenic potential of dental calculus is not clearly defined, but it certainly serves as a plaque-retentive surface. Although Porphyromonas species are known periodontopathogenic bacteria in humans, and proposed (especially P. gulae) putative periodontopathogens in dogs and cats, Porphyromonas species were recently found in dogs and cats associated with healthy periodontium as well as periodontal diseases. Newest studies suggest that in animals, opposite to humans, the shift from Gram- to Gram+ bacteria may be associated with progression of periodontal diseases. Periodontal diseases are the diseases of the tooth supporting apparatus (periodontium) and are the most common diseases of dogs and cats. Periodontium is a complex structure constituted by various tissues (gingiva, junctional epithelium, periodontal ligament, cementum, alveolar bone) that also maintains the integrity of the oral mucosa. Periodontal diseases are plaque-induced, usually chronic, inflammatory alterations of the periodontium. Gingivitis is completely reversible disease with removal of plaque-bacteria. However, if gingivitis is left untreated, it causes irreversible destruction of the periodontium (periodontitis), including bone loss, and may lead to loss of tooth function and ultimately tooth loss. As opposite to gingivitis, periodontitis is (at best) only partially reversible. Periodontitis may develop very early in some breeds of dogs and it is in general more prevalent in small breed dogs. The reasons for the progression of gingivitis into periodontitis are not fully understood, but an interplay between microorganisms and host response is likely playing a major role. With the development of supra- and subgingival dental plaque (biofilm), more and more pronounced inflammatory reaction is noted in the gingival tissue. When gingivitis progresses into periodontitis, a massive inflammatory infiltrate is noted histologically with progressive connective tissue attachment loss and bone resorption. Such findings are not always detected clinically upon examination of an awake animal, and therefore detailed oral examination under general anesthesia with dental radiographs is mandatory to fully evaluate the extent and severity of periodontitis and plan appropriate treatment.

Diagnosis of periodontal diseases

During dental charting and periodontal probing, a detailed examination of dental and periodontal tissues is performed on a tooth-by-tooth basis with a periodontal probe (periodontal tissues examination) and a dental explorer (hard dental tissue examination) to evaluate plaque and calculus, mobility, gingival index, probing depth, gingival recession, furcation involvement/exposure and any hard tissue defects. Clinical examination is complemented with full-mouth dental radiographs (See Proceedings on Detailed oral and dental examination).

When evaluating dental radiographs for periodontitis, special attention is given to the alveolar margin (alveolar bone is normally at or about 1mm below the cemento-enamel junction), periodontal ligament space (lamina lucida) and alveolar bone proper (lamina dura). Rounding of the alveolar margin is the first sign of early periodontitis and is in more advanced cases followed by the widening of the periodontal ligament space and loss of integrity of the lamina dura. Alveolar bone osteolysis is described as horizontal (the alveolar bone level is parallel to where it should normally be), vertical (there is a wedge-like bone loss around the root(s)) or combined.

Recently, studies are revealing, that cone-beam computed tomography (CBCT) provides more detailed information than dental radiography in evaluation of periodontitis, especially in brachycephalic dogs.

Stages of periodontal diseases

As per American Veterinary Dental College (AVDC), there are 5 stages of periodontal disease. Stage PD 0 describes clinically normal gingiva with no gingival inflammation or periodontitis clinically evident. Stage PD 1 indicates that there is gingivitis only without attachment loss. The height and architecture of the alveolar margin are normal. Stage PD 2 indicates early periodontitis with less than 25% of attachment loss or at most, there is a stage 1 furcation involvement in multirooted teeth. The loss of periodontal attachment is measured either by probing of the clinical attachment level, or radiographic determination of the distance of the alveolar margin from the cemento-enamel junction relative to the length of the root. Stage PD 3 describes moderate periodontitis with 25-50% of attachment loss as measured either by probing of the clinical attachment level, radiographic determination of the distance of the alveolar margin from the cemento-enamel junction relative to the length of the root, or there is a stage 2 furcation involvement in multirooted teeth. And Stage PD 4 indicates advanced periodontitis with more than 50% of attachment

loss as measured either by probing of the clinical attachment level, or radiographic determination of the distance of the alveolar margin from the cemento-enamel junction relative to the length of the root, or there is a stage 3 furcation involvement in multirooted teeth.

Basic periodontal therapy

To prevent periodontal diseases, dental plaque must be disrupted as often as possible. The opportunities to provide veterinary dental care are immense, especially as the lack of preventive care is high. The treatment plan in periodontal diseases patients is only done after oral examination with dental charting and full-mouth radiographic survey. The treatment of periodontal diseases always starts with basic periodontal therapy (professional dental cleaning) that includes supra- and subgingival scaling using power and/or hand instruments, and polishing. Before any treatment, the oral cavity should be rinsed with an antiseptic solution. Basic periodontal therapy is performed prior to any surgical procedures to allow more accurate assessment of the tooth structure and provide a cleaner environment for surgery. Regional nerve blocks are performed if any advanced procedures other than professional dental cleaning are planned.

Basic periodontal therapy may be performed with power and/or hand instruments. A variety of power scalers are available. These can be classified as sonic, ultrasonic – piezoelectric and ultrasonic – magnetostrictive. Certain ultrasonic scalers/tips are designed for subgingival use and adapted for periodontal debridement or designed specifically for periodontal debridement. Sonic scalers can be used subgingivally, but this should be done with appropriate tips only and with great care not to remove too much cementum.

Hand instruments used for manual scaling in veterinary dentistry include scalers and curettes. Scalers are designed for the removal of supragingival calculus. Periodontal curettes are finer and rounded instruments to be primarily used for subginigval scaling, root planing and gingival curettage. Mastering the technique of using hand instruments requires specific training.

A plaque-disclosing agent can be used following basic periodontal therapy to help reveal areas of plaque and calculus remnants. Residuous plaque can be removed with polishing, while any residuous calculus will require further scaling. It is a common practice to make the dental surfaces as smooth as possible after scaling. However, the long-term beneficial effect of polishing would appear to be minimal. Also, some loss of the tooth structure (enamel) occurs during polishing. Polishing can be done using a low-speed handpiece with oscilating or rotating cup and pumice, or an air-polisher using fine bicarbonate crystals.

In cases of advanced periodontal disease, basic periodontal therapy/professional dental cleaning is followed by periodontal debridement, root planing, periodontal surgery and extractions as indicated. The treatments are attempted to be finished in one cycle in animals, which is most likely a very aggressive approach. Depending on the extent of periodontal diseases, periodontal treatment and tooth extractions, patients are also treated systemically with analgesics (e.g., NSAIDS, opioids) in addition to local nerve blocks, and in rare selected cases with systemic antibiotics (prophylactic use of antibiotics during the procedure and/or therapeutic use after the procedure). Chlorhexidine gluconate solution should also be used after the procedure and for home care, if any surgery was performed and therefore reinstitution of daily toothbrushing delayed.

Home care

Oral homecare should be instituted early in the life of an animal (when deciduous dentition is present) and continued throughout life. Moreover, without oral home care, the benefits of professional oral care are short-lived as plaque starts to develop within hours after its' removal. Therefore, oral home care should be (re)instituted as soon as possible after professional oral care. The gold standard of oral home care is active mechanical removal of plaque by daily tooth brushing, with or without a toothpaste designed for animals. Also, clients need to be regularly encouraged to keep the habit of daily tooth brushing as compliance is often lost. Ideally, all surfaces of the teeth are brushed, but it is advisable to start with buccal surfaces of the maxillary teeth, that are the most easy to reach. Also, generalized gingivitis is most commonly found on the maxillary canine and fourth premolar teeth.

If an adequate technique and timing of tooth brushing is difficult to achieve due to animal's intolerance (unless tooth brushing is introduced at an early age of the animal and made a daily routine), other oral homecare measures are often recommended, although less efficient than daily tooth brushing.

Diet is generally believed to be related to periodontal health – the more fibrous it is, the more beneficial the effect on periodontal health. It has been suggested, that home-prepared food, as compared to commercial pet food, can increase the probability of an oral health problem in animals. Another study showed that periodontal health did not differ between domestic cats (fed commercially-available foods) and feral cats. Moreover, cats fed with dry extruded kibbles were found to have higher bacterial diversity with higher numbers of *Porphyromonas* spp. and *Treponema* spp. compared to cats fed wet diets, but the association with periodontal health remains unclear, although it was previously suggested that feeding dry diet only may be beneficial for oral health. Several diets are commercially-available and proven to help with reduction of plaque and/or calculus formation. Their efficacy is mostly attributed to the textural characteristics (size, shape, consistency, fiber matrix) that allows for maximal contact with the teeth and addition of polyphosphates that reduce calculus formation by binding salivary calcium.

Edible treats/chews are another possibility; daily addition of certain commercially-available treats to the main meal was shown to reduce accumulation of plaque and/or calculus. If such an oral homecare measure is applied, treats

should be fed in limited amounts as recommended and the amount of the main meal adjusted accordingly not to exceed daily caloric requirements. It is advisable that animals are supervised while eating treats. Generally, any treat or toy given to the animal should be of an appropriate size and hardness to avoid e.g., dental fractures or intestinal blockage.

Further on, several oral rinses, gels, sprays, water additives and also wipe cloths are commercially-available. Data on their efficacy with regards to prevention of plaque and/or calculus accumulation are known for some, although the ingredients are not always fully described. Chlorhexidine is still the most commonly used chemotherapeutic agent with a broad antimicrobial spectrum and anti-plaque activity. It has long been considered to not induce bacterial resistance, although some worrisome data on this possibility are emerging. In animals, a 0.12% solution is commonly used. It is recommended twice daily in the perioperative period, while data on the long-term use lack. Its' bitter taste also makes it poorly palatable, especially for cats. Zinc ascorbate used after professional dental cleaning has also been decribed in cats as an effective anti-plaque agent that also reduces gingivits. Drinking water treated with xylitol each day was found effective in reducing plaque and calculus accumulation in cats, but can cause hypoglycemia and liver failure in dogs.

Dental sealants (barrier gels) are applied to dental surfaces immediately after professional dental cleaning and followed in a prescribed regimen at home. Dental sealants act as physical barriers for accumulation of bacteria, and result in lower average plaque scores in treated animals compared to controls at the end of the study, but the treatments did not impact calculus accumulation nor gingivitis scores.

In general, vast array of products is available on the market and the veterinarian is highly encouraged to practice evidence-based medicine also when recommending a specific oral homecare product to the client. One can also look up the Veterinary Oral Health Council (VOHC) website (www.vohc.org), where certain products are listed, that meet pre-set standards regarding retardation of plaque and/or calculus accumulation. At the same time, it needs to be stated, that obtaining a VOHC seal is voluntary and therefore the lack of VOHC seal on certain products does not indicate that these products are ineffective.

Above all, client education is the key to providing optimum patient oral and dental care together with yearly professional oral care as well as daily oral home care.

References available upon request

Dermatology

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Filippo graduated from University of Bari, in 2001. He moved to UK in 2003 and worked for PDSA before joining the Royal Veterinary College in 2006 as Resident in Veterinary Dermatology. He gained the RCVS Certificate in Veterinary Dermatology in 2009 and became a Diplomate of the European College of Veterinary Dermatology in 2010. Filippo worked in several institutions, including the Animal Health Trust and The Royal Veterinary College; currently he works in four referral centers in London and south of England. He is also an Honorary Lecturer in Veterinary Dermatology, and Past President of the British Veterinary Dermatology Study Group.

Atopic dermatitis in dogs and cats: an update

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Canine and feline atopic dermatitis are very common diseases. The aim of this article is to describe the recent discoveries in our understanding of these conditions and highlight the impact in diagnosis and management.

Canine Atopic Dermatitis (CAD)

Pathogenesis

The International Task Force on Canine Atopic Dermatitis has defined this condition as: "A genetically-predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features associated with IgE antibodies most commonly directed against environmental allergens".

Clearly this is a multifaceted condition resulting from a complex interaction between intrinsic factors, unique to the animal, and extrinsic factors, relating to the environment and cutaneous microenvironment.

Intrinsic factors include:

- Genetic predisposition in breed and line. Most studies in veterinary medicine have been focused on inheritance of genes responsible for development of CAD. and several breeds have been described as predisposed to development of this condition, including Labrador retriever, Golden retriever, West Highland White terrier and German shepherd dogs. The condition is most likely multiallelic and not linked to one single gene.
- Impaired barrier function. Newer theories propose that a defect in the skin barrier has an important role in the pathogenesis. In healthy individuals skin offers an effecting barrier function against bacteria, viruses, parasites and allergens, such as house dust mites, forage mites and pollens. Genetic defects in skin lipids and proteins create a barrier imperfection causing increased entry of the allergens into the body, stimulating an immune response. Briefly the skin can be described as bricks and mortar structure, with epithelial cells making up the bricks and extracellular lipids and proteins making up the mortar. Both human and canine patients with atopic dermatitis have been shown to have abnormalities and deficiencies in the intercellular lipid barrier, showing in particular differences in the way the lipids are formed and organized. Lipids are produced by the epithelial cells into structures called lamellar bodies. The lamellar bodies are extruded into the extracellular space and form organized stacks called lamellae, which help preventing water loss and allergen penetration. Ceramides are a type of lipid that makes up a large portion of the lamellae and dogs with atopic dermatitis have a skin deficiency of ceramides with their lamellae also arranged in a disorderly manner. In human atopic patients, a mutation in the gene encoding for filaggrin (filament aggregating protein) have been identified. In the canine counterpart, alterations in filaggrin expression and higher expression of enzymes involved in filaggrin metabolism have been reported. Although more research is clearly needed, there is increasing, albeit preliminary evidence, to support a role for skin barrier dysfunction in CAD. Along with skin barrier dysfunction, host-microbiome interactions are also emerging as primary alterations in canine AD and it is clear that future studies focused on the development of drugs able to restore the skin barrier and increase the natural defences against pathogenic organisms are needed.
- Aberrant immune responses. Many immunological aberrations have been described in canine with atopic dermatitis. T-helper lymphocytes (Th), divided into two families (Th1 and Th2), through production of various cytokines, play a key role in the IgE immune response to environmental antigens. Studies in humans have shown that in atopic dermatitis patients there is deviation in the immune response toward a Th2 type, with production of cytokines (IL-4 and IL-13) leading to Increased IgE production, expression of high affinity receptors by antigen-presenting cells (Langherans' cells) and mast cell pre-activation. With chronicity Th1 response drives the cell mediated immunity, through production of IL-2, IL-12, Interferon γ and IL-18. Similar pattern is believed to be present in dogs, where the expression of Th2 and Th1 type cytokine profile is not mutually exclusive and both contribute to pathogenesis of CAD with a sequential activation where Th2 leads the initiation phase and Th1 the persistence of inflammatory response.
  In addition to what previously described, pruritus can be elicited by neuronal stimulation. Immune cells release a variety of itch mediators, including interleukin-31. This goes in close proximity to primary afferent nerves in dermis and epidermis where there are itch mediators detected through itch receptors present on sensory nerves. Signals travel along nerve fibres, are received by the dorsal root ganglia on the dorsal horn of

the spinal cord and reach the brain transmitting the pruritic sensation. In a recent paper the role of il-31 was studied and the conclusion was that canine IL-31 induced pruritic behaviours in dogs. This molecule was detected in the majority of dogs with naturally occurring CAD, suggesting that this cytokine may play an important role in pruritic allergic skin conditions in this species, such as atopic dermatitis.

Extrinsic factors include:

- Allergens–there is increasing evidence that increased reactivity to environmental challenges plays an important role, especially through epicutaneous exposure. Important aeroallergens include the House dust mites *Dermatophagoides farinae, D. Pteronyssinus, Euroglyphus maynei.* Forage mites show cross reactivity with house dust mites may contribute to flares up of CAD in house dust mites allergic dogs. Whilst the role of hair and scales and moulds is unclear in the dog, a major role is played by the seasonal allergens such as pollens of different families (tree pollens, grass pollens and weed pollens). **In certain individuals food allergens are also likely to play a role**. In veterinary dermatology historically cutaneous adverse food reactions (CAFR) and CAD have been considered as two different conditions, however this separation has been often an object of debate. CAFR includes both immune-mediated and non-immune-mediated food intolerances and the clinical signs can consist in gastro-intestinal disturbances, urticaria/angioedema, signs mimicking those of CAD. For this reason, from an aetiopathogenetic point of view, we can distinguish between the Food-induced atopic dermatitis (FIAD) and the Non-food-induced atopic dermatitis (NFIAD), with the two forms being clinically indistinguishable.
- Microbial colonization – the development of chronic lesions is often associated with secondary microbial infection with Staphylococci or *Malassezia* yeasts and these infections significantly increase the severity of clinical signs.
- Environmental factors–In medicine, the hygiene hypothesis states that a lack of early childhood exposure to infectious agents, symbiotic microorganisms (e.g., gut flora or probiotics), and parasites increases susceptibility to allergic diseases by suppressing the natural development of the immune system. In particular, the lack of exposure is thought to lead to defects in the establishment of immune tolerance. In veterinary medicine Swedish studies have recently found that living in a rural environment, living in a household with other animals and walking in forest appeared to be protective. In other studies has been shown that feeding non-commercial dog food to lactating bitches had a protective effects, but gender, season of birth, environment, vaccination or de-worming had no effect.

In synthesis, based on the current beliefs, we can attempt to explain the aetiopathogenesis of atopic dermatitis in dogs highlighting that in predisposed individuals a possible defect in barrier function may lead to an increased risk for allergic sensitization followed by development of an aberrant immunological response, with subsequent Inflammation and typical clinical signs.

Clinical signs

The clinical signs are seen in young dogs (between 6 months and 3 years of age) and the condition may have seasonal manifestations initially, usually showing a progressive worsening over time. Early lesions consist in erythematous macules, generalized erythema, small vesicles, oozing in early phases. Recurrent bacterial and yeast infections (Malassezia dermatitis) can occur, leading to signs seen most often in chronicity, including hyperpigmentation lichenification, papular dermatitis. Self-trauma causes excoriations and ulcerations, which perpetuate secondary infections.

Diagnostic criteria

The diagnosis of CAD is based on the finding of a constellation of typical history and clinical signs and on the subsequent elimination of other conditions that might mimic it. Important factors include signalment, disease history (seasonal or non-seasonal depending principally upon the allergens involved as flare factors and the pet's environment), evidence of lacrimation, ocular congestion or sneezing / rhinorrhea that could be indicative of concurrent atopic conjunctivitis and rhinitis. In 2010 Favrot and colleagues published a set of criteria useful in the diagnosis of canine atopic dermatitis:

1. Onset of signs under 3 years of age
2. Dog living mostly indoors
3. Glucocorticoid-responsive pruritus
4. Pruritus sine materia at onset (i.e. a-lesional pruritus)
5. Affected front feet
6. Affected ear pinnae
7. Non-affected ear margins
8. Non-affected dorso-lumbar area

Considering that food allergens can also play a role, an elimination diet should be carried out, for a duration of minimum 6 weeks, using hydrolyzed prescription diet or home-cooked diet, followed by a food re-challenge and re-introduction of the special diet depending on outcome of the re-challenge.

Management options

Management of CAD usually involves a combination of therapeutic modalities. In a recently published guidelines, the options were divided into two categories: treating acute manifestations and treating chronic cases.

- Acute flares. Currently recognized causes of flares of canine AD include fleas, food and environmental (e.g. house dust mites, pollens) allergens; other ectoparasites, such as *Cheyletiella* or *Sarcoptes*, can also contribute to increase pruritus. In addition to addressing these factors, where infections are present, it is recommended that they are treated topically or systemically, according to the clinical signs. When pruritus is not complicated by infections, glucocorticoids should be used, including topical (e.g. hydrocortisone aceponate spray) or systemic (prednisolone or methylprednisolone at anti-inflammatory doses) formulations, according to the clinical signs and lesions' distribution. Medications that are not suitable for management of acute flares, include anti-histamines, essential fatty acids (they take too long to be incorporated into the cells' membrane) and ciclosporin (due to its delayed therapeutic benefit).
- Chronic cases. The mainstay of treatment is allergen-specific immunotherapy, topical, systemic (low-dose alternate-day oral) glucocorticoids, and ciclosporin. Adjunctive treatment includes antibiotics and antifungals, strict flea control, diet trials, antihistamines, shampoos, and fatty acid supplementation. Intradermal and serological tests are both been recommended as useful to identify environmental triggers in view of pursuing allergen specific immunotherapy. Interestingly, there is no evidence that anti-inflammatory therapy interferes with allergen specific immunotherapy; therefore this can be used during the induction phase, before any improvement is seen from the vaccine. Control of localized pruritus can be successfully achieved by use of topical glucocorticoids and tacrolimus and more generalized manifestation benefit from systemic glucocorticoids, to be started as for acute flare, with the aim of achieving a low dose alternate day dosage, and with ciclosporin. This should be started on a daily basis and then, upon clinical signs, reduced gradually. Essential fatty acids, Chinese herbs and anti-histamines are recognized as useful steroids sparring drugs in the long term. Bathing with non-irritating, antiseborrheic or antimicrobial shampoos is also believed to be beneficial, albeit not recommendable as a sole therapy.

New strategies. In view of the recent discoveries in skin barrier defects, it is tempting to speculate that addressing an impaired skin barrier function could produce a beneficial effect. In one human study, the application of a topical moisturizer containing ceramides produced dramatic improvement in clinical scores after 3 and 6 weeks of treatment. In dogs with CAD, topical application of a lipid preparation was shown to be effective in re-establishing a normal skin structure. In clinical practice it is difficult to demonstrate the clinical efficacy of this skin lipid complex spot-on treatment, because topical lipid applications are not used as monotherapy. These formulations are intended to be used as adjunct therapies in combination with other anti-inflammatory drugs, antimicrobial drugs, and immunotherapy as part of the global approach to the management of canine CAD. In a study, conducted on 8 dogs already on treatment with allergen-specific immunotherapy and/or pentoxyfilline, during a 12-week treatment period, their canine atopic dermatitis extent and severity index (CADESI) scores were measured before and after treatment and, the total clinical score progressively decreased, in association with an improvement in clinical signs. The change in the scores for excoriations and erythema was the most dramatic. Because the only change in treatment over the 12 weeks was the addition of the topical spot-on therapy, these results suggest that topical lipids may play a role in the reduction of inflammation. Repair of epidermal barrier function presumably led to the reduction in inflammation seen in this study. These findings are encouraging, but double blinded placebo-controlled or cross-over studies are needed for further confirmation.

Oclacitinib is another drug approved for the treatment of pruritus associated with allergic dermatitis and its clinical manifestations in dogs. This molecule specifically inhibits expression of IL-31, controlling pruritus in dogs with atopic dermatitis. It appears to be highly effective and with a rapid onset of action; in a recently published randomized, double-blinded, placebo-controlled trial in 299 atopic dogs resulted in a 29.5% reduction in pruritus by 24 hours and 64% decreased pruritus by day 14.

For patients that respond to oclacitinib but are incompletely controlled at once daily regime, it might be useful to consider a new biologic product, lokivetmab. This is caninized anti cIL-31 monoclonal antibody. It is aimed at blocking IL-31, administered by monthly subcutaneous injection and based on published studies in appears to provide relief in up to 88% of pruritic atopic patients.

Feline Atopic Dermatitis

What is it?

Pruritus is one of the most common presentations in feline patients in general veterinary practice, and most often itchy cats have hypersensitivity skin diseases. These are commonly caused by environmental, food and/or flea allergens. The pathogenesis of atopic disease in cats has not been fully elucidated and currently, to better define pruritic hypersensitivity in cats where parasites and infections have been ruled out, the term recommended by the International Committee on Allergic Diseases of Animals (ICADA) is Feline Atopic Syndrome (FAS). **This includes hypersensitivity caused by environmental allergens and food items or a combination of both**.

Clinical manifestations and diagnostic criteria

It is generally accepted that cats affected by feline atopic syndrome may manifest the disease with different clinical forms, called reaction patterns. These include: head and neck pruritus (fig. 6), symmetrical self-induced alopecia, miliary dermatitis, and eosinophilic granuloma.

Given that hypersensitivity skin disorders are frequently suspected in feline patients, it would be useful to establish criteria to be used for diagnostic purposes. Recently Favrot and colleagues have made an attempt in this direction, analysing data from different population of cats with disease induced by flea, food and environmental allergens. Although a few differences were found, unfortunately the studies confirmed that the clinical reaction patterns are not pathognomonic of any specific feline hypersensitivity dermatitides and are not specific for any groups of allergens.

As result, diagnosis of feline atopic syndrome is based on ruling out other causes of pruritus and on response to specific therapies.

Management options

In order to establish an effective management plan, the first step should consist in elimination diet trials and provocation testing. Food trials for feline patients follow the same principles applied for the canine counterpart, although it should be highlighted that palatability and lifestyle may be more of an issue.

When and if the food component has been ruled out, treatment of feline atopic syndrome in cats generally relies on different options, including:

- Oral or parenteral glucocorticoids. These are usually highly effective, however high doses or long term therapy may be associated with adverse effects, including diabetis mellitus and skin atrophy.
- Topical glucocorticoids. Hydrocortisone aceponate spray is licensed for use as symptomatic treatment of pruritus and allergic dermatoses in dogs. In a recent clinical trial it was demonstrated to be efficacious and well tolerated in 10 cats with presumed allergic skin disease. More and larger studies are needed to confirm these findings.
- Ciclosporin. This is highly effective and appears to be well tolerated, with most adverse effects limited to transient gastro-intestinal disturbances. Other complications include potential risk for development of systemic toxoplasmosis, viral infections and neoplasia, although at the recommended doses such risk appears small.
- Oclacitinib. This drug is unlicensed for use I feline patients. A recently published double-blind, randomised methylprednisolone-controlled trial on the use of oclacitinib at 1mg/kg q12h in 38 cats with allergic dermatitis did not find a significant difference in efficacy if compared with methylprednisolone given at the same dosage. However, in this study, 25 and 50 percent of cats experienced an increase above the normal range of creatinine and urea, respectively. Pharmacokinetics, pharmacodynamics and toxicity of oclacitinib in cats are not known, and this drug should be used with caution in the feline species.
- Anti-histamines. Data are limited and a recent study showed that cetirizine cannot be recommended for management of atopic syndrome.
- Essential fatty acids supplementation. Data are limited.
- Allergen specific immunotherapy. Some cats respond well to this management; however the evidence of efficacy/safety and the availability/reliability of tests to select the allergens is less than in dogs.

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Diagnostic approach to otitis: history taking, physical examination, otoscopy, microscopic evaluation, cytology, diagnostic imaging

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Abstract

Otitis externa, inflammation of the external ear canal, with or without middle ear involvement, is very common in dogs and quite common in cats. Many different factors can cause or exacerbate otitis and recognition and correction of these is the key to successful management. Scrupulous note of the historical features, thorough examination of the ear and collection of appropriate samples constitute the minimum database. Selected cases may need further investigations, including imaging of the middle ear.

History

It is important obtain a complete history in patients with either acute or chronic otitis externa. Relevant considerations include:

- Owner's complaint – often head-shaking, ear rubbing and/or discharging and malodour
- Signalment – several breeds, due to the conformation of the pinnae and ear canals and due to their susceptibility to other diseases, are predisposed to develop otitis; young dogs are predisposed to otodectic mange and elderly dogs to endocrinopathies
- Lifestyle – outdoor activities such as walks in fields may predispose to foreign body and frequent swimming to moisture of the are canals
- Acute onset with frenzied head-shaking may again indicate foreign body
- Chronic cases with skin disease elsewhere suggests otitis is part of a more generalised skin disease
- Seasonal recurrence suggests atopic disease
- Unsuccessful previous treatments may indicate presence of resistant organisms or onset of drug eruptions to topical medications

Physical examination

Full general and dermatological examination is paramount. This enables to identify underlying primary causes of the otitis and eventual neurological signs of otitis media and otitis interna.

The clinical findings vary with the cause:

- Tumours, parasites and foreign bodies may be evident upon otoscopy
- Erythema of the medial pinna and vertical canal suggests an allergic aetiology
- Dry, brown, granular discharge is seen with *Otodectes* infestation
- Moist brown discharge can be seen with staphylococcal and *Malassezia* infections
- Purulent, greenish, foul odour exudate indicates gram negative bacterial infection
- Chronic cases may have thickened, pigmented skin (and para-aural abscesses
- Cornification disorders may have changes in coat quality, colour and density or scale formation
- Facial nerve paralysis and Horner's syndrome may are indicative of otitis media
- Head tilt, circling, falling toward the affected side, horizontal nystagmus and asymmetric ataxia are indicative of otitis interna
- Some cases of otitis media/interna may also show loss of hearing
- External palpation of the ear canals may reveal pain, thickening and hard consistency, with latter indicative of mineralization of the cartilages

Otoscopy

Otoscopy is visualization of the ear canal with an otoscope. Otoscopes available in veterinary medicine include:

- Closed – Good view; limited access; can perform tympanometry
- Open or surgical – Slight inferior view; excellent access; best choice if you are limited to one otoscope
- Video otoscope – Excellent view and access; can record images

Careful visualisation will identify foreign bodies, *Otodectes*, inflammatory changes, ulceration, stenosis, condition of the tympanic membrane (tough in many cases otoscopy alone is often not sufficient for detecting all changes in the tympanic membrane and otitis media), amount and type of exudate as well as the degree and type of chronic changes. The normal ear canal should have a thin, smooth and pale pink appearance. The most common pathological findings include:

- Swollen, moist erythematous lining of the ear canals suggestive of acute inflammation
- Firm, fibrous, indurated appearance suggestive of chronic changes
- Erythema confined to the vertical portion of the ear canal in absence of exudate, suggestive of allergic otitis (food induced or non-food induced atopic dermatitis)
- Erosions and ulcers accompanied by purulent exudate are seen when Gram negative bacteria complicate the otitis
- 'Cobblestone' appearance to the lining of the ear canals suggestive of sebaceous and ceruminous hyperplasia. In some dogs this may develop into moderate to large, single or multiple polyp-like growths
- Foreign bodies, tumours , parasites

In many cases complete otoscopic examination may be impaired by exudate, stenosis, and excess of hair. If otoscopy is prevented by these findings, is preferable not persist (especially in animals with painful ears). Such cases should be examined under sedation/anaesthesia and, in presence of stenosis, is preferable to review the animal after a 1-3-week (depending on the severity of the clinical signs) course of oral glucocorticoids.

Examination of the visible part of the tympanic membrane may reveal changes (thickening, bulging, loss of transparency, partial rupture) or complete absence.

The integrity of the tympanic membrane can also be assessed by tube palpation. This is done through the surgical otoscope head but is more valuable when done trough the video otoscope. Debris can often mimic a tympanic membrane; a feeding tube or catheter will, however, pass through into the middle ear without resistance. In normal dogs and cats ear the tip of the tube can always be visualized; if the tube tip goes to a point where it cannot be seen that indicates pathology.

Another method to assess the tympanic membrane status is by tympanometry. Air is introduced into the ear canal via a closed otoscope. The tympanic membrane should flex back and forth; reduced movement or a bulging membrane suggests that there is fluid or debris in the middle ear. This is difficult technique to perform and assess, and it is not routinely done.

Microscopic evaluation

The search of parasites (*Otodectes cynotis*, *Demodex* spp.) can be performed examined under low power (10x objective) the otic exudate admixed in mineral oil.

Cytology

Cytology is a quick and easy procedure; it is very useful to identify microbes, inflammatory or neoplastic cells and monitor the progress of treatment. Cytology should be performed from both ears in bilateral otitis and from ear canals and middle ear (when otitis media is present or suspected) as the findings may differ and influence your choice of treatment.

A swab is inserted into the horizontal ear canal to obtain sample of the otic exudate and then rolled onto a glass microscope slide and stained with a modified Wright's stain. The specimen is then microscopically examined. It is essential to remember that cytology is most important in identifying micro-organisms, as the discharge does not always reflect the nature of the infection. Ear cytology is necessary at the initial examination and at each re-assessment. Microbial culture and sensitivity from the horizontal canal is not always required. It is performed in chronic recurrent or unresponsive cases, when otitis media is suspected and when rods are seen on cytology; in these cases *Pseudomonas* is suspected, which may be multi-drug resistant. Studies have shown that the organisms in the external ear canals and middle may be different and/or have different antibiotic sensitivity patterns. If possible, therefore, it is worth taking material for culture from both the external ear canal and middle ear.

Myringotomy

Iatrogenic rupture of the tympanic membrane is indicated when otitis media is suspected to take samples for cytology and culture from the tympanic bulla. It should be performed under general anaesthesia and under direct visualization after lavage of the external ear, when the canal is dry. The preferred method used by the author is using a 6 F urinary catheter cut obliquely to a 60° and attached to a 2 ml syringe containing sterile saline solution. The catheter is advanced trough the ventral and posterior quadrant of the membrane with subsequent aspiration of the fluids. An aliquot can be used for direct cytological examination and the remaining for culture.

Diagnostic imaging

Diagnostic imaging (radiography, CT, MRI) may be used to evaluate the ear, especially the middle ear for bony changes and other irreversible pathology that might indicate the need for surgery rather than medical therapy. According to Benigni and Lamb (2006) ear imaging is indicated in the following cases:

- Recurrent or severe otitis with suspected otitis media
- Para-aural swelling
- Fistulous tracts
- Trauma
- Inability to open the mouth
- Neurological dysfunctions
- Naso-pharyngeal polyp
- Complications following surgery

Techniques available include:

- Radiography – conventional radiography is commonly used but often lack sensitivity. The changes, furthermore, can be very subtle. The radiographic views include a series of left and right lateral oblique, dorso-ventral skull and open mouth rostro-caudal (best view for evaluation of the tympanic bulla) under general anaesthesia. With significant radiographic findings of occlusion and bony change in the ear canals, soft-tissue opacity of the middle ear cavity and lysis or proliferation of the bulla wall, surgical approach may be required as the prognosis with medical treatment alone is guarded.
  Positive contrast canalography evaluate the patency of the tympanic membrane can by introducing soluble contrast material into the ear canals of anesthetized dogs. In presence of ruptures, the contrast material will leak into the middle cavity. Stenosis of the ear canal, however, may block the flow wrongly suggesting that the tympanic membrane is intact.
- CT – this technique provides excellent images of bony structures and it is also very sensitive and specific for stenosis and occlusion of the ear canals and soft-tissue filling of the middle ear. CT, if available, is quick and easy to perform and interpret. However, normal findings do not rule out otitis media.
- MRI – it provides a better resolution of soft-tissue structures compared to CT or radiography. MRI is therefore better for imaging soft-tissue structures such as neoplasia. in or around the ears, but it is less good for imaging and differentiating the cartilage of the ear canal and bony wall of the tympanic membrane. MRI takes longer to perform than CT and is more expensive.
- Ultrasound can also be used. With care and practice it is possible to place the probe on the ventral-lateral surface of the tympanic bulla to detect fluid or soft-tissue, but the technique is difficult and rarely performed.

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Medical treatment of infectious otitis externa and media

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Abstract

Otitis externa, inflammation of the external ear canal, with or without middle ear involvement, is very common in dogs and quite common in cats. Ear disease is seen in both first opinion and referral practice and, due to its frequently recurrent nature, constitutes a frustrating problem for owners and veterinarians alike. Many different factors can cause or exacerbate otitis and recognition and correction of these is the key to successful management. Based on history and clinical presentation, management of ear diseases include medical and surgical options. The aim of these notes is to describe the medical interventions available in course of otitis externa and media, discussing principles of ear cleaning, ear flushing, and use of topical and systemic medications, mentioning the issues related to ototoxicity.

Medical treatment of infectious otitis externa and media.

Once an otic infection has been diagnosed, medical options include topical and systemic therapy, co-adjuvated, when appropriate, by ear cleaning.

Ear cleaning – when?

Whilst is commonly accepted that cleaning is not necessary in healthy ears, it is beneficial in the following conditions:

- Seborrheic ears
- Hairy ears
- Stenotic ears
- Pendulous ears
- Purulent discharge

Ear cleaning is an important part of any treatment regimen as it can remove debris and pus and permit complete diagnostic evaluation of the ear canal and tympanic membrane.

The cleaning fluids most commonly contain:

- Ceruminolytics, surfactants and foaming agents e.g sodium docusate
- Astringents or drying agents e.g isopropyl alcohol
- Antimicrobial agents e.g. parachlorometaxylenol (PCMX)

In a study (Swinney *et al*. 2008) the antimicrobial efficacy of different ear cleaners against *Staphylococcus intermedius*, *Pseudomonas aeruginosa* and *Malassezia pachydermatis* was evaluated. Antimicrobial activity appeared to be associated with the presence of isopropyl alcohol, parachlorometaxylenol and a low pH. Manual cleansing can be done at home by the owners; however it is important to instruct them on how to perform the cleaning and how often to use the different preparations. Although these are normally not recommended to be used more than every 48h, in one study (Cole *et al.* 2003) one cleaner (EpiOtic, Virbac) used up to twice daily caused no adverse effects. Manual cleansing doesn't remove tightly adherent debris or material present in the deep portion of the ear canal and therefore is best used as routine cleansing at home once ear flushing has been performed.

Ear flushing

Ear flushing is indicated when the entire external ear canal and/or the middle ear need thoroughly cleaning. It should always be performed under general anaesthesia with an endotracheal tube placed and cuffed, to avoid the fluids running from the ear to respiratory tract though the Eustachian tube. In presence of hyperplastic, stenotic or particularly inflamed ear canals, it is recommendable to provide systemic glucocorticoid treatment (0.5–1mg/Kg once daily) 2-3 weeks prior to the flushing. Ear flushing is best to be performed by using a video-otoscope or, if not available, with a urinary catheter or a feeding tube connected to a syringe and fluids (sterile saline), preferably through a three-way tap. Before ear flushing is performed, some cases may require use of an ear cleansing solution to emulsify and remove debris. If the ear drum cannot be visualized, care should be used as ear cleaners are not licensed for applications in the middle ear and are all potentially ototoxic.

Myringotomy

Iatrogenic rupture of the tympanic membrane is indicated when otitis media is suspected and/or confirmed by diagnostic imaging techniques, to take samples for cytology and culture from the tympanic bulla and to allow flushing of the middle ear cavities. It should be performed under general anaesthesia and under direct visualization after lavage of the external ear, when the canal is dry. The preferred method used by the author is using a 6 French urinary catheter cut obliquely to a 60° and attached to a 2 ml syringe containing sterile saline solution. The catheter is advanced trough the ventral and posterior quadrant of the membrane with subsequent aspiration of the fluids. An aliquot can be used for direct cytological examination and the remaining for culture.

Topical therapy

In the majority of cases of infectious otitis externa, topical therapy alone is sufficient. Antimicrobial agents rarely can reach, sistemicallly, therapeutic concentrations in the skin of ear canal and topical therapy, choosen empirically based on otic cytology and otoscopic examination, represents an appropriate choice. Antibiotic sensitivity data reflect serum level needed systemically and it is less useful with topical drugs where concentrations 100 to 1000 times superior to the MIC (Minimum Inhibitory Concentration) may be reached. Topical therapy ussually is characterized by high efficacy and, with regard to the antimicrobial agents, by no systemic side effects in presence of an intact tympanic membrane.

Ingredient of topical antibacterials

Fusidic Acid

- Bacteriostatic
- Effective against Gram positive cocci
- Mechanism of action: interference with bacterial proteins synthesis

Aminoglycosides

- Bactericidal
- Large spectrum
- Mechanism of action: interference with bacterial proteins synthesis
- Impaired in acidic environment – cleansing agents should be used at least one hour prior to their use
- Topical agents include mainly neomycin and gentamicin. Amikacin is not available as topical preparations but injectable formulations, diluted in sterile saline, can be used topically.

Polimixin B

- Bactericidal
- Effective against Gram negative bacteria
- Mechanism of action: alteration cytoplasmic membrane permeability
- Ototoxic
- Inactivated by cellular debris , therefore the association with ear cleaning is important

Fluoroquinolones

- Bactericidal
- Large spectrum
- Mechanism of action: inhibition of DNA replication
- Effective against Gram positive and Gram negative bacteria
- Topical agents, available as veterinary formulations, include, marbofloxacin and orbifloxacin. Enrofloxacin injectable solution dilute in sterile saline can be used topically.

Carboxypenicillins

- Expanded-spectrum penicillins
- Activity against gram-negative organisms (including *Pseudomonas spp*)
- Mechanism of action: penetrate the gram-negative cell membrane.
- Reconstituted ticarcillin, diluted with sterile water, is the carboxycillin for which topical use has been most commonly reported in the treatment of canine *Pseudomonas* otitis

Topical Antimycotics

Azoles

- Amidazoles (clotrimazole, miconazole, posaconazole and ketoconazole)
  - Mechanism of action: inhibition of ergosterole synthesis

Polienic

- Nistatine
  - Mechanism of action: binds to ergosterole causing alterations of the cellular wall permeability

Other topical antimicrobials

- **Silver Sulfadiazine (SSD)**–This has broad-spectrum antibacterial activity (most notably against *P. aeruginosa*). Concentrations as low as 0.02% have shown 100% efficacy against *P. aeruginosa* and *Staphylococcus spp*. It is available as a cream and, although not readily miscible in water, a homogeneous emulsion can be achieved with gentle mixing
- **Tromethamine–ethylenediamine-tetraacetate (TrisEDTA)–**This is commonly used as either a pre-soak or a carrier vehicle in the treatment of gram negative infections. EDTA promotes increased permeability to extracellular solutes and increased sensitization to antibiotics, whereas Tris serves as a buffer. The in vitro antimicrobial activity of a commercial ear antiseptic containing chlorhexidine (0.15%) and Tris-EDTA (Otodine Vetruus) has been evaluated (Guardabassi *et al.* 2010); according to the results, this product was active against all the pathogens most commonly involved in canine otitis. In a more recent study (Clark et al. 2016), the association of Tris-EDTA with chlorhexidine did not show beneficial effect against *Staphyloccus pseudointermedius.* Furthermore, more recently (Boyd et al. 2019) Tris-EDTA appeared to have detrimental effect on the efficacy of silver sulfadiazine against *Staphyloccus pseudointermedius.* It is important to highlight that the clinical interpretation of this results requires further investigations.

Glucocorticoids

Glucocorticoids have antiinflammatory, antipruritic and antiproliferative properties. They can also reduce sebaceous and ceruminous gland secretions. Can be sistemically absorbed, with the adrenal glands function suppressed up to 2 weeks or more after administration of some glucorticoids for more than one week. Long term treatment can cause cutaneous atrophy, comedones, demodicosis.

Their potency depends on:

- Intrinsec potency
- Concentration
- Vehicle

An example of a potency scale is:

- Hydrocortisone: 1
- Prednisolone: 5
- Triamcinolone: 5
- Dexamethasone: 25
- Bethametasone: 25
- Fluocinolone: 100

According to manifactcurer's data, hydrocortisone aceponate (Cortavance, Virbac) has a potency similar to dexamethasone ands bethametasone.

The reader should remember that all the UK licensed polipharmaceutical topical ear medications are no licensed to be used in absence of tympanic membrane and owners should be made aware of the risks of using these medications when the tympanic membrane cannot be assessed.

Sistemic therapy

Antibiotics

As stated by Morris (1994) "Unless the ear canal epithelium has been eroded or ulcerated extensively, systemic (oral) antimicrobials are unlikely to achieve therapeutic concentrations within the fluid and waxy exudates of the external canals in which the infectious organisms are harboured."

Systemic antimicrobial treatment is indicated in case of:

- Stenosis
- Ulcerations and deep infections
- Otitis media

Considering that the middle ear (tympanic bulla) contains a highly vascular mucous membrane lining, drugs may diffuse from the from the vascular compartment to the bulla space better than in the external ear canals. The choice of systemic antibiotics for treating the middle ear diseases is also indicated as the tympanic bulla may present a problematic access to topicals. The choice should be based on culture and susceptibility testing and, results pending, empirical treatment, based on examination of cytological specimen from the bulla content, should be started.

Antibiotics recognized effective for the treatment of otitis media include:

- Enrofloxacin 5-20mg/kg once daily
- Marbofloxacin 2-5 mg/kg once daily
- Ciprofloxacin (off label) 10-20 mg/kg once daily
- Orbifloxacin 2.5 mg/kg once daily
- Cefalexin 20-30 mg/kg twice daily

In case of multiresistence:

- Ceftazidime (off label) 30 mg/kg four times daily
- Ticarcillin (off label) 40-80 mg/kg three times daily
- Meropem (off label) 8 mg/kg twice daily

Antimicotics

The administration of systemic antimycotic agents is needed in curse di otitis media caused by *Malassezia* spp. or when topical therapy is not an option.

Drugs used include:

- Ketoconazole (off label) 10 mg/kg once daily
- Itraconazole (off label) 5mg/kg once daily
- Fluconazole (off label) 2,5-5 mg/kg once daily

Glucocorticoids

Administerd systemically they can:

- Reduce stenosis
- Reduce oedema
- Reduce hyperplasia
- Allow otoscopic examination
- Allow better cleaning process

The initial treatment consists in doses of 0.5-1 mg/kg once daily depending on the severity of clinical signs. Dose and frequency of administration should be reduction until discontinuation when the medication is no longer needed.

Ear wicks

Ear wicks are made of polyvinyl alcohol (PVA) and are characterized by a hard compact structure. They are inserted in the ear canal under general anaesthesia and then soaked with a solution usually containing antibiotics with or without TrizEDTA and/or glucocorticoids. The expansion produces a structure that adapt to the contours of the ear canal, releasing slowly the medicaments. In this author's experience, ear wicks can be a useful alternative to daily topical therapy in those patients that do not tolerate administration of topical medications. It is paramount that the ear canals and (in presence of otitis media) the tympanic bullae, are aseptically cleaned prior to the placement as, if the canal is not adequately flushed, the wick can act as a lid trapping infections. Additionally, in dogs with large ear canals, they often do not expand sufficiently to fill the ear canal in its entire diameter.

Ototoxicity

An ototoxic agent can cause damage to the ear in any of its anatomical components. Usually ototoxicity can be divided cochlear damage with consequent deafness or vestibular damage with consequent vestibular syndrome. In both cases, the damage occurs to the inner ear. The ototoxic agent can reach the inner ear via haematogenous route or directly through openings in the tympanic membrane. In particular, given that the middle and inner ear component can be damaged by topical medicaments, it is important that, before administration of a topical, the clinician performs otoscopic examination.

Systemic ototoxicity

Examples of molecules that cause ototoxicity after topical administration are aminoglicosides antibiotics, furosemide, cisplatin, vinblastin, vincristin.

Local ototoxicity

- Cleaning agents. According to Mansfield *et al.* (1997) the only non ototoxic agent is squalene. With regard to chlorhexidine, recent studies have demonstrated that, if used at a 0.2% or inferior concentration doesn't carry risk of ototoxicity.
- Antibiotics. aminoglicosides can cause cochlear damage, with the exclusion of gentamicin that in a study (Strain *et al.* 1995) failed to cause damage when instilled in the middle ear of dogs for 21 days. Agents with recocognized ototoxic potential are polimixin B in the guinea pig and ticarcillin in the cincilla.

Agents with low ototoxic potential are fluoroquinolones, some cefalosporines (e.g. ceftazidime), the antifungal clotrimazole, miconazole, nistatine e tolfaftate, the steroids desametasone e fluocinolone, and TrisEDTA solution.

In pathologic condition, even the use of simple saline solution during ear flushing may cause, although infrequently, complications. For this reason is always important to inform owners about potential risks of ear flushing and topical therapy.

Finally, it is paramount to highlight that the majority of the studies on ototoxicity have been performed on laboratory animals or has been extrapolated by human studies. Despite these studies represent guidelines for the clinician, further studies on other species are needed.

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Dermatological emergencies

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Dermatological emergencies are not common in general practice as in most cases dermatological conditions are chronic in nature. However, when presented as acute problems, although non-life threatening, skin issues may alarm the owners who will subsequently seek veterinary attention. On the other side, there are other conditions, often rare, that may appear mild initially but that may prove serious or fatal at a later stage. Given that often serious conditions can be difficult to differentiate between each other, the process of history taking is very important, including specific attention to previous treatment as adverse drug reactions can be one of the most serious dermatological presentations. Very important is also taking skin biopsy of early lesions and submit the specimens to pathologist with a special interest and expertise in dermatohistopathology.

Urticaria and angioedema

Urticaria and angioedema are uncommon conditions in small animals. They can be triggered by both immunological and non-immunological processes and the pathological changes are restricted to the dermis in urticaria and can involve the connective tissue in angioedema.

Pathogenesis. The causative agents may be non-identified in up to 80% of human cases; similar numbers are anecdotally reported in veterinary patients. The pathomechanism can be of immunological or non-immunological nature and clinical signs are classically due to the result of local mast cells and/or basophils degranulation leading to vascular dilation and recruitment of inflammatory cells. Immunological reactions are classic type 1 hypersensitivity disorder triggered by vaccinations, allergens drugs, topical agents, arthropod bites. Non immunological reactions can be triggered by arthropod venom, food items, drugs, dermatographysm, or by environmental factors (cold-induced urticaria, actinic urticaria).

Clinical signs are acute in onset and classically consist in pruritic wheals or large areas of oedematous swellings. They can be localized or generalized, with angioedema tending to be localized to the head. Respiratory distress can occur if the angioedema involves the nares, larynx, or pharynx.

Diagnosis is based on clinical appearance, disappearance of the signs on diascopy and, when necessary, supportive histopathology; however, in most cases history and clinical signs play a major role. Differential diagnoses for urticaria include: bacterial folliculitis (especially for short coated breeds), early cases of erythema multiforme, mast cell tumours, cutaneous mastocytosis, focal mucinosis. Differential diagnoses of angioedema include early stages of juvenile cellulitis, early stages of bacterial cellulitis, neutrophilic immunologic vasculitis.

Treatment. Prompt identification and correction of the offending factors is crucial for successful management, however most often is important to proceed with symptomatic treatment, including systemic glucocorticoids (dose and route administration are dependent on the severity of the clinical signs), anti-histamines (these have been described as ineffective in treating acute cases but may be helpful in chronic cases or to prevent future reactions), in case of vasculitis pentoxyfilline (15mg/kg three times daily) and in case of angioedema, given the risk of laryngeal oedema, intravenous glucocorticoids (methylprednisolone succinate 1mg/kg or dexamethasone sodium phosphate 0.25mg/kg).

Canine juvenile cellulitis

Canine juvenile cellulitis (CJC) is an uncommon pustular and granulomatous disease affecting mainly the face, pinnae and lymph nodes, seen usually in puppies. However, there are rare reports of dermatoses resembling CJC in adult dogs. This condition has been described with increased occurrence in some breeds (Golden retriever, Dachshund, Gordon setter).

The aetiology and pathogenesis of CJC are unknown; an infectious aetiology has been considered but not demonstrated, and the prompt response to high doses of oral prednisolone supports a non-infectious aetiology. Causative link with a vaccine against distemper virus, adenovirus and parainfluenza virus has also been suggested. The fulminant onset is a typical characteristic of CJC.

Commonly the initial feature is acute swelling of the face, especially on the eyelids, lips and muzzle, with submandibular lymphoadenopathy. Within 24 to 48 hours papules, pustules and crusting develop rapidly. At presentation typical cutaneous lesions usually appear on the head (muzzle, pinnae, and periocular areas); the inner aspect of the pinnae is commonly oedematous and shows presence of crusting and purulent exudate; additionally, involvement of the feet,

abdomen and thorax, preputial and perianal areas has been reported. Secondary bacterial infections are possible; pyrexia and depression, along with joint pain, are inconsistent clinical signs.

The clinical differential diagnoses of CJC include mainly deep pyoderma, demodicosis and adverse drug reaction; in early stages, when papules and pustules are absent, it has also to be differentiated from angioedema. For adult dogs sterile granuloma pyogranuloma syndrome, eosinophilic furunculosis of the face should also be considered. Diagnosis is based on history, clinical signs and is confirmed by histopathology.

Therapy of CJC requires immune-suppressive doses of glucocorticoids (prednisone or prednisolone at 2 mg/Kg), to be administered until remission of the clinical signs is achieved. Combination of prednisolone and ciclosporin has also been effective. If there is cytological evidence of secondary bacterial infection, systemic antibiotics should be given.

Prognosis is generally good, although relapses after discontinuation of treatment have been reported.

Pyotraumatic dermatitis

As previously mentioned, sometimes common and non-life-threatening diseases, due to their acute onset, can alarm the owners and therefore can be presented as emergencies. Pyotraumatic dermatitis "hot spots" is an example.

This condition is well known in general practice, affecting mainly young dogs with higher prevalence in breeds such as St. Bernards, Golden Retriever and Rottweilers. Dense coat seems to be a predisposing factor. Pyotraumatic dermatitis is considered a complication of underlying problems, most commonly allergies. Clinically it is characterized by acute onset with well circumscribed areas of alopecia with moist matted hair on cheek, neck, dorso-lumbar region, and flanks.

Diagnosis is based on history and clinical signs but histopathology may be needed to differentiate cases with surface pyoderma from cases with folliculitis and furunculosis consistent with deep pyoderma.

Clinical management consists in clipping and use of topical antiseptic agents; however lesions can be often painful and therefore caution should be made with handling and sedation should be considered at least initially. Use systemic antibiotics is needed when deep pyoderma is present or suspected and, markedly pruritic cases, in absence of deep pyoderma, should be treated with a short course of prednisolone at anti-inflammatory doses.

Primary irritant contact dermatitis

Another condition that can be alarming for owners is primary irritant contact dermatitis. This is a heterogeneous disease with various clinical manifestations and usually history is important to allow identification of the causative factors, which often include soaps, insecticides, topical antimicrobials, caustic substances.

Typical clinical manifestations are erythema and papules seen as primary lesions, with chronic cases showing lichenification, excoriations, crusts and ulcerations. Typically lesions occur on glabrous areas where the skin is easily exposed to the offending substances.

Differential Diagnoses include other hypersensitivity disorders, ectoparasitic diseases and infections such as Malassezia dermatitis.

Treatment of choice include removing the offending substance and washing the affected area; with pruritus anti-inflammatory doses of systemic prednisolone may be indicated.

Eosinophilic Furunculosis of the Face

Eosinophilic furunculosis of the face (EFF) is an uncommon skin disease in dogs. It is characterized by peracute onset and predominantly nasal and muzzle distribution of lesions. EFF is believed to represent some type of hypersensitivity reaction due to possible contact with arthropods (including bees, hornets, wasps, ants) and spiders, but cause-effect relationship has not been proven.

Affected dogs present with papules, nodules and plaques with various degrees of erosions, ulcerations, crusting, serum leakage and haemorrhage, present on the muzzle and often periocularly. However, similar lesions may be seen also on the pinnae, ventral abdomen, lips and interdigital areas. Pruritus can be variable. Severely affected dogs may present pyrexia and depression.

The differential diagnoses of EFF include mainly bacterial nasal folliculitis and furunculosis, dermatophytosis and demodicosis when the lesions persist and auto-immune diseases with predominant facial lesions; however, EEF presents a fulminant onset whereas autoimmune diseases commonly develop gradually. Although histopathology is required for definitive diagnosis, cytology, with large numbers of eosinophils, is of value in supporting a clinical diagnosis of EFF, and, histopathology results pending, can provide justification for the use of glucocorticoids, when other symptomatic treatments have failed to prevent progression of the disease.

Rapid response within ten to fourteen days to moderately high doses of prednisolone is typical of this disease. In some cases scarring alopecia may be seen.

Prognosis is excellent because of the prompt response to the therapeutic agents.

Erythema Multiforme

Erythema multiforme (EM) is an uncommon disease characterized by eruption of the skin and/or mucous membranes that been reported in humans, dogs, cats and horses. EM is considered to be a cutaneous reaction pattern associated with a T cell-mediated hypersensitivity reaction directed against altered keratinocytes antigens. It has been recognized in associations with infections, drug therapy (especially trimethoprim-potentiated sulphonamides, penicillins and cephalosporins), neoplasia, connective tissue diseases and adverse food reactions.

EM is frequently characterized by pleomorphic eruptions. Typically there is acute onset of maculo-papular lesions that spread peripherally and clear centrally, producing annular or arciform patters. Other clinical presentations include urticarial plaques, vescicles, bullae and ulcers. Feline EM is reported to exhibit predominantly vesciculo-bollous and ulcerative lesions but generalized exfoliative dermatitis with alopecia also has been seen. Severely affected animals may be depressed and anorectic.

The clinical differential diagnoses of EM in this case included mainly paraneoplastic diseases, early lesions of bullous autoimmune diseases and epitheliotrophic lymphoma. Due to the pleomorphic nature of the clinical signs, histopathology is essential for making a definitive diagnosis. Interface dermatitis and apoptosis are typical features of EM where apoptosis is prominent at all levels of the epidermis, contrary to thymoma-associated exfoliative dermatitis which shows milder transepidermal apoposis. There are cases of EM featuring large histiocytic round cells in clusters within the epidermis mimicking lesions of epitheliotropic lymphoma with apoptosis.

Treatment of EM is based on identification and removal of the offending factor and on use of supportive care measures. In idiopathic cases glucocorticoids used with or without azathioprine have been successfully used; anecdotal reports suggest the use of ciclosporin. Intravenous human immunoglobulin administration (1gr/Kg during a four-hour period for two consecutive days) has been reported successful in a feline case.

The prognosis is variable and depending on the nature of the lesions and on the identification and correction of the triggering factor.

Toxic Epidermal Necrolysis

Toxic Epidermal Necrolysis (TEN) is a rare immune-mediated disease characterized by extensive, painful vesiculo-bullous and ulcerative lesions affecting both the skin and the mucosae. It has been reported in humans, dogs, cats and cattle and is most commonly associated with drug eruptions, although in humans cases associated with vaccine reactions, neoplasia, infections and pregnancy. These appear to be possible also in dogs and cats.

The pathomechanism of TEN is not exactly known and there cellular immunologic factors involved primarily in death of keratinocytes. The pathways leading to the pathological changes are different and have been extensively studied in humans; pathogenesis is still unknown in the dog. Stephen Johnson Syndrome (SJS) and SJS-TEN overlap are considered the same entity, albeit characterized by less severe clinical manifestation.

There is no apparent age, breed or sex predilection and typical presentation include acute onset, pyrexia, anorexia, lethargy and depression. Dermatological clinical signs consist in erythematous macular dermatitis, focal to widespread muco-cutaneous vesicles with epithelial detachment and consequent ulcerations. A positive Nicholsky sign is often present. Other clinical signs may include loss of claws, corneal ulcerations and ulcerative otitis. Internal involvement may manifests as renal failure, haepathopathy and blood dyscrasias. Fluid and electrolyte losses and secondary infections can be also often seen.

Differential diagnoses include urticaria, thermal burns, deep infections, other immune-mediated blistering skin diseases, vasculitis, epitheliotropic lymphoma , cutaneous drug reactions. Histopthological lesions typically consist in hydropic basal cell degeneration, full thickness necrosis of the epidermis with dermo-epidermal separation, vesicles and ulcerations. Cell-poor interface dermatitis may occasionally be present.

Treatment is similar to the one for second degree burns and symptomatic and supportive measures to counteract the fluids, colloids and electrolytes losses are vital. Antibiotic cover is important to prevent secondary infections. In humans use of systemic glucocorticoids has been associated with increased morbidity and mortality. In veterinary cases intravenous immunoglobulines have been reported effective in dogs and cats.

The prognosis of TEN is guarded to poor depending on the underlying cause.

Cutaneous drug eruptions

An adverse drug reaction (ADR) is any undesired consequence derived from the administration of a drug. They can be divided into two different categories:

- Undesired pharmacological effects, dose dependant, foreseeable and relatively frequent
- Toxic effects, unforeseeable and of idiosyncratic nature

A drug eruption is a drug reaction that involves the skin.

Pathogenesis. Generally any drug can cause undesired effects, although certain drugs are more frequently associated

to dermatological manifestations. The pathomechanism can be immunological or non-immunological. Immunological drug reactions include hypersensitivity mechanisms of type I to IV. Non immunological drug reactions may clinically mimic those of their immunological counterpart but are non-elicited by their interaction between the drug and the immune system. Some examples include drugs that can elicit release of mast cell mediators, drugs that can activate alternate pathway of complement activation, drugs able to alter the metabolism of arachidonic acid, drugs able to suppress regulatory lymphocytes Diagnosis

Diagnosis is based on history of drug administration, clinical signs supported, when needed, by histopathology, and resolution after drug withdrawal. Reproducibility of the clinical signs after drug re-challenge is important but is usually not advised for ethical reasons.

The list of differential diagnoses can be extensive as the clinical signs are various including urticaria and angioedema, erythroderma and exfoliative reactions, maculo-papular eruptions, vasculitis, auto-immune diseases (pemphigus foliaceus, systemic lupus, diseases of the dermo-epidermal junction), Well's-like Syndrome (canine eosinophilic dermatitis with oedema), erythema multiforme-Stephen Johnson Syndrome-toxic epidermal necrolysis, pruritus, injection site reactions, fixed reactions, contact reactions.

Given the extreme variability of clinical signs and the various criteria needed to address a drug reaction, an "adverse drug reaction probability scale" was developed by Naranjo and colleagues in human medicine. This is a method for estimating the probability of an adverse reaction and in order to do so a series of questions should be addressed, giving a pertinent score to the answers.

Naranjo algorithm

	Yes	No	Do not know	Score
1. Are there previous conclusive reports on this reaction?	*+1*	*0*	*0*	
2. Did the adverse event appear after the suspected drug was given?	+2	-1	0	
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	*+1*	*0*	*0*	
4. Did the adverse reaction appear when the drug was re-administered?	*+2*	*-2*	*0*	
5. Are there alternative causes that could have caused the reaction?	*-1*	*+2*	*0*	
6. Did the reaction reappear when a placebo was given?	-1	+1	0	
7. Was the drug detected in any body fluid in toxic concentrations?	*+1*	*0*	*0*	
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	*+1*	*0*	*0*	
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	*+1*	*0*	*0*	
10. Was the adverse event confirmed by any objective evidence?	*+1*	*0*	*0*	

Scoring

> 9 = definite ADR

5-8 = probable ADR

1-4 = possible ADR

0 = doubtful ADR

Treatment is based on withdrawal of the suspected drug. Fluid therapy is needed until an improvement of the general condition is obtained and antibiotic cover (not related to the possible responsible drug) may be needed in cases with ulcerations and pustular lesions. The use of systemic glucocorticoids, apart from cases of urticaria and autoimmune-disease, is controversial.

Prognosis is usually good but can be guarded in cases of anaphylactic shock, erythema multiforme or toxic epidermal necrolysis.

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Ulcerative skin disease in a dog receiving prednisolone

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Signalment

Four-year, six-month old, 23 kg male neutered, English Springer Spaniel.

Owner's complaint

Ulcerations on planum nasale and foot pads.

History

Day 0.

Three months previously, following onset of stiff gait, cervical pain, pyrexia and hypersalivation, a diagnosis of steroid-responsive meningitis-arteritis had been made by a specialist in veterinary neurology; the dog had received oral prednisolone (1 mg/kg BID, reduced to 0.5 mg/kg BID after three weeks) with an initial remission of the clinical signs. Two months later the dog had developed ulcerations on his feet and, one month later on the planum nasale, which persisted despite topical therapy with fucidic acid. One month prior to referral, haematology, blood biochemistry, thoracic radiographs and abdominal ultrasound had revealed elevation of liver enzymes and an enlarged, hyperechoic liver, consistent with steroid-induced hepatopathy. The neurologist prescribed S-adenosine methionine (200 mg BID orally) to support liver function.

Vaccination, flea prevention and worming were regular and the diet was commercial dried dog food. No in contact regular animals were present and the owners had not developed skin lesions.

Physical examination

General physical examination was unremarkable apart generalized mild muscle wastage, more marked over the temporal regions. Dermatological examination revealed patchy alopecia on the dorsal aspects of the pinnae, dorsal neck, dorsal midline and left flank. Comedones were noted diffusely on the ventral abdomen and on the plantar aspects of all four feet. The coat was dull and scaling was present on the trunk. The ventral abdomen showed thinning of the skin. The planum nasale showed depigmentation of the alar folds and of the dorsal surface; the right alar fold showed a deep irregular ulceration (figure 1). A large deep ulceration was noted on the metacarpal pad of the right fore foot (figure 2). The pads of digits 2 and 3 of the left fore had more superficial ulcerations (figure 3) and the metatarsal pad of the right hind showed a deep circular ulcer covered with sero-haemorrhagic exudate (figure 4).

What are your differential diagnoses?

Differential diagnoses

Muscle wastage, thinning of the skin, alopecia:

- Iatrogenic or naturally occurring hyperadrenocorticosm.

Scaling, comedo formation, alopecia and poor coat quality:

- Primary keratinisation defect, or secondary to hyperadrenocorticism or hypothyroidism
- Demodicosis
- Dermatophytosis
- Ectoparasites : *Cheyletiella spp*, lice (these were considered as cause for the scaling)

Ulcerations:

- Sub-epidermal or intraepidermal ulcerative dermatitides or interface dermatitides, vasculitis, drug eruption
- Deep infections (fungal, bacterial, mycobacterial)
- Cutaneous lymphoma

Considerations:

The history was consistent with iatrogenic hyperadrenocorticism and the scaling, comedones and poor coat quality had been present since two months after treatment with prednisolone.

Adult-onset demodicosis and dermatophytosis were considered due to the immunosuppressive treatment.

The nasal and pedal ulcerations were suggestive of immune-mediated conditions; there was history of drug exposure. Could this be an adverse drug reaction?

Although due to the immunosuppressive treatment deep fungal and bacterial/mycobacterial infections were considered, these normally present as nodular, discharging lesions affecting both haired and non-haired skin.

What tests would you perform?

Laboratory results

- Multiple skin scrapings and hair plucks from the trunk and feet – unremarkable
- Cytology from the scaly and erythematous areas on the trunk – nucleated keratinocytes
- Cytology from lesions on footpads – red blood cells, mainly non degenerated neutrophils and occasional coccoid bacteria
- Multiple 6 mm punch biopsies from the footpads and planum nasale for histopathology – pyogranulomatous, mainly histiocytic dermatitis with intracellular fungal elements (figure 5). Further biopsies samples were submitted for macerated tissue fungal (to a mycology reference laboratory) and bacterial culture.

Haematology, biochemistry, T4 and TSH were planned but postponed due to the current treatment with prednisolone.

Diagnosis and prognosis

Deep mycosis. Prognosis guarded due to concurrent immunosuppressive treatment, possible inefficacy of medical and surgical managements and recurrences.

Treatment plan

Dilemma:

What would you do with the immunosuppressive treatment?

Cefalexin (15mg/kg/BID) was given pending histopathology results; prednisolone reduced and discontinued by the neurologist over an 8-week period. S-adenosine methionine was discontinued.

Day 11.

Bacterial culture yielded growth of a staphylococcus with a large sensitivity pattern, including cefalexin; on the receipt of the histopathology and fungal culture and sensitivity results pending, treatment was started with itraconazole (5 mg/kg once daily with food). We advised to monitor the dog for signs of anorexia, nausea, vomiting or abdominal pain and to contact us in case of concern.

Cefalexin was continued as before.

Re-evaluations and final outcome

No changes to treatment unless indicated.

Day 47.

Ulceration on the planum nasale resolved, reduced ulcerations on metacarpal pad of the right fore, on pads of digits 2 and 3 of the left fore and on metatarsal pad of the right hind . Coat dull with scaling (trunk mainly).

Skin scrapings repeated with no evidence of *Demodex*.

Fungal culture yielded *Gliomastix sp.* sensitive to amphotericin B, itraconazole and posaconazole.

Final diagnosis: pyogranulomatous dermatitis caused by *Gliomastix sp.*

Cefalexin and prednisolone discontinued.

Day 68.

Single healing ulcer on digit 3 of left fore foot. Decreased scaling and comedones. Haematology, biochemistry, T4 and TSH within normal limits.

Day 99.

Reduced temporal muscle wasting, ulcerations resolved, depigmentation on right nostril (figure 6), and metacarpal pad of right forefoot (figure 7). Reduced scaling and fewer comedones on ventral abdomen only. Serum biochemistry unremarkable.

Day 134.

Small depigmented patch on left side of planum nasale and occasional comedones on ventral midline. Itraconazole discontinued.

Day 228.

Follow-up call. No skin lesions; minimal temporal muscle wastage.

Day 358.

Follow-up call. No abnormalities reported.

Discussion

Gliomastix spp. is not a common animal pathogen. The natural habitat includes plant litter, wood, soil and cellulose (1-3) and it has also been isolated from the conjunctiva of dogs (4) and horses (5) and from a porcine aborted foetus (6). Infections with saprophytic fungi usually occur secondary to traumatic implantation or wound contamination but in this case there was no history of recognized trauma. This patient had no previous history of skin disease and the infection may have been secondary to the use of immuno suppressive doses of prednisolone.

Glucocorticoids result in alteration of the concentration, distribution and function of peripheral leucocytes (7). Prednisolone, given in this case at immunosuppressive doses, may have significantly reduced the patient's cell mediated immunity with consequent lack of defence against fungal infections.

Although the majority of reports of deep mycoses in the literature describe animal presenting with nodular, often discharging lesions (8,9,10), mucocutaneous and footpads oriented ulcerative lesions have been reported (11) as evolution of primary papular and nodular lesions. In this case, the lack of nodules and draining tracts and the presence of ulcerations confined to the planum nasale and footpads were suggestive of an immune-mediated disease, although some of the alopecic areas on the trunk may have represented early lesions; a biopsy performed on those sites may have helped in clarifying this point.

The history of immunosuppressive treatment was compatible with the presence of an opportunist infection, as reported in the literature (9, 12, 13, 14,15). In a recent retrospective study, an opportunistic invasive cutaneous fungal infection was diagnosed in 15 of 113 (13%) of dogs with selected immune-mediated diseases treated with immunosuppressive drugs. In this study, and in a preceding case series (14) dogs were significantly more likely to develop an opportunistic invasive fungal infection if they had been treated with cyclosporine. Our patient was not treated with cyclosporine but was maintained with substantial high doses of prednisolone for several weeks.

The histological lesions resembled those of other opportunistic fungal infections; the different species are said not to be distinguishable on histological grounds. The sub-committee on nomenclature of fungal diseases gives the correct reporting phraseology as Pathology A caused by fungus X or fungus X pathology A (16). In this case the fungus was identified based on the macroscopic and microscopic morphological features. Further test (included molecular biology techniques) may have given more accuracy, however clinically the most important factors for the prognosis are sensitivity results and host immuno state.

Wide surgical excision for nodular solitary lesions may be curative (17), although long-term antifungal treatment may be required to prevent recurrence of the lesions (18). In this case, due to the widespread and non-nodular nature of the lesions, prolonged systemic antifungal treatment alone was chosen. The response to drugs is unpredictable and these should be chosen based on in vitro susceptibility testing. At the time of presentation in the UK there were no licensed systemic antifungal medications available in canine medicine; therefore, following the cascade, off-licence therapy using itraconazole was started. This medication was chosen initially empirically because of its wide spectrum of action (19, 20) and its fewer side-effects when compared to ketoconazole (21) and this choice was confirmed by the sensitivity testing results. Although generally well tolerated, anorexia, lethargy, increased blood urea and liver enzymes have been reported in dogs (22). Elevation of liver enzymes is often dose-related. In a study of dogs with blastomycosis (22), a similar efficacy of itraconazole at 5 mg/kg SID compared with 10 mg/kg SID was noted, with substantially less hepatotoxicity. Additionally in dogs, doses of 10 mg/kg SID produced vasculitis, which did not occur when given at doses of 5 mg/kg SID (22). In this patient the liver enzymes had been monitored once the treatment with prednisolone was discontinued and ALT remained normal. Recurrences are reported (23), and in this case the treatment was continued for 8 weeks beyond clinical cure with no relapses noted 6 months after discontinuation.

Due to its unusual presentation this case highlights the variety of clinical signs associated with deep mycoses and suggests that fungal diseases should be considered a differential in animals on immunosuppressive treatment when presenting with ulcerations. Additionally, despite the therapeutic challenge of managing this alongside with immunosuppressive treatment, it demonstrated the efficacy of itraconazole.

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Figure 1. Deep irregular ulceration on the right alar fold of the planum nasale.

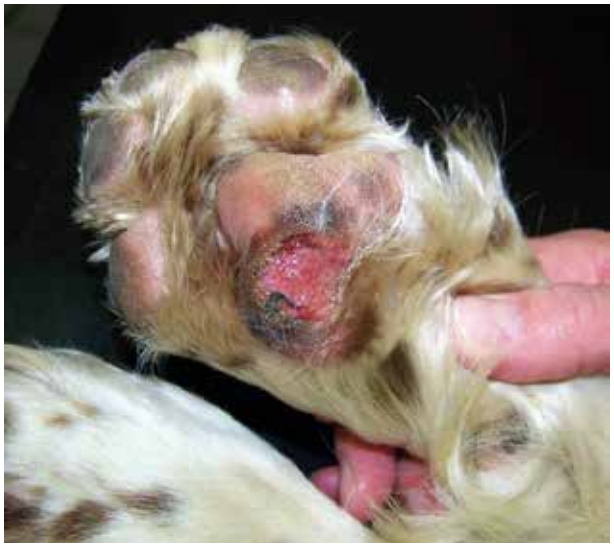

Figure 2. Large deep ulceration on the metacarpal pad of the right fore foot.

Figure 3. Ulcerations on pads of digits 2 and 3 of the left fore foot.

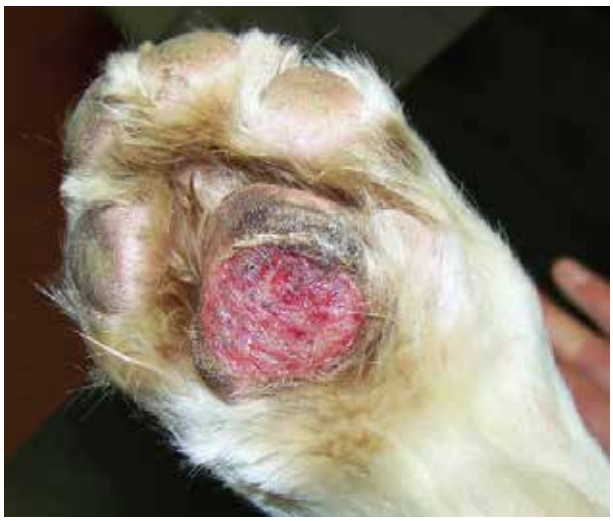

Figure 4. Deep circular ulcer covered with sero-haemorrhagic exudate on the metatarsal pad of the right hind foot.

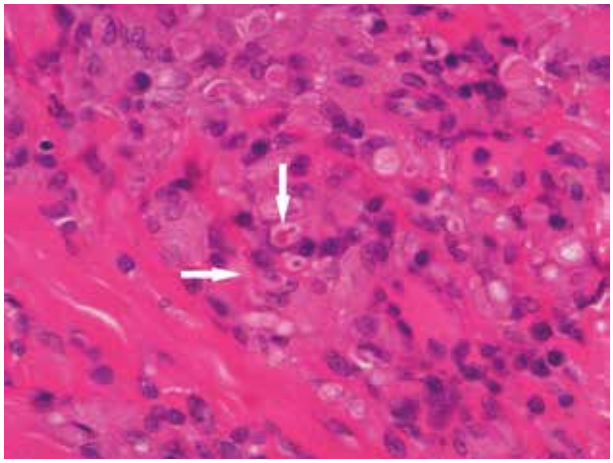

Figure 5. Histopathology: granulomatous reaction containing pink spherical budding organisms (arrow). Note the surrounding pale haloes and the occasional hypae-like structures (notched arrow). Haematoxylin and eosin.

Figure 6. Day 99: planum nasale: ulcerations resolved but depigmentation remains.

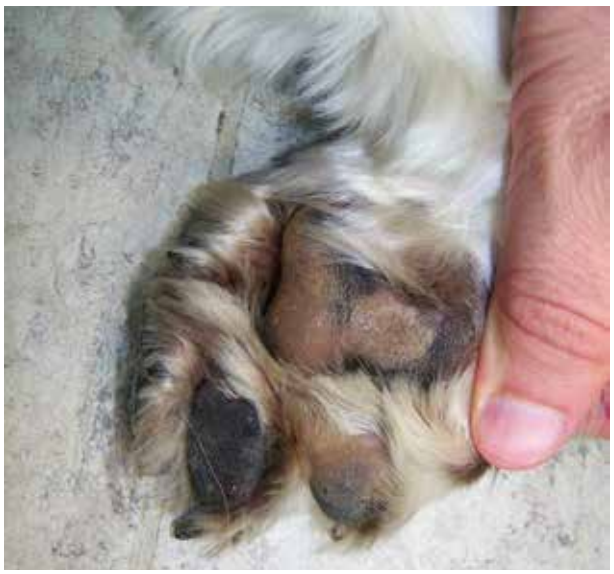

Figure 7. Day 99: depigmentation on metacarpal pad of right fore foot.

Crusting skin disease in a dog: treatment and complications

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Signalment

Nine-year old, 14.6 kg female neutered Cavalier King Charles Spaniel.

Owner's complaint

Multifocal crusting and pruritus.

History

Day 0.

This patient presented with a long history of pruritus evolving, in the last eight months, into generalised crusting eruptions. No seasonality had been noted and the condition had progressively worsened. The crusting, initially truncal, had later involved face, feet and ventrum. Previous treatment consisted of chlorexidine/miconazole shampoo twice weekly, short lasting dexamethasone injections (0.2 mg/kg, the last given 20 days prior to referral), cefalexin, clindamycin, marbofloxacin (1.3 mg/kg SID given from five days prior to presentation) and daily applications of a polymyxin-B/miconazole/prednisolone product; only the latter had provided some improvement. The dog was otherwise well in herself.

Vaccination and worming were regular; no ectoparasiticidal treatment. There were no other in-contact animals and the owners had not developed skin lesions. The lady owner was a nurse and worked in a hospital.

Physical examination

The dog was overweight and a 3/6 systolic heart murmur was noted. General examination was otherwise unremarkable. Dermatological examination revealed patchy alopecia, erythematous annular lesions with crusting eruptions (figure 1) with mainly truncal and neck distribution. Focal alopecia and erythema were noted on all limbs, along with crusting, involving also the perianal skin, the interdigital areas and the claw-folds. Crusting and alopecia were noted on the peri-orbital areas and dorsal muzzle (figure 2), axillae, abdomen, inner aspects of the thighs and margins of both pinnae. The perivulvar skin was folded, lichenified and moist, with erythematous papules, thick yellowish crusts and pustules (figure 3). Generally the coat was matted in yellowish crusts (figure 4).

What are your differential diagnoses?

Differential diagnoses

Crusting eruptions and pruritus:

- Scabies
- Sterile pustular disease (pemphigus foliaceus, drug reaction, other sterile neutrophilic or eosinophilic pustular disorders)
- Bacterial pyoderma
- Allergic skin diseases with infections

Considerations:

Sterile pustular diseases can be accompanied by pruritus in presence of infections; bacterial pyoderma was considered as secondary to immune-mediated condition, to an endocrine disorders (including hypothyroidism) or to an allergy. The presence of resistant bacteria was also considered.

Patchy alopecia and erythema could be caused by the above conditions or also by:

- Demodicosis
- Dermatophytosis
- Epitheliotropic lymphoma

Heart murmur:

- Degenerative mitral valve disease (most likely)
- Congenital mitral valve malformation
- Bacterial endocardiosis

What tests would you perform?

Laboratory tests

- Multiple hair plucks, skin scrapes and coat brushing – unremarkable
- Cytology from the crusts on trunk and claw beds – neutrophils, acantholytic cells
- Cytology from pustules on the perivulvar area –neutrophils with intracellular coccoid bacteria, acantholytic cells
- Fungal culture of hair and crusts – no pathogens
- Bacteriology culture and sensitivity from perivulvar area – heavy, mixed growth of *Proteus spp*, *Staphylococcus aureus* and *Enterococcus faecalis* sensitive to enrofloxacin, amoxicillin/clavulanate acid and potentiated sulphonamides
- Haematology – slight anaemia
- Serum biochemistry – slightly decreased calcium, urea and creatinine; moderately increased ALP
- T4 and TSH – within normal limits

History, clinical findings and test results were suggestive of pemphigus foliaceus, complicated by a bacterial infection on the perivulvar area. Sarcoptic mange could not be excluded. Histopathology was indicated.

Dilemma: *skin biopsies could not be taken straight away. What would you do in the interim?*

Enrofloxacin (5mg/kg SID) and selamectin (6mg/Kg once monthly) were started.

Day 7.

Under local anaesthesia (lignocaine 1ml at each site), three 6mm punch biopses were taken from the crusted areas on the trunk. Results pending, prednisolone at anti-inflammatory dose for pruritus relief (0.5 mg/Kg SID) was prescribed.

Histopathology – morphological diagnosis of superficial pustular dermatitis with acanthocytes (figure 5). Atrophic dermatosis and cyclical arrest.

Diagnosis and prognosis

Pemphigus foliaceus. Prognosis variable but usually guarded, due to lack of response to treatment or unacceptable side-effects of medications used.

Dilemma: *what would be the cause for the atrophic dermatosis?*

Would you treat it?

Atrophyc dermatosis possibly due to prior topical and systemic glucocorticoid treatment. Ischemic dermatopathy?

Treatment plan

Dilemma: *in view of cardiac problem, how would you treat the skin disease?*

Prednisolone 1 mg/kg SID. A low dose was chosen to avoid onset of cardiac decompensation.

Day 14.

Follow up call. Owners updated on diagnosis and new dose of prednisolone.

Re-examinations and final outcome

No changes in treatment unless reported.

Day 20.

Hair re-growth, decreased crusting, no pruritus, no pustules; vulvar folds moist with cytology showing cocci, rods and acantholytic cells.

Topical treatment (once daily on perivulvar area) with an antimicrobial, moisturizing and soothing spray.

Day 50.

Follow up call. Crusting decreased, marked polyuria/polydipsia.

Dilemma: *would would you do?*

Urinalysis (by cystocentesis) revealed a specific gravity of 1.040 and 3+ proteinuria; urine culture negative for bacterial growth. Urine protein to creatinine ratio reased, likely to be referable to steroid therapy rather than a primary nephropathy.

Prednisolone decreased to 0.8 mg/kg SID, antibiotics for two more weeks.

Day 78.

Muzzle (figure 6), limbs (figure 7) and abdomen showed no lesions. Patchy alopecia with mild crusting on trunk. Increased respiratory rate, pendoulus abdomen (figure 8), mild exercise intolerance.

What would be the cause of the reported clinical signs?

For the increased respiratory rate and distended abdomen decompensated heart failure and glucocorticoid side-effects were considered. Pulmonary thromboembolism was also considered, albeit less likely.

Dilemma: *would you investigate further and how would you modify the treatment?*

Thoracic radiographs showed left sided compensated cardiomegaly (figure 9) ruling out CHF as cause for the tachypnoea. An echo-cardio (which could have been helpful in determining if PHT is present or not) was offered but declined.

Bloodwork revealed acute inflammatory leucogram with regenerative left shift, mild non regenerative anemia, slightly decreased urea and creatinine, elevated ALP.

Prednisolone replaced by dexamethasone (0.05 mg/kg SID) and azathioprine (2mg/kg SID) added.

Day 98.

Reduced extent and severity of the skin lesions, livelier demeanour; polyuria/polydipsia decreased.

Mild neutrophilia and lymphopenia, decreased chloride and creatinine, hypercholesterolemia, markedly elevated ALT and ALP.

Dilemma: *would you modify the treatment?*

Dexamethasone decreased to 0.05 mg/kg EOD and azathioprine decreased to 2mg/kg EOD.

Day 112.

Follow up call. Bloodwork (referring practice): mild lymphopenia, persistently increased cholesterol. Dexamethasone reduced to 0.05 mg/kg ETD.

Day 113.

Residual alopecia over shoulders, improved demenour.

Day 141.

Weight 14.9 kg, polydipsia and polyphagia decreased. Mild alopecia and focal crusting over shoulders. Marked hypercholesterolaemia, moderate hypertriglyceridaemia, raised ALP and ALT.

Dilemma: *would you do any other test to monitor treatment side effects?*

Abdominal ultrasonography revealed multiple, tiny, hyperechoic foci in the liver and echogenic sediment in the gall bladder; the former finding was interpreted as bile duct calcification, attributed to chronic inflammation or steroid therapy.

Dexamethasone reduced to 0.025mg/kg ETD.

A low calorie diet to treat obesity and hypertriglyceridaemia was started.

Day 167.

Demeanour improved and dog keener to exercise.

Patchy alopecia only.

Day 189.

Weight 13.6 kg. Alopecia reduced.

Mils lymphopenia, increased lipase, mildly elevated ALP, decreased creatinine. Dexamethasone discontinued.

Day 202.

Follow up call. Dog very active, residual alopecia.

Day 227.

Weight 12.9 kg. Alopecia over the the shoulders with mild erythema (figure 10). Hair re-growth and absence of lesions on perivulvar skin (figure 11). Repeated haematology and blood biochemistry performed at referring practice showed unremarkable results.

Day 275.

Weight 12.6 Kg. Hair re-growth.

Day 351.

Mild alopecia on shoulders. Hair re-growth evident on rest of body (figure 12). Haematology and blood biochemistry performed at referring practice showed unremarkable results.

Discussion

Pemphigus foliaceus (PF) is an uncommon skin disease in dogs. However, it is perhaps the most common auto-immune dermatosis in dogs and cats (1).

The breed of this dog is not reported as at high risk for developing PF (2); the age at onset is within the range reported in three large case series (1, 3, 4). This dog showed typical clinical signs consisting in crusting and pustules, usually appearing on the head (nasal planum, pinnae, and periocular areas) and on the trunk. Most affected sites are the face, and trunk (4), but in this case the perivulvar skin was also markedly affected. This dog was pruritic, and this can be seen in one fourth to one half of dogs with PF (3). Histopathology is essential for diagnosis. Therapy of generalised PF, as presented in this case, usually requires life-long systemic immuno-suppressive treatment. Oral glucocorticoids alone are reported to be effective in 30-40% of cases (1, 3). This patient initially showed only a mild improvement with glucocorticoids alone. A higher dose may have given better results but to avoid onset of cardiac decompensation and due to the development of hypercholesterolemia and hypertriglyceridemia, a switch to an equivalent dose of dexamethasone was preferred. This was however gradually withdrawn due to the persistent hypercholesterolemia and hypertriglyceridemia. As no abnormalities in the lipid status were noted before starting the treatment, the likely cause of these was considered the lipolysis induced by chronic steroid therapy (5) and this was confirmed by normalization of the parameters at discontinuation of the glucocorticoids. When glucocorticoids are contraindicated, cannot be reduced to safe life-long levels or in refractory cases, cytotoxic drugs have been proposed as adjunctive treatment (6). Although in one study (4) azathioprine did not lead to a significant difference in the time needed to achieve remission when compared to the use of glucocorticoids alone, this dog was succesfully controlled by ongoing treatment with azathioprine. It is possible to speculate that the increased liver enzymes, attributed to the corticosteroid activity, could also have been caused by azathioprine-induced hepatitis; a small open trial (7) reported the use of azathioprine monotherapy in 12 dogs with atopic dermatitis. Serum levels of ALP and ALT rose above normal in 10 of 12 dogs (83%). Three dogs developed clinical signs of hepatitis, which resolved once azathioprine was withdrawn. In other dogs the high liver enzyme activity was not associated with clinical signs of liver disease. In a more recent retrospective study (8) of a total of 34 dogs treated with azathioprine, with a median onset of 14 days, 5 dogs (15%) developed laboratory evidence of hepatotoxicity, with one dog developing also clinical signs suggestive of hepatitis. In three of the dogs with hepatotoxicity, reducing the azathioprine dose by 50% led to liver enzyme stabilization or reduction. In our patient a low dose maintenance therapy resulted in a remission of almost all skin lesions, normalization of the liver enzymes and no recurrence of the hypercholesterolemia and hypertriglyceridaemia.

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Figure 1. Thick yellow crusts associated with circular and annular areas of erythema.

Figure 2. Crusting and alopecia on the peri-orbital areas and dorsal muzzle.

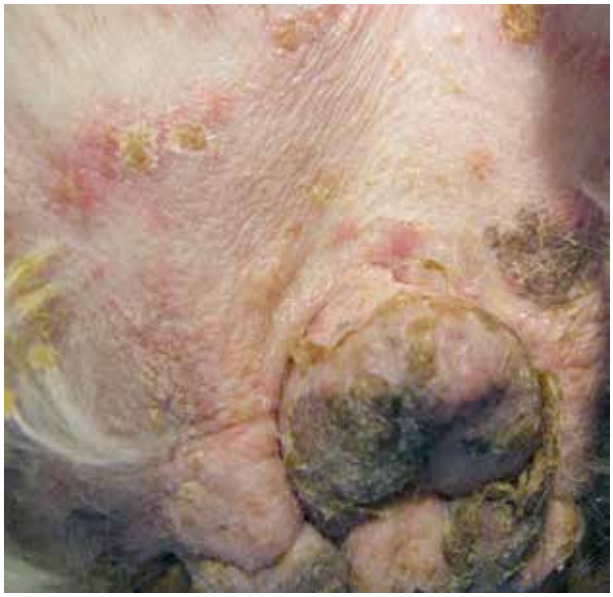

Figure 3. Erythematous papules, crusts and pustules affecting moist and lichenified perivulavr skin.

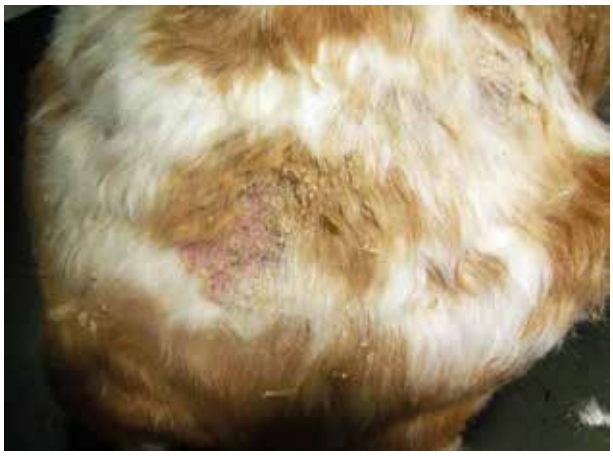

Figure 4. Coat matted in yellowish crusts. Note the alopecic patch.

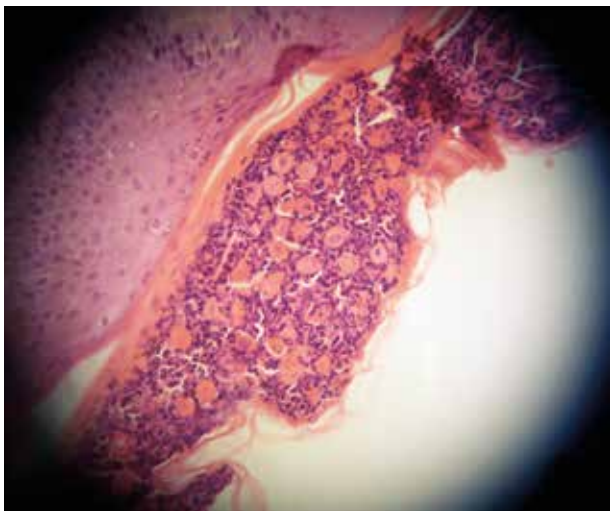

Figure 5. Histopathology: intracorneal pustule containing large numbers of neutrophils and acantholytic keratinocytes. Haematoxylin and eosin.

Figure 6. Day 78: absence of lesions on the muzzle.

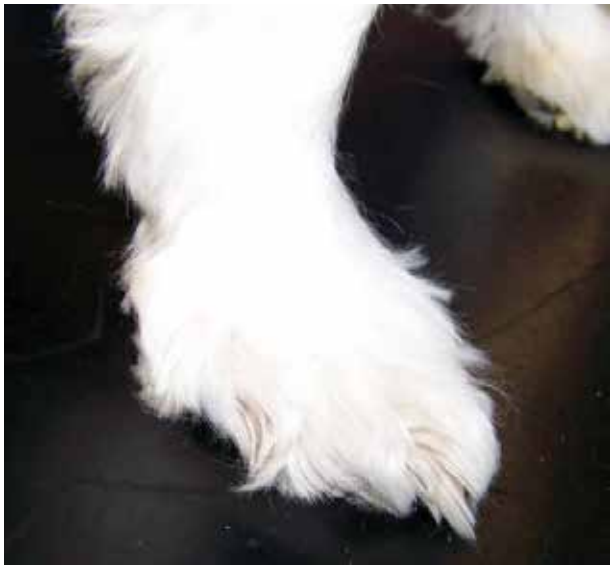

Figure 7. Day 78: right fore foot: absence of lesions.

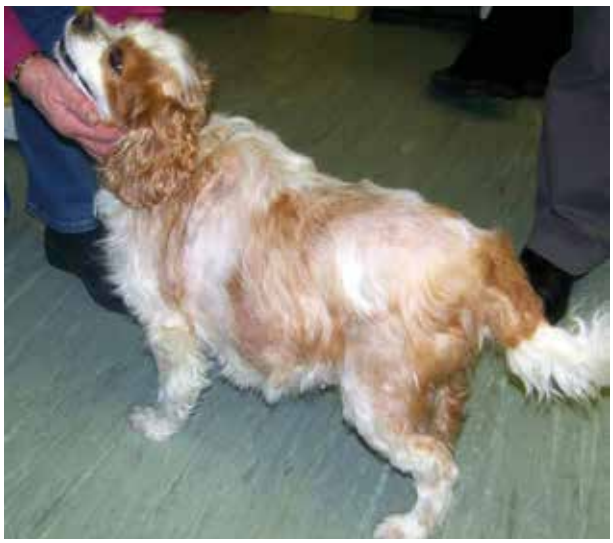

Figure 8. Day 78: pendoulus abdomen and alopecia over the trunk.

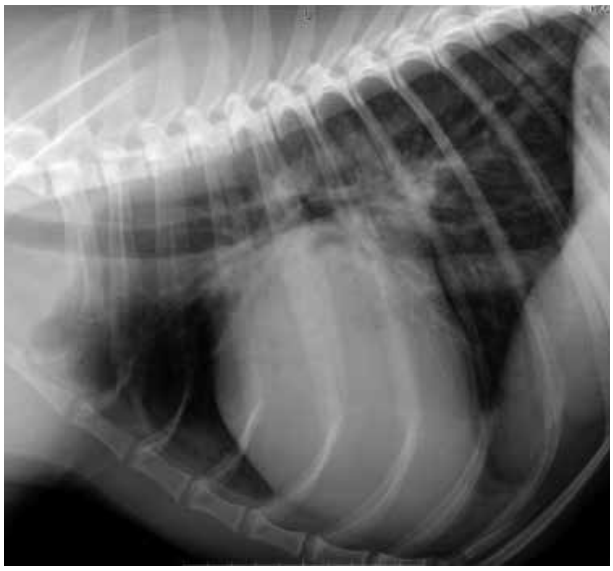

Figure 9. Day 78: Left sided cardiomegaly.

Figure 10. Day 227: alopecia and mild erythema over the shoulders.

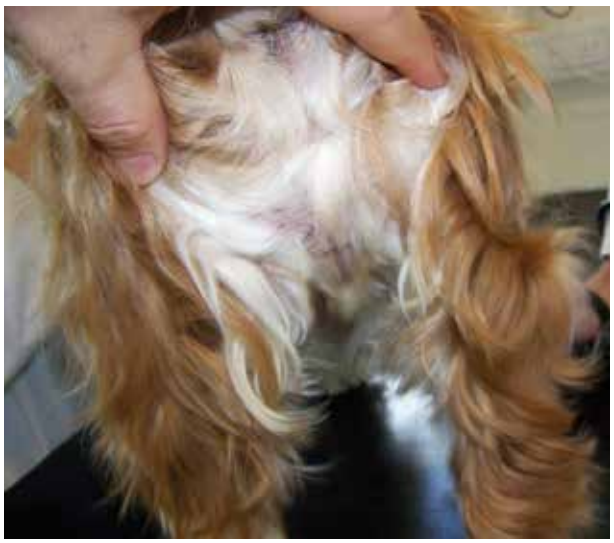

Figure 11. Day 227: hair re-growth and absence of lesions on perivulvar skin.

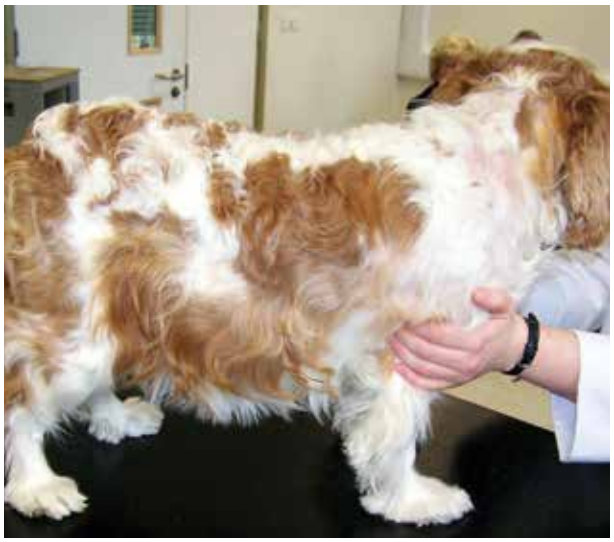

Figure 12. Day 351: mild alopecia on shoulders. Hair re-growth evident on rest of body.

Endoscopy

Vassiliki Stathopoulou (GR)

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I have qualified from Aristotle University of Thessaloniki in 2000 and have been working since as an internist and later as head of the Endoscopy and Gastroenterology Department in a referral clinic in Athens (www.plakentiavet.gr). My clinical interests include canine and feline gastroenterology/hepatology, clinical nutrition as well as diagnostic and interventional endoscopy in companion animals. I have participated in several advanced postgraduate intensive courses in Veterinary Endoscopy (University of Giessen, ESAVS, Improve International) and hold a GP Certificate in Small animal Internal Medicine (2009), a GP Certificate in Endoscopy and Endosurgery (2010) from the European School of Veterinary Postgraduate Studies and a PgC in Small Animal Medicine (2015) from Harper Adams University. I am a member of the Veterinary Endoscopy Society (VES), the Comparative Gastroenterology Company (CGS) and the European Society of Comparative Gastroenterology (ESCG). My passion is sharing knowledge and I've been an invited speaker every year at the annual Greek congress as well as in various seminars, webinars and a trainer in postgraduate endoscopy courses in Greece. I have served as the President of the Organizing Committee of the 8th Greek forum, and during the last 5 years I have always served as a member of the scientific committee. I was honored to be a co-author at Dr. Rallis (Professor of Internal Medicine at AUTH University, Greece) book on Pancreatic Diseases and my chapters were focused on endocrine and exocrine pancreatic neoplasms.

Esophageal strictures in cats-the “whys” and the “hows”

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DEFINITION

Esophageal stricture is a pathologic narrowing of the esophageal lumen as a result of the production of fibrous connective tissue or masses.[1]

PATHOPHYSIOLOGY

Benign esophageal strictures occur on grounds of severe esophagitis, where inflammation disrupts the esophageal mucosa and exposes the submucosa and the muscular layers.[1,2] Malignant strictures from neoplastic proliferating tissue occur rarely in cats.

CAUSES

1. **Gastroesophageal reflux (GOR) during general anesthesia** is a common cause for stricture formation in cats.[3]

- In a series of seven cats with benign esophageal stricture, recent anesthesia for ovariohysterectomy was in reported in five cases. Decreased Lower Esophageal Sphincter (LES) tone as a result of many preanesthetic and induction agents may lead to GOR and subsequent direct acid injury to the esophageal mucosa.[4]
- Head down position during the operation and intraabdominal surgical manipulations are other predisposing factors.
- In one study, the use of laryngeal mask airway device in 40 cats, 12-15 weeks of age, in which both induction and maintenance of anesthesia was obtained by isoflurane, resulted in GOR in 50% of the cat population, compared to 22% of cases with endotracheal intubation.[5]
- Clinical signs appear up to 21 days post the anaesthetic episode. Esophagitis due to GOR and subsequent stricture formation typically occur in the segment of the thoracic oesophagus, located 5-10 cm cranial to the LES.
- Barret esophagus which is a major complication of severe and persistent gastroesophageal reflux disease in humans occurs rarely in cats. Three cats were reported to have Barrett-like esophagus, in which two cases were associated with hiatal hernia and one with cardiac failure.[6]

2. **Drug-induced esophagitis**

- Drug induced oesophagitis (DO) is a well-documented pathological entity in people, with over seventy drugs implicated in the aetiopathogenesis, although no strictures have been reported.[7] Antimicrobials have been implicated in 50% of published cases, in which any other anatomical or functional abnormality of the oesophagus had been excluded.
- The incidence of DO and subsequent benign oesophageal stricture (BOS) formation in cats is not known. Several published reports implicate oxytetracycline, doxycycline, clindamycin in cats in contrast to dogs, for which no confirmation is evident in literature.[3,8,9,10,11] Prolonged contact of the oesophageal mucosa to a drug and its direct corrosive effect are the main causes of DO and BOS, whereas parenteral administration of the same drugs does not have the same result. The intrinsic tissue resistance of oesophageal mucosa to the offending drugs reduces the risk of oesophagitis. Oesophageal mucus bicarbonates, multiple layers of oesophageal epithelium, strong cell to cell connections, intracellular lipids, glycoproteins, mucosal perfusion, prostaglandins and leukotriene metabolism products cintribute to tissue resistance.[12]
- Doxycyclin hydrochloride licensed for companion animals in the form of tablets (Ronaxan, Merial) creates an acidic solution in the neutral, under normal circumstances, oesophageal PH and its corrosive, ulcer-forming effect in the feline oesophageal mucosa has been experimentally documented.[8] Furthermore, doxycyclin accumulationin the basal membrane of the oesophageal squamus epithelium has been noted, revealing another potential side effect of this drug.[13]
- Clindamycin does not alter oesophageal PH and causes minimal mucosal irritation. Its aetiopathogenetic mechanism on BOS is associated with increased transit time through the oesophageal lumen and increased duration of contact with the oesophageal mucosa.[7] The pharmaceutical formulation (capsule), dry swallowing, oesophageal hypomotility due to systemic disorders or dehydration at the time of administration are intrinsic factors in the aetiopathogenesis of side effects attributed to this drug.[9]

- In people there are reports of DO associated with amoxicillin/clavulanic acid with an aetiopathogenetic mechanismsimilar to that of clindamycin. There is only one report in cat of suspected amoxicillin/clavulanic acid associated oesophageal injury in cats.[14]
- Studies have indicated that dry swallowing of capsules or tablets in cats can result in retention of the drug in cervical oesophagus (88%) or the oropharynx (8%) for a duration of 30-240 seconds.[15] In a different study more than 50% of capsules administered to healthy cats were trapped in the cranial thoracic oesophagus.[10] A comperative study demonstrated that flavor-coated capsules/tablet administration with a pill gun (FlavoRox Pill Glide, FLAVORx, Columbia, Md) or the offering of treats with drug pockets (Greenies Pill Pockets, Nutro Products, Franklin Tenn) can ensure an average oesophageal transit time of less than 60 seconds.[1]

3. **Esophageal foreign bodies**

- Esophageal foreign bodies (FB) are less commonly found in the esophagus of cats compaired to other sites of the gastrointestinal tract. Reported FB are strings, needles, fish hooks, bones and trichobezoars that can be lodged in the esophagus during vomiting.[1,16] Common locations that the FB may be embedded include the thoracic inlet, the heart base, the esophageal hiatus in the diaphragm.[17] Chronic esophageal FB have also been reported in cats with intermittent regurgitation, hypersalivation, dysphagia and progressive weight loss.[18]

4. **Vascular ring anomaly**

- Vascular ring anomalies are congenital malformations of the great vessels of the heart that entrap the esophagus and the trachea. The most commonly reported anomaly is persistent right aortic arch, where circular extraluminal compression of the esophagus by the right fourth aortic arch leads to physical obstruction of the esophagus and the trachea.[19] A double aortic arch has been described in a Siamese cat.[20]

5. **Prolonged vomiting of gastric contents (hiatal hernia both acquired and congenital, chronic gastritis, IBD, hyperthyroidism, megaesophagus, dysautonomia, metabolic disorders, triaditis)[2]**

- All causes of chronic vomiting may lead to severe esophagitis and esophageal strictures.

6. **Esophageal neoplasia**

- Squamous cell carcinoma is the most common primary esophageal tumor in cats and is often located in the caudal two thirds of the esophageal lumen.[21] It typically affects middle aged to older cats. Mucosal biopsies are difficult to obtain. Brush cytology may be diagnostic. They respond poorly to chemotherapy or radiation. Palliative esophageal stenting could short term alleviate the symptoms.

CLINICAL SIGNS

- Progressive regurgitation
- Dysphagia
- Salivation and ptyalism
- Odynophagia and neck extension
- Liquid meals better tolerated than solid meals
- Aspiration pneumonia-fever
- Weight loss, malnutrition.

DIAGNOSIS

- Standard lateral radiographs rarely reveal the stricture site, especially in multiple strictures[22], thus necessitating barium series and endoscopy in order to confirm the diagnosis.[23]
- Endoscopy may also detect mucosal erythema, erosion, hemorrhage. Strictures appear as a ring of white fibrous tissue that reduces the diameter of the esophageal lumen.[24]

TREATMENT

- Treatment of esophageal strictures is achieved by surgery, boougienage, dilation balloons, the distal tip of the endoscope and stent placement. [1,3,12]
- A bougie is a narrow, long, oblong mechanical dilator available in different sizes (from 9 to 12 mm used in cats) that is gently proceeded through the narrowing, over a guide wire. The initial size of the selected bougie is approximately at the same size of the stricture and progressively bougies of increasing diameter are used. In one retrospective case series of eight cats treated with bougienage, the median number of procedures was 4,5 and it was sucessful in lysis of the stricture in 75% of cases.[25]
- Restoration of oesophageal lumen diameter by balloon catheter dilation is the method of choice, as radially directed rather than shearing axial forces are exerted on the oesophageal mucosa, minimizing theoretically the risk of oesophageal rupture. Although endoscopist feel that this is a safer technique than bougienage, there are no data in literature to support this assumption. The balloon can be placed through the biopsy channel of the endoscope or along side but the procedure will always take place under endoscopic visualisation and general anesthesia. There is a variety of balloon sizes available.In one stydy the size was

selected so that the inflated diameter was 4mm longer than the stricture diameter.[26] The balloon is inserted to the stricture and is inflated until it reaches the manufacturer's rated pressure. It stays inflated for 1-2 minutes until the stricture dilates sufficiently. Sequentially larger balloons are useduntil the mucosal tearing and bleeding suggests lysis of the stricture.

- **Cuffed endotracheal tubes should not be used to substitute balloon catheters.**
- Potential complications during the dilation procedure include esophageal rupture mainly in cats, pneumothorax, pneumomediastinum, mild tissue injury and oesophageal wall bleeding.[23,24,25]
- The total number of dilation sessions can vary and it depends on the initial size of the stricture, the "aggressiveness" of the dilation procedure manipulations, the tissue responses of the affected animal and the chronicity of stricture.[23] The average sessions required in cats range from 4-6 [11]. A higher number of sessions than what is reported in the literature as maximum (8-11 sessions) [1,9,10,23] should be considered in the absence of alternative techniques such as stent placement.[14]
- Dilation intervals range from every 3 days to once a week to decrease the stricture reformation.
- Topical injection at the site of the dilated stricture of triamcinolone in a four-quadrant pattern might reduce the frequency of restricturing.[2]
- Intralesional application of mitomycin-C serves the same purpose.
- Patients refractory or unresponsive to balloon dilation may benefit from stent placement. Biodegradable self-expanding stents with or without drug elution (paclitaxel) may have successful results in cats.[27] Possible complication is stent migration.
- Future novel treatments will be based on regenerative medicine in which extracellular matrix scaffolds and autologous muscle tissue will be used to prevent tissue reformation.[28]
- Following dilation therapeutic regime for esophagitis is administered, comprising of omeprazole, sucralfate suspension, cisapride to increase LES tone and enhance gastric emptying and a broad -spectrum antibiotic. the use of systemic corticosteroids is controversial. To achieve analgesia 2% lidocaine gel is placed at the site of the dilated stricture with a urinary catheter under endoscopic guidance.
- Surgical resection of the esophagus and anastomosis is only performed as a last resort, due to high failure rates.

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Chronic vomiting in dogs: case based approach

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DEFINITION

Emesis is defined as a retrograde, active and forceful ejection of food or fluid from the stomach or the duodenum. Persistent vomiting lasting longer than one week or occurring intermittently for several days or weeks with poor response to symptomatic treatment is defined as chronic vomiting.[1]

ETIOLOGY/PATHOPHYSIOLOGY

Vomiting is initiated via the vomiting center, located within the medulla oblongata of the brainstem. Its activation can derive from various stimuli receiving input from humoral or neural pathways. The vomiting reflex includes 4 main components : (a) visceral receptors within the gastrointestinal (GI) tract (b) vagal and sympathetic afferent neurons (c) the chemoreceptor trigger zone (CRTZ) and (d) the vomiting center. The humoral pathway is mediated via activation of the CRTZ, which is located within the area postrema on the floor of the fourth ventricle and is affected by blood born toxins (uremia, endotoxemia, ammonia, cytotoxic agents) or drugs (digoxin, apomorphine). Furthermore the neural pathway is mediated via activation of the emetic center and is affected by stimulation of various organ and tissue receptors of the gastrointestinal tract, sensitive to strech, osmotic and chemical stimuli and pain, as well as central nervous system disease. Finally, vomiting induced by the vestibular apparatus and the cerebrum is believed to travel through the CRTZ to the vomiting center.[1,2,3,4]

Prior to the initial diagnostic evaluation, it is imperative to differentiate between true vomiting and regurgitation. Regurgitation is the passive retrograde expulsion of food from the esophagus. Vomiting is associated with clinical signs of nausea (ptyalism, retching, lip licking), violent abdominal contractions and the presence of yellow gastric fluids, digested blood or bile in the vomitus.[5,6]

SIGNALMENT/HISTORY

- Young animals are more likely to ingest foreign bodies or have an infectious disease (e.g parvoviral or distemper viral gastroenteritis)
- Breed predispositions should be taken under account: e.g brachycephalic breeds are prone to pyloric outflow obstruction due to hypertrophic gastropathy, Yorkshires are predisposed to intestinal lymphagiectasia, Rottweilers exhibit a higher incidence of eosinophilic IBD etc.[5,7]
- History should elicit the duration, frequency and time of vomiting episodes, as well as the relationship of vomiting to food or water consumption and its content. Vomiting episodes early in the morning in a fasted animal are indicative of gastroesophageal reflux or bilious vomiting syndrome. Vomiting of indigested or partially digested food 8 or more hours after the meal suggest gastric motility disorders or obstruction. Concurrent diarrhea and profound weight loss are compatible with intestinal disease. Signs of weakness, depression, polyuria/polydipsia, jaundice are related to systemic, metabolic or endocrine disorders as well as severe inflammatory process of the upper gastrointestinal tract. Fecal odor in the vomitus has been reported in jejunoileal disorder.[5,6,7,8]
- Hematemesis and melena implies gastric, duodenal ulceration, liver disease or coagulopathies.
- Access to toxins, drugs (e.g NSAIDs), dietary indiscretion.

PHYSICAL EXAMINATION

- Inspection of the oral cavity and pharyngeal structures (e.g ulcers in uremia, icteric mucus membranes in liver disease, pale membranes in anemia and gastric hemorrhage, sublingual foreign bodies)
- Abdominal palpation may reveal abdominal distention, masses, kidney size and shape, thickened intestinal loops, pain(e.g peritonitis,pancreatitis), liver and urinary bladder size.
- Cardiac auscultation may detect bradycardia or other disturbances that could be a sign of septic shock, adrenocortical insufficiency or other metabolic disease.
- Severe weight loss and poor hair coat indicate chronic malabsorption/maldigestion disorders
- Peripheral lymphadenopathy could be suggestive of a neoplastic or an inflammatory process etc.
- Rectal examination may provide evidence of melena, hematochezia, diarrhea, prostatomegaly etc.[1,5,6,7,8]

DIFFERENTIAL DIAGNOSIS of chronic vomiting[9,10]

Extraintestinal diseases

- Renal disease
- Hepatobiliary disease
- Pancreatitis
- Hypoadrenocorticism
- Diabetic ketoacidosis
- Peritonitis
- Any disease eliciting pain in the abdominal cavity
- Pyometra
- Electrolyte abnormalities: hypo/hyperkalemia, hypercalcemia, hyponatremia
- Toxicity
- Drug induced (e.g NSAIDs, chemotherapeutics etc)
- Neurologic causes (cerebral edema, CNS tumors, vestibular disease, meningoencephalitis)
- Neoplasia (pancreatic adenocarcinoma, gastrinoma, systemic mastocytosis)

Gastrointestinal diseases

- Infectious diseases (parvo virus, *Helicobacter spp*, Histoplasmosis)
- Inflammatory Bowel disease (lymphoplasmacytic, eosinophilic, granoulomatous)
- Obstructive GI disease (foreign bodies, intussusception, anatomical or functional pyloric stenosis)
- Food intolerance/sensitivity
- Neoplastic disease (e.g GI Lymphoma, adenocarcinoma)

DIAGNOSTIC APPROACH[5-10]

1. Hematology/Biochemistry/Urinalysis/Fecal parasitologic examination

- Anemia may suggest chronic GI bleeding, concurrent metabolic disease
- Peripheral eosinophilia can occur in GI parasitism, systemic mast cell disease, eosinophilic gastroenteritis, hypoadrenocorticism.
- Leucocytocis has been reported in IBD, chronic pancreatitis, cholocystitis, cholangiohepatitis, prostatic inflammation etc. whereas leukopenia may be detected in early stages of viral gastroenteritis or late stages of septic inflammatory processes.
- Azotemia and hyperphosphatemia suggest chronic renal failure
- Hyperkalemia and hyponatremia in a vomiting patient suggest hypoadrenocorticism, oliguric/anuric renal failure, occasionally enteritis caused by trichuris or salmonella.
- Increased liver enzyme activity, low urea nitrogen concentration, hypoglycemia, hypoalbuminemia, hyperbilirubinemia are consistent with hepatic disease.
- Hypoalbuminemia, hypoglobulinemia, hypomagnesemia indicate protein losing enteropathy (severe IBD, lymphoma, lymphagiectasia, histoplasmosis)
- Hypochoremic metabolic alkalosis combined with hypokalemia occurs in gastric outflow obstruction.
- Hypocholesterolemia suggests severe small intestinal disease or hypoadrenocorticism
- Urinalysis is useful in detecting primary renal disease, DKA.
- Paradoxical aciduria in an hypokalemic, hypochloremic, alkalotic patient suggests gastric outflow obstruction.

2. Further tests

- ACTH stimulation test to confirm hypoadrenocorticism.
- Canine pancreatic lipase immunoreactivity to rule out pancreatitis
- Bile acids concentration pre and postprandial to establish the diagnosis of hepatic dysfunction.

3. Imaging [11,12]

- Lateral and ventrodorsal radiographs of the abdomen may identify radiodense foreign body, gastric outflow or intestinal obstruction with partial or total ileus.
- They allow evaluation of the liver size, the presence/absence of ascites, displacement of abdominal organs.
- Survey thoracic radiographs may detect neoplastic lesions, megaesophagus, esophageal foreign bodies.
- Contrast barium studies can be used to diagnose delayed gastric emptying, motility disorders, foreign bodies, sliding hernias etc.
- Abdominal ultrasonography may evaluate the gastric and intestinal wall layering, the size of the mesenteric lymph nodes, abdominal masses and other parenchymal abnormalities of the liver, pancreas, kidneys, gallbladder.
- CT and MRI may help in the localization of lesions in parenchymal organs.

4. Upper GI endoscopy[13]

- Upper GI endoscopy allows direct viualisation of the gastric and intestinal mucosa, evaluation of the rugal folds, ulcers, erosions, masses, friability, granularity, mucosal edema, the presence of foreign bodies, dilated lacteals in small intestinal lymphagiectasia, identification of pyloric stenosis.
- Biopsies are retrieved from the pylorus, body, incisura angularis, the fundus as well as from the small intestine even if macroscopically the mucosa seems normal.

5. Laparoscopy/laparotomy

- To acquire full thickness biopsies from the small intestine.
- For surgical interventions (eg intussuseption)

TREATMENT

1. Diet

- Small frequent meals of a low fat highly digestible diet. Prolonged fasting should be avoided and feeding should start as soon as the vomiting episodes seize and the animal can tolerate oral feeding.
- To assist feeding in an anorectic patient esophagostomy, gastrostomy and enterostomy tubes should be placed.
- In patients with IBD or food allergy an elimination diet (novel protein, hydrolyzed) should be initiated.

2. Fluids

- Crystalloids are used to restore volume, replace deficits and correct electrolyte disturbances.
- If metabolic acidosis is confirmed, lactate Ringer's solution is indicated.
- In hypokalemic patients, potassium supplementation is required; 20 mEq of KCL/lit of fluid can be safely added for replacement and maintenace.
- Blood transfusion in patients with ongoing GI bleeding.
- Human recombinant albumins to stabilize hypoalbuminemic patients.

3. Antiemetic agents[14,15]

- **a_2-adrenergic antagonists (prochlorperazine, chlorpromazine, Yohimbine, atipamezole):** their site of action is in the CRTZ and the emetic center. They are very potent but containdicated in dehydrated or hypotensive patients without previous fluid support and should be avoided in patients that have exhibited seizures.
- **D2-dopaminergic antagonists (metoclopramide, domperidone,trimethobenzamine, prochlorperazine, chlorpromazine):** their site of action is in the CRTZ and the GI smooth muscles. Metoclopramide blocks receptors in the CRTZ but also has an effect on the viscera, increases the lower esophageal sphincter tone, decreases pyloric sphincter tone, increases gastric and duodenal amplitude and contraction. Metoclopramide is a weak antagonist of 5-HT_3 receptors and does not seem to be effective in chemotherapy-induced emesis. Patients receiving metoclopramide or domperidone may exhibit extrapyramidal signs as a side effect.The prokinetic activity of metoclopramide seems to be limited to the liquid phase of gastric emptying as a study showed no effect on gastric emptying rate of digested solids. This category of drugs appears to be the less efficacious in cats as the D2 dopaminergic and the a_2 adrenergic receptors are not well developed in this species.
- **H_1- histaminergic antagonists (diphenhydramine, dimenhydrinate, prochlorperazine,chlorpromazine):** their site of action is in the CRTZ and the emetic center.
- **M_1-cholinergic antagonists (pirenzepine, scopolamine, aminopentamide, prochlorperazine, chlorpromazine):** their site of action is in the vestibular apparatus and the CRTZ.
- **5-HT_3 serotonergic antagonists (ondansetron, dolasetron, granisetron, tropisetron):** their site of action is in the CRTZ and the vagal afferent neurons. Potent antiemetics for the chemotherapy- induced emesis. Sedation and head shaking are possible side effects of their use.
- **5- HT_4 serotonergic agonists (cisapride):** its site of action is the myenteric neurons. It promotes release of acetylcholine in the intestinal wall which results in prokinetic activity. It is more potent than metoclopramide in stimulating gastric emptying and increasing the lower oesophageal sphincter pressure. It stimulates oesophageal peristalsis in cats where the distal oesophagus is smooth muscle. The canine oesophagus is striated muscle, thus inhibiting the effect of cisapride on the oesophageal function of this species. It has no central effect, therefore it is not efficacious on nausea or emesis induced by uremia or motion sickness. Reported side effects are abdominal pain, diarrhea and cardiac arrythmia (humans).
- **ENKμ,δ- enkephalinergic (butorphanol):** Its site of action is in the CRTZ.
- **NK_1 neurokinin antagonists (maropitant):** Its site of action is in the CRTZ and the emetic center. It inhibits emesis through both humoral and neural pathways therefore it is effective against both central and peripheral causes of vomiting. It should be used with caution in animals with liver and heart disease.

4. Antisecretory agents[16, 17, 18]

- **Antacids (aluminum hydroxide, magnesium hydroxide, calcium carbonate, sodium bicarbonate).** They react chemically with gastric acid to increase gastric PH.They bind to bile acids, decrease pepsin activity in the stomach and stimulate the secretion of endogenous prostaglandins. The level of Acid Neutralization Capacity that they provide for ulcer healing has never been clearly established. Frequent dosage and poor

palatability make antacids an unattractive option for their use in dogs and cats. They may interfere with the absorption of tetracycline, digoxin, prednisolone, cimetidine, ranitidine.

- **Prostaglandin analogues (misoprostol).** Gastric prostaglandins play a significant role in increasing mucosal blood flow, mucus production and bicarbonate secretion. It has both prophylactic and therapeutic role in the prevention and treatment of gastrointestinal ulceration attributed to the use of NSAIDs. Its use is contraindicated in dogs receiving gentamycin or other nephrotoxic drugs and in pregnant animals as it can cause abortion. The incidence of dose depended diarrhea has been reported.
- **Chemical diffusion barriers (bismuth, sucralfate).** Sucralfate has little effect on gastric acidity and is mainly a gastromucosal protectant. Sucrose octasulfate reacts in the stomach with hydrochloric acid to form a paste-like complex that has greater affinity for damaged tissue than normal mucosa. It also stimulates prostaglandin release, increases mucus production and bicarbonate secretion. The use of liquid sucralfate is preferable in acid-induced esophagitis in cats and it has been reported that it has outperformed a PGE_1 analogue and cimetidine. Sucralfate binds to fluoroquinolones and tetracyclines and decreases their absorption. Digoxin, theophylline, phenytoin should be given orally at least 2 hours prior sucralfate.
- **H_2- Histamine antagonists (cimetidine, ranitidine, famotidine, nizatidine).** They competitively inhibit acid secretion by the gastric parietal cells. Ranitidine and nizatidine have anticholinesterase activity which supposedly results in some prokinetic activity, nevertheless this has never been proven in "in vivo" studies and re-evaluation of the original papers which suggest this effect, do not confirm it . In a recent study ranitidine was unable to increase gastric PH>3 or >4 better than saline. Since ranitidine is 12 times more potent than cimetidine and has a longer half- life, the efficacy of cimetidine is healing gastric ulceration is questionable. Ranitidine interferes with hepatic metabolism of theophylline, phenytoin, warfarin and should not be used concurrently with these drugs. In one recent study of healthy dogs, ranitidine has proved to be significantly less effective than famotidine, pantoprazole or omeprazole in increasing intragastric PH. Famotidine is has minimal hepatic metabolism and its absorption is not affected by feeding or fasting. Famotidine should be used with caution in patients with impaired renal function and may trigger cytopenias if administrated in combination with other myelosuppressive agents.
- **Proton Pump Inhibitors (omeprazole, lansoprazole, pantoprazole, esomeprazole).** They irreversibly inhibit acid production by the gastric parietal cell. They are absorbed in the small intestine and being weakly alkaline they will concentrate and persist in the acidic parietal cell, prolonging their duration of action. The antisecretory effect continues for 3-4 days after treatment is seized. Omeprazole tablets should not be split as they are stomach acid resistant and should be given on an empty stomach as gastric content will decrease oral bioavailability. Enteric-coated omeprazole paste registered for use in horses has not been assessed for use in cats and dogs. Lansoprazole comes out in formulations more suitable for dogs and cats (acid-resistant granules in a capsular form or orodispersible tablets) and can be given with food. Their onset of activity is slow (72 hours) therefore in order to reach a therapeutic concentration sooner, their use is every 12 hours and not once daily as it used to be reported. Long term use of PPI's in humans has been theoretically related to hypergastrinemia and subsequent gastric mucosal and muscular hypertrophy, yet this rebound hypersecretion was not reported in one dog study. Concurrent administration with ketoconazole or itraconazole may decrease the bioavailability of the latter.

5. Antimicrobials (metronidazole, tylosin, oxytetracyclin, enrofloxacin)[19]

- They are indicated for *Helicobacter*- associated gastritis, intestinal dysbiosis, granulomatous colitis in Boxer dogs, antibiotic-responsive enteropathy and as an adjunct to corticosteroids in the treatment of Inflammatory Bowel Disease (IBD).

6. Prokinetic agents[20]

- **Dopaminergic D_2 antagonists (metoclopramide, domperidone)** They are indicated in gastroesophageal sphincter disorders, in gastric emptying disorders as metoclopramide increases the amplitude and frequency of antral contractions and coordinates gastric, pyloric and duodenal motility, in small intestinal transit disorders because of its effect on the antropyloroduodenal coordination and in CRTZ-induced emesis.[21]
- **Serotonergic 5-HT_4 agonists**
  Cisapride is indicated in gastroesophageal sphincter disorders, in gastric emptying disorders, in small intestinal motility disorders (postoperative ileus, pseudoobstruction), in colonic motility disorders (improves early stages of idiopathic megacolon in cats) and in cis-Platinum induced emesis. Cisapride is a smooth muscle prokinetic with limited application to canine idiopathic megaesophagus, because the canine esophagus is a striated muscle.[22]
  Mosaprid restores gastric motility in dogs with vincristine induced gastric hypomotility.
  Prucaloprid stimulates gastric emptying in dogs and enhances defecation frequency in cats and dogs, having a direct effect on the colon.
- **Motilin-like drugs (erythromycin).** Erythromycin increases gastroesophageal sphincter pressure in cats and dogs and is indicated in patients with gastroesophageal reflux, in gastric emptying disorders as it induces antral contractions and in colonic motility disorders. It has been reported that administration of oral erythromycin after meals, accelerates gastric emptying of solids in dogs.[23]
- **Acetylocholinesterase Inhibitors and Cholinomimetic Agents. (ranitidine, nizatidine, bethanechol).** Indications for their use are esophageal, gastric and colonic motility disorders.
- **Nitric oxide donors (AMU-301).** It is indicated in diabetic gastroparesis.

7. Immunosuppresive drugs

- **Glucocorticoids (prednisone/prednisolone, dexamethasone, methylprednisolone acetate, methylprednisolone sodium succinate, budesonide).** Indicated in conjunction with dietary changes to treat biopsy-confirmed IBD. However, side effects are usually marked, especially in large breed dogs, and studies have shown that only about 30% of dogs that failed diet and antibiotic treatment will respond to steroids.
- **Calcineurin inhibitors (cyclosporine).** Indicated in patients with stomatis, myasthenia induced megaesophagus, IBD and anal furunculosis. Cyclosporin can exacerbate vomiting and diarrhea when used at high dosages. Plasma trough concentration of cyclosporine should be measured 1-2 hours post administration.
- **Antimetabolites (azathioprine).** Azathioprine is myelotoxic, therefore when administered the clinician should monitor CBCs for neutropenia and thrombocytopenia every 2 weeks for the first month of treatment and once a month thereafter. Evidence for azathioprine induced pancreatitis or hepatotoxicosis in dogs are limited.
- **Alkylating agents (chlorambucil).** It is often used in cats when response to glucocorticoids is poor or when the side effects of steroids need to be controlled (e.g diabetes mellitus).
- **Other immunosuppressive drugs**
  Mycophenolate mofetil (MMF) There are anecdotal reports of its use in dogs with myasthenia gravis- induced megaesophagus and IBD.[25]
  Leflunomide Possible application to refractory IBD patients.

8. Other drugs

- **Iron supplementation** in animals with GI bleeding that develop microcytic hypochromic anemia
- **Cobalamin B12 and folate supplementation** in IBD patients
- **Vitamin D supplementation** in dogs with protein losing enteropathies as a result of disorders in calcium homeostasis.

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Exotics

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Urinary tract disorders in small mammals

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Disorders of the urinary tract in rabbits and rodents (esp. guinea pigs) is a common health disorder.[1,2] With the increasing popularity of rabbits and rodents as pets and suboptimal husbandry conditions for many of them (e.g. nutrition and water intake),[3] it would not be surprising for veterinary practitioners to treat more rabbits and rodents with urinary tract disorders than in the past.

The presentation will show common and uncommon urinary tract disorders, diagnostics included, seen by the authors in rabbits and rodents, such are urolithiasis, encephalitozoonosis, nephropathies, cystitis, urinary tract neoplasia, penile disorders and others. Selected urinary tract diseases in exotic companion mammals are described.

Urolithiasis

In rabbits and guinea pigs, calcium is excreted via the kidneys; therefore, most (> 99%) uroliths consist of various calcium salts (predominantly calcium carbonate [69.4%]) or are compound uroliths containing calcium (23.0%).[4-6] Even, calcium sulphate urolithiasis in a rabbit was described.[7] Only a few reports exist regarding uroliths composed of substances other than calcium, such as silica and struvite.

Rabbits differ from dogs, cats, and ferrets in calcium metabolism. In rabbits, almost all available calcium is absorbed from the diet (independent of vitamin D3) by passive diffusion through the intestine wall, and only when the dietary amount of calcium is low does active calcium transport occur. Excess calcium is excreted via kidneys. Moreover, with excessive calcium intake by rabbits, the intestinal calcium absorption rate does not change, but instead urinary calcium excretion greatly increases. Serum total calcium concentration in rabbits is greater than that in other mammals and, for healthy rabbits, is suggested to be within the range of 2.1 to 3.5 mmol/l.[4] Altogether, rabbits eliminate a consistently high amount of calcium in urine, and this mineral can bind with other constituents if the conditions are appropriate for crystallization.

Urine supersaturation with crystallogenic material is an etiopathogenetic factor common to all individuals with urolithiasis, regardless of species or mineral type. The degree of supersaturation is strongly related to the degree water metabolism, which in otherwise healthy individuals is associated with drinking behaviour.[8] In an experiment involving rabbits and different feeding regimens, faecal dry matter content was significantly higher in rabbits with water provided via nipple drinkers than in rabbits with water provided in an open dish.[9] These findings provided an argument against the use of nipple drinkers for rabbits, particularly after an episode of urolithiasis. Moreover, with restricted water access, rabbits in the same study had significantly greater water intake when provided in open dishes versus nipple drinkers. It is realistic to suppose that many pet rabbits do not have optimal access to drinking water and that drinking from a nipple drinker and eating dry food predisposes pet rabbits to thickening of urine, with subsequent crystalline sand formation. Similar situation exists in guinea pigs.

In female rabbit urethra enter the vagina; therefore, the vulva is the common opening for both, uropoetic and genital system and the presence of the blood in the urine can be of uterine origin.[2] In the contrary, guinea pig females had vagina and external urethral orifice localized independently. At the authors practice, uroliths in female guinea pigs are, apart from the urinary bladder, located proximally to the urethral external orifice.

Diagnosis is based on thorough clinical examination, palpation of the abdomen (with the emphasis on urogenital tract) and urethra included.[9] Most of the uroliths are opaque and abdominal radiography is the part of the diagnostic protocol. Abdominal ultrasound can reveal other organ changes, include urinary bladder wall thickening, etc. and shows exact urolith location. Urinalysis and mineral analysis of the urolith can aid the further steps in the urolithiasis management and prevention.[8] Blood chemistry and haematology should be always performed to check the kidney function and white and red blood cell counts, leukocyte differential counts and reticulocyte count included. Authors have a very good experience with IDEXX analyzators, which can count and analyse blood from commonly kept exotic pet animals.

Therapy consist of patient stabilization, fluid therapy, surgical removal of the urolith and dietary management.[10,11] Benzodiazepines should be included in the anaesthetic protocol as they release uropoetic tract muscles. Use of urine acidifiers (ammonium chloride 0.5 g/kg PO q24h or potassium citrate 10 mg/kg PO q12h) must be closely monitored to do not exceed the fatal dose. In case of oxalates, dietary restrictions can be made. For urolith removal, endoscopy and/or lithotripsy can be also used.[13] Urinary diet for herbivore pets (rabbits) exists, can be recommended, but evidence-based information about the its use is missing.

Urine "sludge" in rabbits

Urinary "sludge" is characterized by formation of pasty-like urine resulting with dysuria and pain.[12] Thea aetiology is multifactorial and, apart of the cystitis, the most common cause is "immobility" from several reasons (e.g. pain due to dental disease, spondylosis, pododermatitis, obesity and lack of space for exercise and movement). Formation of urinary sludge lead to urinary bladder atony, cystitis, pain, gastrointestinal stasis, lack of movement and urine scalding.

Diagnosis is based on palpation and radiography. Therapy consist of the primary cause treatment, analgesia (buprenorphine 0.03 mg/kg q8 hod IM; meloxicam 0.4-0.8 mg/kg SC/PO q12h), fluid therapy and urinary bladder flushing. Activity level should be increased, and body weight monitored. Leafy fresh greens, grass and fresh juice can be added into the drinking water to support drinking. Clients can learn how to massage abdomen to support void the bladder. In some cases, betanechol can be used. Removing of the calcium rich vegetables from the diet is not recommended by the authors, due to large water content of these vegetables.

Encephalitozoonosis

Encephalitozoon cuniculi is an obligate intracellular pathogen that has wide host distribution, but primary affects rabbits. It was also described in guinea pigs. Encephalitozoon cuniculi is a single-celled, spore-forming, obligate intracellular fungi that belongs to the genus Microsporidia. Encephalitozoonosis in laboratory and pet rabbits is of clinical significance worldwide. Nowadays, infections with *E. cuniculi* are being recognized with increasing frequency in pet rabbits.[14,15]

Infected rabbits show a range of clinical signs from chronic infections, which can persist asymptomatically for years, to sudden deaths. Predilection sites in rabbits are the central nervous system, kidneys and eyes. The most commonly recognized neurological sign is a vestibular disease because of granulomatous brain inflammation. Kidney disease is characterised by granulomatous interstitial nephritis. Signs of ocular disease include lens rupture, uveitis and cataracts. Differential diagnoses include pasteurellosis, otitis due to ear mites, herpes-viral meningitis, larva migrans and toxoplasmosis.[14,15]

Post-mortem diagnosis of encephalitozoonosis in rabbits is based on the histopathological examination or PCR. Nevertheless, a definitive antemortem diagnostics is difficult. Direct detection of organisms in the urine or faeces is not dependable because spores excretion is sporadic, however some clinicians use also this method in clinical practice.

The standard method is the serological testing,[14-16] which is the commonly used method for in vivo diagnosing. Several serological tests, including indirect immunofluorescence, carbon immunoassay and ELISA were developed. They are usually used for detection of only IgG isotype of specific antibodies that merely indicate exposure to infection but do not confirm the organism as a causative agent of a disease. A definitive antemortem diagnosis of encephalitozoonosisis important for specific therapy, accurate prognosis and assessment of zoonotic risk. The intravital diagnosis is usually obtained by a combination of clinical examination excluding the main differential diagnoses, and serological testing which is mostly based on detection of specific IgG antibodies. However, presence of this isotype of antibodies is indicative for chronic/latent infection, but not of clinical disease. Moreover, the antibody titre levels are not suitable for establishment of E. cuniculi as the causative agent of the displayed symptoms because a considerable percentage of animals within a rabbit population appear to be infected and show remarkably high titres, that can persist for several years even in the absence of clinical signs.

In rabbits infected with E. cuniculi under experimental conditions, the specific antibody response is initiated soon after infection. Based on general kinetics of humoral immune response, detection of only IgM antibodies indicated early (acute) infection, simultaneous detection of both IgM and IgG allowed identification of the infection as active (acute, reactivated infection or reinfection) and detection of alone IgG specific antibodies denoted chronic/latent infection. Some authors recommend also use a combination of titres of IgM and IgG and elevated CRP levels as when examined alone, the positive predictive values of IgM, IgG, and CRP varied from 88% to 90%. The use of combinations of these tests decreased the sensitivity of the diagnostic panel but increased the specificity—resulting in a positive predictive value ranging from 92 to 100%.[17,18] These data suggest that the use of multiple immunological tests appears helpful in diagnosing ECUN in rabbit patients exhibiting clinical signs consistent with infection

It was demonstrated, that E. cuniculi infection was prevented with prophylactic administration of fenbendazole (20 mg/kg PO) prior to experimental infection.[19] Rabbits remained seronegative after 21 days and spores were not recovered in brain tissue on postmortem tissue analysis. Information regarding spore recovery from the kidney and histologic analysis for any tissue was not provided. In the therapeutic trial of fenbendazole orally dosed at 20 mg/kg body weight daily for 4 weeks, there were no spores noted in the brain based on histologic evaluation. Based on these findings, current treatment practices advocate the use of fenbendazole for E. cuniculi prevention. Therapeutic efficacy of combined treatment of fenbendazole, oxytetracycline, enrofloxacin, and dexamethasone or prednisone showed 54.2% clinical recovery rate.[16]

Because the risk of steroid-induced immunosuppression can be significant in E. cuniculi-infected animals, authors recommend using nonsteroidal anti-inflammatory drugs. The use of midazolam or diazepam is commonly employed to control seizure activity and to act as a mild sedative in animals with severe vestibular disease that is causing flailing/rolling. In case of seizures, use of short-active steroids (prednisolone) for the first 24 hours in combination/or without benzodiazepins can control acute cases (rolling, ataxia) can be also used. Environmental modifications should be

made to provide severely centrally vestibular animals with protection. Soft padding and non-metal cage barriers should be employed with these animals to prevent accidental ocular and limb trauma.

E. cuniculi is environmentally resistant, but spores can be killed effectively using a number of disinfection protocols. Spores are susceptible to 0.1% bleach at a contact time of 10 minutes, and ethanol (70%) effectively kills spores with a contact time of 30 seconds. Sodium hydroxide (1%), formaldehyde (0.3%), and hydrogen peroxide (1%) effectively kill spores with a contact time of 30 minutes.

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Respiratory diseases in rabbits

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Anatomy and physiology

Several challenges arise when evaluating a rabbit with respiratory disease. The respiratory system has not such a high degree of ventilatory reserve as dogs and cats, which can make respiratory diseases difficult to treat.

Rabbits are obligate nasal breathers, which mean that the normal anatomical position of the epiglottis causes it to be engaged over the caudal rim of the soft palate, sealing the oral pharynx from the lower airways.[1-6] Therefore, rabbits with advanced upper airway disease will attempt to breathe through their mouths, which prevent feeding and drinking and could be quickly fatal.[1,2]

The nostrils of rabbits contain sensory pads and at the tip of the nose is also a "blind spot", which makes this region very sensitive to touch. Inadvertent occlusion of the nasal passages during any procedure, including oral exam, can lead to respiratory compromise due to the ineffectiveness of mouth breathing.[1-3]

Rabbits have maxillary and ethmoid paranasal sinuses.

Rabbit lungs have no small septa (lungs are not lobulated), right lung have four lobes and left lung have three lobes; air flow volume is higher in the left lung. The cranial lung lobes are small and are commonly superimposed with mediastinal fat. The caudal lung lobes have a pronounced vasculature.[4] Pneumonia is always lobar, so clear radiographic determination whether the infection is bronchogenic or haematogenic is not possible in rabbits.

Rabbits have relatively small thoracic cavity, and at rest breathe mostly through the activity of diaphragm and showing minimal movement of the chest wall when breathing. The normal respiratory rate at rest is 30 to 60 breaths per minute. On auscultation, rabbits have more pronounced upper airway and bronchial sounds and may sound somewhat harsh. Significant respiratory compromise may occur if a rabbit is placed in dorsal recumbency for surgery when the gastrointestinal tract is distended or in obese animals, so elevating thorax above the abdomen is recommended.[1,5,6]

The cranial border of the heart, which is localized between 2(3)nd to 5(6)th intercostal spaces, is less distinct due to the presence of thymus and fat. Cardiac size is evaluated based on vertebral heart score.

The thymus persists through the life.[6]

Aetiology and pathophysiology

A list of differential diagnoses for nasal discharge and dyspnoea is given in a Table 1.[3,6-11] Cause of dyspnoea could be of primary origin or secondary, where diseases primarily affecting other organs can result in respiratory embarrassment even if the respiratory system is healthy

Pathophysiology of dyspnoea originated from lack of oxygen or excess of carbon dioxide in the body. The animal tries to resolve the problem with either increased ventilatory rate or increased ventilatory depth or both.

History and clinical signs

The history of patients with respiratory disease can be problematic, because some owners can have a difficult time in recognizing any abnormalities. Any stridor, presence of nasal discharge or recent onset of snuffling might indicate nasopharyngeal disease. Weight loss, anorexia and the presence and rate of progression of respiratory distress or exercise intolerance should be ascertained.

Rabbits are obligatory nasal breathers,[5] so any obstructive disease of the nasal cavity could be life-threatening. It is imperative that animals with severe respiratory distress must be stabilized before time is taken to obtain a thorough history. Stabilization may include oxygen therapy, appropriate medications (diuretics), and then a brief history.

Respiratory disease (RD) could be associated with restrictive or obstructive pattern. Determination, which pattern the animal exhibiting, can help to narrow the list of differential diagnoses.

Because of small thoracic cavity are rabbits predisposed to ***restrictive diseases***, which prevent the lungs expanding, and lead to short, rapid and shallow breaths. These signs could be associated with pneumonia, lung oedema, pleural effusion, pneumothorax, mediastinal and lung tumours or abscesses or due to increased pressure of abdominal organs into the diaphragm. ***Obstructive disease***, which is present in cases of airway passages narrowing, leads to slower and deeper breaths. Upper obstructive RD is associated with increased inspiratory effort and open mouth breathing, whereas lower RD with increased expiratory effort, however inspiratory problems could be also seen.

Wheezes are usually heard on expiration and indicate obstruction or narrowing of small airways. Crackles are caused by the opening of small airways during inspiration and are heard with bronchial inflammation and pneumonia.[3]

Diagnosis

The physical examination is extremely important in assessing respiratory health. Even before approaching the animal, an attempt should be made to observe the animal while talking to the owner.

The mucous membranes should be checked for any indication of cyanosis or pallor. Both nostrils should be checked for air flow and signs of discharge. Unilateral or bilateral nasal discharge is usually indicative for upper respiratory rather than lower respiratory or systemic disease.

Due to rabbit regular grooming, signs of discharge could be seen only as wet hair on the front paws. Facial symmetry should be evaluated. Oral cavity and all maxillary teeth should be evaluated for the presence of any associate pathology with nasal cavity. Palpation of the skull, cervical area, thorax and abdomen could reveal tumours, skeletal injury or enlargement/distension of abdominal organs.

A properly fitted and functioning stethoscope is of great importance in the thorough examination of the heart and lungs. Care must be taken to identify the origin of potentially confusing sounds that commonly arise as a result of shivering, twitching or movements of stethoscope against the body. During the auscultation entire thorax at different places should be examined even in small rabbits to exactly identify the source of abnormal sound. Wheezes (musical sounds) are generated primarily by airway narrowing, stenosis, or obstruction. Crackles (short, explosive, non-musical sounds) are typically produced by a delayed opening of small airways attributable to an abnormal fluid-air interface (pneumonia, pulmonary oedema). Knowledge of the timing (systolic, diastolic) and location of abnormal heart sounds (murmurs, arrhythmias) allows practitioner to establish a differential diagnosis rapidly. In rabbits, the arterial pulse is evaluated bilaterally to assess heart rate, rhythm and arterial pulse quality. However, heart disease can be present without auscultable abnormalities, and not all murmurs are associated with heart disease (most commonly due to anaemia).[3]

Many diagnostic methods are available to the clinician to help identify and describe the type of respiratory disease. It is imperative with small mammals that the potential hazard of any test be considered, because minor stress can lead to collapse of these patients. Haematology and plasma/serum biochemistry is often unremarkable, however the most important contribution is to uncover systemic diseases that might be affecting the respiratory system, such as anaemia, leukaemia or presence of liver and kidney failure. Urinalysis and analysis of acid-base blood parameters showing metabolic disturbances. ELISA tests are available for the antibody detection for *P. multocida* in rabbits and for *M. pneumoniae* in rats; however a paired blood sample examination is necessary to evaluate an increase in particular antibody titres.[3]

Although our ability to closely describe patterns and abnormalities in the rabbit thorax are limited compared to our abilities in ferrets, radiography is still very important imaging method for the evaluation of a patient with respiratory disease. It is preferable to ensure that the patient is in most cases under sedation or anaesthesia when performing radiography due to proper positioning. It is preferable to use benzodiazepins, opioids, propofol (rabbits) and isoflurane anaesthesia. The optimal views for thoracic examination are dorsoventral and right and left lateral and for nasal cavity dorsoventral/ventrodorsal, right lateral and two lateral oblique and rostrocaudal view.[12,13] Intraoral radiograph of the nasal cavity can be very helpful in the evaluation of the nasal cavities and incisor and molar apices.[13] Cranial cardiac borders are often indistinct and cranial mediastinum is soft tissue opacity, especially if a large amount of fat is present. In some rabbits with chronic respiratory disease we could identify indistinct bronchial pulmonary pattern throughout the lungs. In a more severe case of chronic respiratory disease, focal areas of pulmonary consolidation could be seen. In cases of caudal lung lobe inflammation and some systemic diseases (e.g. that causes anaemia) are cranial parts of the lungs extremely aerated. It is very important to remember that radiography should not be performed prior to basic patient stabilization. Interpretation of radiographs may document the presence of cardiomegaly, pulmonary oedema, pleural effusion, or prominent pathological lung patterns.

Computed tomography (CT) is of great importance as using this method one can evaluate nasal passages, conchae, paranasal recessi, dentition, skull and dentition. In case of chronic sneezing, authors recommend using CT. Endoscopy of the respiratory tract is indicated especially in cases of nasal or tracheal foreign bodies, chronic respiratory diseases or respiratory neoplasia. Endoscopy is a very useful tool not only for direct pathology visualization but also for guided biopsy or treatment.

Echocardiography and ECG in particular are useful to document cardiac function and to assess mediastinal masses. Echocardiography should not be performed if a patient has marked respiratory distress.

Cytology (nasal swab, bronchoalveolar lavage, fine needle aspiration, effusion determination) and bacteriology/mycology together with antibiotic sensitivity testing is important from the point of diagnosis, treatment and also prognosis. In case of biopsy or any mass removal histopathological examination should be made in all cases.

Therapy

Frequently, after evaluation of the historical and physical examination findings, laboratory examination and interpretation of the thoracic radiographs, it is possible to determine whether heart or lung disease or other disease is the most likely cause for the respiratory distress.

If pulmonary infiltrates compatible with oedema are present on thoracic radiographs, the rabbit should be treated with diuretics, oxygen, cage rest and possibly vasodilators. In authors practice, furosemide (4–5 mg/kg IM or IV q 2–6 hours) is frequently used. Placement of an intravenous catheter is in rabbits essential and may often be placed with minimal restraint into the marginal ear vein, cephalic or saphenous vein.

Oxygen is most easily administered by placing the animal into the oxygen cage.

If a moderate to large volume of pleural effusion is present, it should be removed in order to improve the stability of the patient as well as to help aid in reaching the final diagnosis. Thoracocentesis (21 gauge needle) is recommended to perform under the control of ultrasound.[1,2,6]

Antibiotics or other drugs should be administered systemically or topically based on the disease severity and exact cause.

For nebulisation it is preferable to use amynoglycosides alone or in combination with bronchodilatators. Moreover, nebulisation itself keep mucosal membrane "hydrated" and acts as an excellent expectorant.

In chronic cases of nasal disease or in case of periapical infection is indicated to perform rhinotomy/sinusotomy and solve the problem surgically.

Rhinotomy/Rhinotomy/Sinusotomy in rabbits

Rhinotomy is in rabbits indicated in cases of chronic sneezing, non-responsive upper respiratory disease or in cases of neoplastic disorders.[14-16] Based on computed tomography findings a dorsal ("true") or lateral (mostly "sinusotomy,") is performed. Care should be taken do asses also middle ear cavity as some of patients have concurrent otitis media/interna (commonly subclinical). Intubation during the procedure, thorough nasal or paranasal recessus flushing, and wound marsupialization/or intranasal catheter placement is necessary to reach optimal therapeutical outcomes. For exact diagnosis and proper therapeutical protocol, bacteriology, antibiotic sensitivity testing and, if indicated, histopathological examination should be performed in all cases.

Pasteurellosis of rabbits is one of the most significant bacterial diseases throughout the world. To date, pasteurellosis in rabbits is mainly caused by serogroup A and, to a lesser extent, by serogroup D and F strains. The organism is transmitted through direct contact with animals shedding the organism from nasal or vaginal secretions. *P. multocida* is then spreads to other tissues: to the lower respiratory tract by aerogenous routes; to the middle ear via the Eustachian tube; hematogenously; local extension; and to the genital tract by venereal spread or nasal inoculation.[17]

Common clinical signs include nasal discharge, sneezing and conjunctivitis. More serious forms of the disease are pneumonia, pleuritis, otitis media, meningitis, septicaemia and pyometra. Some other bacteria that could be present in the respiratory infection of rabbits are *Staphylococcus aureus*, *Bordetella bronchiseptica, Mycoplasma sp.* and *Klebsiella pneumoniae*.

The diagnosis is based on clinical signs, thoracic and tracheal auscultation, radiography, rhinoscopy and bacterial culture.

Therapy includes supportive care, nebulization (aminoglycosides) and antibiotic treatment (local or systemic). Use of trimetoprim-sulpha (30 mg/kg PO q12h) or fluoroquinolones (marbofloxacine 10 mg/kg PO, IMq 24h) is recommended. In more severe cases parenteral administration of beta-lactams provide better outcomes (PNC G 50.000 IU/kg IM q12h).[3]

Nasal discharge, Upper airway disease		
	Bacterial infection (Rhinitis/Sinusitis)	*P. multocida* *S. aureus* *B. bronchiseptica* *Pseudomonas sp.* Mycobacterium sp.
	Viral infection	myxomatosis, calicivirosis
	Mycotic infection	aspergillosis, candidosis
	Parasitic	*Pneumonyssus sp.* infection
	Nasopharyngeal polyps	
	Neoplasia	osteoma, osteosarcoma, fibrosarcoma
	Dental disease	periapical infection incisor maloclussion elodontoma
	Foreign bodies	hay, seeds, prickles
	Skull fractures	
	Traumatic injury	
	Lung oedema	
	Improper housing	Dust Improper humidity Nasal irritants
Lower airway disease		
	Aspiration	
	Bacterial infection (Pneumonia/Bronchitis)	*P. multocida* *S. aureus* *B. bronchiseptica* *K. pneumonia* *Mycobacterium avium* *Chlamydophila sp, Mycoplasma sp*
	Viral infection	myxomatosis
		calicivirosis
	Mycotic infection	aspergillosis
	Lung neoplasia	mesothelioma
	Tracheal neoplasia	adenocarcinoma
	Metastases	uterine adenocarcinoma lymphoma
	Laryngeal paralysis	
Heart disease		
	Cardiomyopathy	idiopathic
	Infectious	P. multocida S. aureus Salmonella sp. Streptococcus viridans coronavirosis
	Parasitic	*E. cuniculi*
	Degenerative	*Valvular disease*

Table 1: Possible causes of dyspnoea in rabbits.

Pleural disease		
	Pneumothorax	
	Chylothorax	
	Pyothorax	
	Neoplasia	uterine adenocarcinoma lymphoma
Mediastinal disease		
	Lymphoma	
	Thymoma	
	Thymic carcinoma	
	Uterine adenocarcinoma	
Systemic disease		
	Gastric dilatation	
	Caecal distension	
	Hepatomegaly, Liver failure	
	Brain disease	encephalitis (herpesviral, *E. cuniculi, Baylascaris procyonis*) neoplasia
	Kidney failure	
	Anaemia	fleas vaginal bleeding trauma, any other causes
	Hyperthermia	
	Lymphoma/Leukaemia	
	Metabolic acidosis	
	Stress, Shock, Pain	
	Skeletal injury	
	Diaphragmatic hernia	
	Acute smoke inhalation	
	Status antefinem	

Table 1: Possible causes of dyspnoea in rabbits.

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Small mammal ophthalmology

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The small exotic pet population has grown dramatically in last years in size because of their increasing popularity as laboratory and pet animals. This popularity stimulated clinicians and researchers in the animal's general health knowledge, ophthalmology included. As the ophthalmic and ocular associate structures diseases are common disorders in exotic companion mammals, the most commonly encountered ocular problems are described with the focus on rabbits and commonly kept rodents (esp. rats, guinea pigs and chinchillas). Detailed information are focused on normal anatomy and physiology, thorough ophthalmic examination, disease recognition, diagnostic procedures and optimal medical and surgical treatment.[1-5]

Ophthalmic examination in small exotic mammals follows the same principles used in companion animals.[2] However, ocular examination of some species is difficult because of small size of the eye, restraint difficulties, and the use of large conventional diagnostic instruments. In these cases, the eye is best examined using source of magnification. Slit lamp biomicroscopy of the eye adnexa, cornea and anterior segment could be performed, but ophthalmoscopy with the use of standard methods could be more problematic. The tonometer (TonoVet) is small enough to provide accurate measurements of intraocular pressure in even the small rodents, however conscious animals should be examined as anaesthesia has a great impact on intraocular pressure. One of the possibilities how to examine ocular structures and caudal ocular segment, apart from fundoscopy, is endoscopic ocular examination (oculoscopy).[6] Below, the procedure of endoscopy is described in the animal in general anaesthesia in a lateral recumbency:

Oculoscopy[6]

The tip of the telescope is slowly moved toward the eye and is supported by the operator's fingers. The tip of the telescope should always be kept approximately 1 to 2 mm from the cornea and should never touch the corneal surface due to possible corneal damage. The eye should be examined in various angles, by gently moving the telescope in different directions. The conjunctiva, eyelids, lacrimal puncta, corneal surface, anterior eye chamber, and iris are evaluated by this technique. The light necessary for the examination depends on the density of the pigmentation of the iris and retina. For most oculoscopies, the percentage of light set on the light source is about 75% to 100% and should corresponded with 130 to 175 lumens. In albinotic animals, the percentage of light set on the equipment should be lower to avoid corneal damage. Light reflectance, if present, can be controlled by slightly changing the endoscope tip position. For detailed visualization of the lens, vitreous, and retina, a mydriatic agent (0.5%–1% tropicamide) is applied topically to the cornea of rabbits. In rats (Rattus norvegicus), atropine 1% is preferred over tropicanamid because of its better mydriatic effect. At the end of the procedure, administration of topical ophthalmic gels containing retinol or dexpanthenol is recommended to ensure that the corneal surface will not get dry and that any minor corneal damage will heal. The complete examination of each eye takes approximately 5 minutes.

Rabbit Ophthalmology

Anatomy[2,4,7-10]

The orbits of the rabbit are situated in either side of the skull and their openings are directed at 85 degrees angle to the transverse plane of the head. Rabbit eye appears compressed in its anterio-posterior dimension and possesses, in contrast to men, and active retractor bulbi muscle and acino-tubuilar gland of the third eyelid (Harder's gland) are present. The conjunctiva is divided in palpebral and bulbar conjunctiva and is relatively thin (10-40 μm). The cornea of an adult rabbit has a power of 40-43 dioptres. The rabbit lens accommodation is limited (0-1.5 dioptres). Retina is merangiotic. The external ophthalmic artery is the chief arterial supply to the orbital structures, including the bulbus. The venous sinus surrounds the muscle cone and covers Harder's gland.

Rabbits are able to resist blinking for long intervals because they have a very stable tear film. Tears of a rabbit are a clear and slightly alkaline solution, with an average pH of 7.5 with electrolyte concentration similar to that of plasma. There is a single nasolacrimal punctum in the rabbit. Swab taken from the conjunctival sac of healthy pet rabbits contain mostly DNase-negative *Staphylococcus sp., Micrococcus sp., Bacillus sp., Stomatococcus sp., Neisseria sp., Pasteurella sp., Corynebacterium sp., Streptococccus sp.* and *Moraxella sp.*[11]

Ophthalmic examination

Ophthalmic examination should always follow history, physical and neurological examination.[2] In rabbits is often difficult to demonstrate reduced vision because individuals can compensate for severe visual disability. General eye examination should start with gross observation of the position and symmetry of the eyes and adnexa. Aspects of

neurological examination that relate to ocular diseases include assessment of vision, eye movement and cranial nerves. Reflexes which should be tested are menace response, visual placing reaction, palpebral and pupillary reflex.

The basic equipment requirements for examination consist of a room that can be darkened, focal light source and some form of magnifying device. Additional equipment and various disposable items (direct and indirect ophthalmoscope, slit-lamp, tonometer, fluorescein, local anaesthetics, mydriatics., etc.) are also needed.

Adequate manual restraint is essential during the ophthalmic examination. Sedatives should be avoided; however, if it is necessary, potential drug effects on eye structures should be taken into consideration. Corneoconjunctival cytology and culture is helpful in cases of conjunctivitis or dacryocystitis. The Schirmer tear test (2-11 mm/minute) and phenol red test (15-27 mm/15 seconds) is applicable in rabbits.[12] Normal intraocular pressure in rabbits is in the range of 15-23 mm Hg. Examination of the bulbar surface of the nictitating membrane is performed after instillation of topical anaesthetic. Cornea, anterior chamber, iridocorneal angle and iris are examined by direct or indirect ophthalmoscopy. Mydriasis is achieved with the topical use of a 0.5-1% tropicamid solution. Even that approximately 60 % of rabbits have atropinesterase, authors have good experience also with the use of atropine eye drops. After the effect of mydriatic agents, lens, vitreous and fundus are examined thoroughly. Fundus is evaluated with the use of an indirect ophthalmoscope and 30-40 D lenses, slit lamp or with oculo-endoscopy. Fluorescein staining of the cornea with the use of the full-strength 2% solution or direct touching of a fluorescein-impregnated strip to the cornea should be avoided because it can result in artificial staining of the cornea.

Electro-retinography is receiving greater emphasis in experimental studies. Photography play an important role in the documentation of ophthalmic lesion.

Diseases

Corneal erosion and ulceration

Due to relatively large and protruding eye globe, even minor problems associated with blinking or tear production or traumatic injury resulting quickly in corneal oedema and subsequent erosion or ulcer formation.[13] Clinical signs could include blepharospasm, conjunctival hyperaemia, keratoconjuktivitis sicca or epiphora and different stage of corneal opacity and corneal vascularization. The fluorescein or phenol red staining examination reveal diffuse uptake of the dye in the affected area. Presence of small number of faint focal or hazy stained areas is in rabbits normal. Cytological examination and bacteriological culture will aid further antibiotic selection. Superficial debridement is performed with cotton-tipped swabs. Treatment consists of administration of broad-spectrum antibiotics (gentamicin, fluoroquinolones, tobramycin, chloramphenicol, sulphonamides), anti-inflammatory eye drops (indomethacin, diclofenac) and agents supporting corneal healing (retinol). Acetylcysteine could be also used. In case of non-healing ulcers autologous serum administration or surgery (keratectomy, corneal flaps) is a choice.

Epiphora

Epiphora is caused by an overproduction or and inadequate removal of tears. In rabbits, it is frequently due to an inadequate removal of tears caused by blockage of the tear ducts by apical elongation of the incisors or periapical cheek teeth pathology. In cases of conjunctivitis and keratitis, epiphora is present due to overproduction of tears from the eye irritation.[4] Purulent epiphora is associated commonly with bacterial infection and kerato-conjunctivitis.[14] Skin in the area of medial eye canthus could be wet and alopecic. Wet dermatitis could be result of chronic skin irritation. In cases of nasolacrimal duct obstruction, milky discharge is commonly present. This secret comes from Harderian gland and physiologically contains lipids, which are macroscopically seen as a white opacity of tears.

Diagnosis is based on clinical examination, oral cavity examination, ocular examination or conjunctival swab examination. Imaging methods could reveal incisor apical elongation or periapical pathology. Dacryocystography with the use of 1 ml of contrast iodine media is a useful procedure for the visualisation of the nasolacrimal duct.[15,16] Epiphora could be present also in cases of myxomatosis, foreign body in conjunctival sac or trichiasis.

If the epiphora is due to the ocular diseases, then treatment of the primary cause will usually solve the problem. If systemic infection is present, peroral or parenteral antibiotic administration is recommended. For the treatment of pasteurellosis, the antibiotics of the first choice are trimethoprim-sulpha drugs (30 mg/kg PO/SC BID for 2-3 weeks); for the treatment of treponematosis, penicillin G (40.000-60.000 IU/kg IM SID till BID for 5 days) is one of the most effective drugs. Daily washing with anti-inflammatory solutions and clipping of the hair in the affected skin area will minimize skin inflammation.

Epiphora caused by blockage of the tear ducts often respond to medical treatments with antibiotic eye drops, but many require flushing the ducts under anaesthesia.[16] If a dental disease is a cause, proper treatment is necessary to solve the problem. Intravenous cannula, lacrimal cannula or metal irrigation cannula with blunt end could be used for the irrigation of the nasolacrimal duct, which should be performed under sedation or general anaesthesia. The syringe is filled with sterile saline and cannula is inserted into nasolacrimal duct or in cases of small diameter of nasolacrimal duct close to nasolacrimal punctum. Milky fluid or pus should come from ipsilateral nostril if the procedure is successful. In some cases, gentle digital pressure in the area of lacrimal sac is necessary to force the fluid to go further the duct to clear the blockage. If the flushing is unsuccessful, administration of anti-inflammatory eye drops and/or antibiotics and re-attempt the flushing after 4-7 days of treatment. Flushed material can be used for cytological examination or culture. Depending on the severity of the disease repeating this procedure is necessary on 3-10 days

intervals. Authors of the present paper recommend using eye protective gel containing retinol or dexpanthenol and anti-inflammatory drugs after each procedure to protect superficial eye structures.

Exophthalmos

Documented cases of retrobulbar mass lesions include retrobulbar abscess associated with periodontal disease, malignant lymphoma and a coenurus cyst of *Taenia serialis*. Exophthalmos could be in rabbits also associated with thymoma, hypertension, stress and Harderian gland neoplasia. To determine the extent and nature of retrobulbar mass or exophthalmos, ophthalmoscopy, radiography, computed tomography, ocular ultrasonography (12-20 MHz probe) and lesion biopsy for cytological and histopathological examination are necessary.

Cataracts

A cataract is any opacity within a lens which could vary in size with variable vision impairment (incipient, immature, mature or hypermature). Aetiology could be of congenital, post-inflammatory, parasitic (*Encephalitozoon cuniculi*), metabolic or idiopathic origin.

Rodent Ophthalmology

Ocular anatomy[2,5,10,17-20]

The eye of all rodents shows the main characteristics of all mammalian eyes. Eyes are localized on lateral side of the head allowing a rodent to have a large visual field with limited binocular vision. The eyes of rats, mice and hamsters protrude more from the head that those of degus and guinea pigs. In guinea pig and chinchillas is the infraorbital region more massive than in rat-like rodents. The globes of mice and chinchillas have a large corneal surface (approximately 50%). The orbital shape is almost circular in guinea pigs, chinchillas and degus in contrast to ovoid shape in small rodents. Small rodents and chinchillas have in general shallow orbit which predispose these animals to the traumatic eye injury. *Tapetum lucidum* was described so far only in one large American rodent paca (*Cuniculus paca*). Other rodents do not have any type of *tapetum lucidum*.

The basic anatomical and physiological characteristic of the rodent eyes are summarized in Table 1.

The Harderian gland is located within the bony orbit. In contrast to rabbits, secretions from this gland include the reddish to brownish pigment porphyrin. In case of stress or any disease, the excessive porphyrin secretion is called chromodacryorrhoea.

Mice have extensive periorbital venous sinuses behind the globe of the eye, while rats have a more discrete plexus of vessels. In rodents, which are used for research purposed is this periorbital region used for blood sampling, however in clinical practice it is not recommended as other safer blood sampling techniques were described.

		Chinchilla	Guinea pig	Rat	Mouse
Blink frequency		2.6±0.84 /10 min.	2-5 times /20 min.		
Intraocular pressure	mmHg	17.71±4.17	16.5± 3.2	18.4±0.1	19.3±0.4
Schirmer tear test	mm/min	1.07±0.54	0-12		
Red thread tear test	mm/15s		21.26 ±4.19		
Esthesiometry	mm	12.4±4.6	20.0±60		
Central corneal thickness	mm	0.34±0.03	0.23±0.01*	0.16±0.03	0.075-0.10
Anterior chamber depth	mm	2.01±0.2	1.3±0.01*		0.035
Axial lens thickness	mm	5.49±0.43	3.68±0.05 *		2.8
Internal vitreous chamber depth	mm	3.69±0.52	3.50±0.11*		
Axial globe length	mm	11.4±0.7	10.17±0.03	5.15±0.23	2.98
Pupil		Vertical	circular	circular	circular
Third eyelid		rudimental			
Retinal vascular pattern		anangiotic	anangiotic	holangiotic	holangiotic

Table 1: Selected ocular characteristics for small rodents (*7-week-old animals).

Vision

Rats have two classes of cone, one containing an ultraviolet (UV)-sensitive photopigment (blue UV) and the other containing a pigment maximally sensitive in the middle wavelengths of the visible spectrum (green). Evidence of dichromatic colour vision in the rat was already proved. UV light entrainment of circadian rhythms is possible even in species that lack UV cones (Syrian hamster). Rats have poor visual acuity and have an enormous depth of focus (7 cm to infinity). The vision of rats is blurred in comparison to the human eye. The albino individuals are severely visually impaired with their retina degenerated. In cases of prolonged period of bright light, albino rats could develop phototoxic retinopathy (light induced retinal damage).

Ocular diseases in rodents[21-25]

Primary or secondary ocular diseases are in rodents quite common, despite its growing population visiting veterinary clinics. Some of the primary ocular diseases are, however, incidental findings during the closer ophthalmic examination (e.g. heterotopic bone formation in guinea pig ciliary body) and it seems that have minimal impact of the animal's health.

Congenital disorders

Microphthalmia or anophthalmia was recorded in all rodent species.

Chromodacryorrhoea

Chromodacryorrhoea is characterized by abnormal secretion of porphyrins by the Harderian gland as a reaction for stress, systemic diseases or ocular/Harderian gland inflammation. It is commonly seen in rats and gerbils. These secretions may be observed around the eyes, around the nares after passage through the nasolacrimal duct, on the forelimbs or as hair "impregnation" after the animal has groomed its face or body. Because of contact of porphyrins with day light, a skin became photo-sensibilised and also contact dermatitis could develop, especially in gerbils. In rats, infection with the coronavirus sialodacryoadenitis virus (SDAV) may also cause chromodacryorrhoea, often accompanied by periorbital swelling, blepharospasm, keratoconjunctivitis, megaloglobus, retinal dystrophic changes, and hyphaema. SDAV is highly contagious and spreads rapidly by aerosol, direct contact and fomite transmission.

Epiphora

Epiphora is caused by an overproduction or and inadequate drainage of tears. In chinchillas, guinea pigs and degus, it is frequently due to an inadequate drainage of tears caused by obstruction of the tear ducts by apical elongation of the premolars and first molars.

Eyelid disorders

Eyelid traumatic injuries are common, especially in cases territorial behaviour or fights form other reason between two cage mates. Entropion is seen esp. in obese guinea pigs with the lipid accumulation in the lower eyelid. This condition does not seem to have negative effect on the animal vision and is not associated with conjunctivitis.

Conjunctival hyperplasia

Follicular conjunctival hyperplasia is, at the authors practice, seen the most commonly in guinea pigs. The reactive lymphoid follicle inflammation acts as a foreign body and readily lead to the corneal erosions. Treatment of choice is affected conjunctiva excision and corticosteroid administration (if no corneal erosion is present).

Corneal disorders

Because of shallow orbit and minimal blinking, rodent eyes are prone to injury, scarring and ulcers. Linear corneal opacity is commonly seen also in cases of neurological disease and lack of blinking, especially in rats with hypophyseal adenoma. Keratitis is mostly associated with dacryocystitis (esp. in guinea pigs) or with corneal injury followed by blepharospasm. Corneal lipidosis is seen mostly in guinea pigs with the suggested aetiology of inherited lipid dystrophy. Corneal dermoid is rarely seen condition in rodents.

Purulent conjunctivitis is in rats and mice commonly associated with *Mycoplasma pulmonis* or *P. pneumotropica* infection, in guinea pigs we could detect also *Chlamydophila caviae*.

Transient mild conjunctivitis was also recorded in degus exposed UV-light for 12 hours a day, but this condition disappears with three days.

Heterotopic bone formation in guinea pigs

Heterotopic bone formation in the ciliary body is seen as a white irregular lesion close to the limbus. It may vary in the

size. The formation of this heterotopic bony tissue probably occurs as a result of vitamin C secretion into the anterior eye chamber. It was suggested that guinea pigs over supplemented with vitamin C could developed such lesions with higher incidence, but it was not proved yet.

Lens disorders

Different stages of cataracts and nuclear sclerosis are seen in older rodents; however congenital cataracts could be also seen.

Hystricomorph rodents lack the ability to properly digest sugar because of divergent evolution in the insulin structure and different physiological activity of insulin. Degus fed on high dietary sugar readily develop hyperinsulinemia with subsequent cataracts, kidney damage and type 2 diabetes mellitus (DM). Degus have physiologically increased aldosterone reductase activity in the lens. This enzyme converts glucose to sorbitol, which increases the osmotic pressure and water influx in the lens, and in the case of high glucose concentrations results in cataract. In cases of cataracts in degus, it was noted the association with feeding high dietary sugar (simple carbohydrates – fruits, carrots, orange and apple juice, banana, etc.) and lens opacity formation. When comparing the incidence of DM and cataracts in degus, it appeared that the lens is very sensitive to a high-sugar diet and cataracts also developed independently of DM. Plain viscachas,[26] the largest species of the family *Chinchillidae*, developed cataracts as a result of a high-energy diet (apples, carrots and bread) as well as degus, and changing to a high-fibre diet resulted in a significant reduction in lens pathology.

Lens luxation was at the authors practice mostly associated with traumatic injury and uveitis.

Glaucoma

Glaucoma is not so common in rodents like in dogs and is mostly associated with uveitis and anterior synechiae causing angle-closure glaucoma or with persistent pupillary membranes causing pupil-block glaucoma.

Posterior segment disorders

From posterior segment disorders a variety of congenital and acquired were described, such are: persistence of the hyaloid vasculature, coloboma, preretinal loops, saccular aneurysm, tortuous retinal vessels retinal dystrophy, retinal detachment and optic nerve hypoplasia/aplasia.

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Gastrointestinal disease in small mammals

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The most common disorder of gastrointestinal tract in herbivorous exotic companion mammals is ileus. Ileus is defined as disruption of the normal propulsive gastrointestinal (GI) motor activity from non-mechanical mechanisms (synonyms: paralytic ileus, functional ileus, gastrointestinal stasis) or because of bowel obstruction (synonyms: mechanical ileus, mechanical obstructions). The cause of the obstruction may be external to the bowel (extrinsic), within the wall of the bowel (intrinsic), or due to a luminal defect/foreign body that prevents the passage of gastrointestinal contents. Obstruction of the intestine can be partial or complete. The most common cause of the bowel obstruction in exotic companion mammals is a presence of intraluminal foreign body.

In rabbits, the term gastrointestinal syndrome or rabbit gastrointestinal disease syndrome was recently used to define a complex of clinical signs, symptoms, and concurrent pathologic conditions affecting the digestive apparatus of the rabbit. The following pathologic conditions can be included, and often occur in combination: gastric impaction, gastric gas accumulation, intestinal impaction, intestinal gas accumulation, intestinal obstruction, primary gastroenteritis, adhesions, neoplasia, pancreatitis and liver disease. It is true that the pathophysiology of the primary GI stasis etiology and secondary diseases is in exotic companion mammals very wide and they are even more complex than already described.

Non-mechanical obstruction (gastrointestinal stasis)

Gastrointestinal stasis in herbivorous exotic companion mammals (rabbits, guinea pigs, chinchillas) is commonly associated with inappropriate diet (low fiber, high in digestible carbohydrates). However, gastrointestinal stasis could be associated with any stressful situation or condition that stimulates the sympathetic nervous system including pain, systemic disease or surgery.

The GI motility decrease, the digesta retention is prolonged and the normal balanced ecosystem in bowel (especially cecum) is disrupted. Cecal pH is altered and allow potentially pathogenic bacteria to overgrowth (*Clostridium sp., E. coli*). This bacterial overload could lead to clinical enteritis/typhlitis or to enterotoxaemia.

In case of prolonged digesta retention in stomach, there is a risk of gastric ulcers development, which leads to another source of pain.

Gastrointestinal hypomotility results in gas formation in intestines (mostly caecum) or stomach. Gas distension is painful and stimulates the sympathetic nervous system and deteoriate the situation.

Secondary impaction can be produced by over accumulation of normal gastrointestinal contents due to alterations in motility, or desiccation of normal contents due to dehydration.

Metabolic acidosis is common sequela of negative energetic balance due to anorexia esp. in rabbits and herbivorous rodents.

Mechanical obstruction

Primary mechanical obstruction of the stomach is commonly seen by the authors in ferrets. Various foreign bodies of different origin (mostly rubber, foam, earplugs) are located within the stomach of the ferret. Foreign bodies are causing permanent or temporary pyloric obstruction or can be passed distally into the duodenum or jejunoileum, where can cause permanent obstruction.

In rabbits, the most common site of the GI obstruction seen at the authors practice is in the proximal duodenum. In case of distal GI is the obstruction located in the distal part of the cecum or proximal colon. However, this obstruction is commonly secondary due to caecal content dehydration and caecolithe formation (seen in rabbits and chinchillas). Caecolithe formation can be seen in with megacolon, which is hereditary disease of some spotted rabbits (English spotted, German giant, Czech Spotted etc.) and is associated with disrupted inervation of the GI tract. In guinea pigs, signs associated with GI obstruction are present in case of gastric dilatation/torsion.

Blood glucose levels and mechanical GI tract obstruction

As rabbits showing signs of stress had higher blood glucose, glycaemia could be a measurable parameter that can be used to assess the severity of a rabbit's condition and help to differentiate between gut stasis and intestinal obstruction in rabbits that are anorexic. Severe hyperglycaemia (>20 mmol/l) is associated with conditions with a poor prognosis. Rabbits with confirmed intestinal obstruction had a mean blood glucose of 24.7 mmol/l. The rabbits with confirmed gut stasis have a mean value of 8.5 mmol/l. Other haematological and plasma chemistry parameters are disturbed with chronic problems (the obstruction is present for more than 24 hours).

It was stated that the pellets of impacted hair that acutely obstruct the small intestine of rabbits are a completely different condition from the hairballs (gastric trichobezoars) or impacted stomach contents that develop during periods of gastric hypomotility. It seems, that these pellets are formed by compression of ingested hair during passage through the large intestine, and the excreted pellets containing the compressed hair are accidentally reingested during cecotrophy. This would explain why the pellets are similar in size to hard feces and are so compressed. Small hair pellets can pass through the digestive tract whereas larger pellets may obstruct the intestine causing pain, which slows gut motility and further reduces the chance of the pellet moving along the intestinal tract. In some cases, the obstruction does move through the small intestine, resulting in a spontaneous recovery as it passes into the hindgut.

Obstruction leads to progressive dilation of the GI tract proximal to the blockage. Swallowed air, and gas from bacterial fermentation, can accumulate, adding to stomach or intestine distention. As the process continues, the stomach/intestine wall becomes edematous, normal absorptive function is lost, and fluid is sequestered into the bowel lumen. In severe cases, the perfusion to the GI wall is reduced and obstructions leads to ischemia, which will eventually lead to necrosis and perforation. In ferrets, with pyloric or duodenal obstruction, ongoing emesis leads to additional loss of fluid containing sodium, potassium, chlorides, hydrogen ions and to metabolic alkalosis. In rabbits and rodents which cannot vomit, the gas and fluid accumulation leads quickly to stomach dilatation and cardiovascular collapse. In rabbits and guinea pigs, stomach dilation readily leads to metabolic acidosis. These fluid losses (vomiting or into the GI tract) can result in hypovolemia. Bacterial overgrowth can also occur in the proximal duodenum, which is normally nearly sterile. Gastric mucosa erosions and/or ulcerations can develop due to reduced vascular supply of the stomach.

Surgical gastrointestinal diseases are commonly in small mammals associated with acute onset of the anorexia and apathy. Weight loss is usually not present. However, even chronic foreign body in a stomach of a ferret, could cause chronic gastritis, blood loss, and progressive weigh loss. Obstructive gastrointestinal diseases are very painful and animals are presented with hunched posture, reluctance to move, sternal recumbency and painful abdomen. Breathing is usually shallow and mucosal membranes pale (CRT more than 3sec.) All patients should be stabilized before surgery as much is possible. In older patients, screening for other diseases such are endocrine and cardiac diseases in ferrets, kidney, liver and cardiac diseases in rabbits, kidney, liver and ovarian cystic disease in guinea pigs, kidney and respiratory diseases in rats should be performed before the surgery.

As with any abdominal surgery, the abdomen should be fully explored and all organs should be evaluated for any signs of a disease. Any other procedures, such are lymph node or liver biopsies, pancreatic insulinoma nodulectomy, etc., should be performed before opening of the gastrointestinal system. Extending the incision cranial to the tip of the xiphoid may result in diaphragmatic perforation and subsequent pneumothorax, so care should be taken during abdominal wall incision. Before entering contaminated gastrointestinal viscera, stomach or intestines should be exteorized outside of the abdominal cavity and in close vicinity wet gauzes should be placed to prevent abdominal contamination. At the end of procedure sterile instruments, new gloves and sometimes new drapes are necessary for routine gastrointestinal and abdominal wall closure. It is possible to close stomach mucosa separately with continuous suture pattern or with the use of two layers inverting suture for stomach wall closure. Intestines are closed or anastomosis is performed with single interrupted sutures. After the closure of the gastrointestinal system affected organ and abdominal cavity is thoroughly flushed with warm saline and abdominal wall is routinely closed in two layers.

Treatment of ileus

- Recognizing the pain (anorexia, inactivity, hunched posture, staring, reduced comfort behaviour, pressing of the belly against the ground, changes of the facial mimic, hiding, other behaviour changes)
- Try to find out the primary (or secondary) aetiology
- Anxiolytics, first line analgesia/sedation
  - Midazolam (0.2-0.5 mg/kg IM) + ketamin (rabbits, rodents 3-5 mg/kg IM)
  - Opioids
    - Butorfanol 0.2-0.5 mg/kg IM
    - Buprenorphine 0.01-0.05 mg/kg IM (preferred)
  - Fentanyl/fluanisone 0.2-0.3 mg/kg SC
- Oxygen
- Thermal support
- IV access and IV fluids
  - Do not use saphenous or femoral veins in case of gastric dilatation
  - e.g. Lactated Ringer's, saline

- Diagnostics
  - Abdominal radiography
  - Abdominal ultrasound (more helpful in ferrets)
  - Haematology
  - Blood chemistry
    - Pain is in rabbits associated with marked hyperglycemia (see in the text)
  - Urinalysis (esp. pH)
  - Blood acid-base balance
- Treat the primary disease/diseases
- Pain medication
  - NSAIDs (use in hydrated patient)
    - Meloxicam 0.1-0.3 mg/kg SC q12h (use with care in ferrets)
  - Opioids
    - Buprenorphine 0.01-0.05 mg/kg IM q6-8h
    - or CRI–Fentanyl 5–10 mg/kg/min, ketamine 1–2 mcg/kg/h
    - Hydromorphone 0.1 mg/kg SC, IV
    - Tramadol 10 mg/kg PO q8-12h
- Prevention of gastric ulceration
  - Ranitidine 5 mg/kg IM q12h
  - Famotidine 1–3 mg/kg PO q12-24h
- Prokinetics (only in case of non-obstructive ileus or postoperatively)
  - Metoclopramide 0.5-1 mg/kg IM q8h
  - Ranitidine 5 mg/kg IM q12h
  - Itopride 10 mg/kg PO q12h
  - Trimebutine 1-2 mg/kg PO q12h
  - (CRI lidokain 0.01 mg/kg/min IV)
- Simethicone 65–130 mg PO q3-12h
- Feeding (only in case of non-obstructive ileus or postoperatively)
  - Recovery diet (force-feeding–syringe, nasogastric tube)
  - Herbivores–fresh grass, vegetables and fruits
- Surgery
  - Gastroscopy in ferrets
  - Gastrotomy/enterotomy
  - Authors are, in general meaning, not afraid of so called "problematic rabbit gastrointestinal surgeries". The main issue is how much and how long is mechanical obstruction present, if intestine wall is necrotic, if cardiovascular changes developed, if there is a presence of gastric ulcers, hepatic lipidosis and/or metabolic acidosis and if the animal suffering from any other concurrent disease.
  - Foreign body "milking" distally
- Stress release/anxiolysis
  - Quite hospitalization
  - Benzodiazepines (see above)
  - (feromones)
- Antibiotics
  - When indicated (not used by the author routinely)
- Probiotics
  - Although probiotics used in small herbivores do not contain the most common bacteria found in healthy animals, it seems to be useful to use them to supress the overgrowth of E. coli and other pathogenic bacteria.
  - The process of transfaunation (collecting caecotrophs from a healthy animal and offering them to an anorectic patient) can be considered in some circumstances, however it is discutable.

Optimal management of GI stasis need to be determined based on particular clinical case. Dosages and therapeutical protocols used in this paper are recommended and used in the author's practice, however, need to be adjusted when indicated or not used at all.

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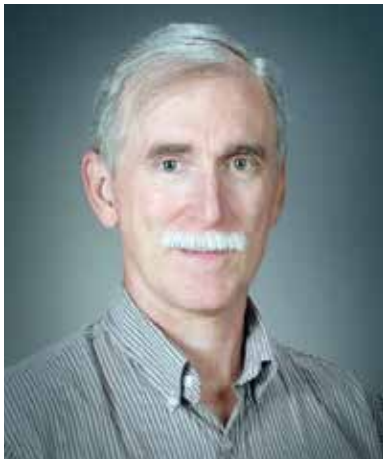
Gastroenterology



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Regurgitation: much, much more than megaesophagus

Michael D Willard, DVM, MS, DACVIM

Esophageal Weakness

Acquired esophageal weakness is usually (but not always) easy to distinguish from obstruction radiographically, especially when a barium contrast radiograph is performed. However, the severity of the radiographic lesion (i.e., the degree of dilatation) does not always correlate well with the clinical severity. Acquired esophageal weakness is typically difficult to resolve because it is hard to find the underlying cause. Myopathy, neuropathy, myasthenia gravis, dermatomyositis, dysautonomia, esophagitis, Addison's disease, *Spirocerca lupi*, tick paralysis, central nervous system disease, or infiltrative non-obstructive esophageal tumors are possible causes. Generalized myopathies and neuropathies often affect the esophagus because it is composed of striated muscle in the dog. Signs of lower motor neuron disease in these patients are sometimes seen and can include loss of muscle mass, weakness, an inability to bark, or a change in the quality of the bark. Some clients report that their animal has laryngitis, which may seem likely because these pets typically have repeated respiratory infections due to aspiration pneumonia. Treatment of the myopathy or neuropathy should resolve the problem, but symptomatic therapy for the esophageal dilatation is indicated.

Generalized myasthenia gravis usually presents as weakness during exertion which resolves after resting; however, generalized myasthenia can present in a variety of ways, including apparent lameness or permanent weakness. Electromyography and assay for circulating antibodies to acetylcholine receptors are the most definitive tests. Localized myasthenia in the dog is a syndrome in which the esophagus is the only muscle which is obviously weak. Up to 25-30% of dogs with acquired esophageal weakness have this syndrome. Third degree heart block may also be seen in some patients with megaesophagus due to myasthenia. This is diagnosed in dogs with esophageal weakness by detecting serum antibodies to acetylcholine receptors. The antibodies are relatively stable and require little special handling other than refrigeration. If myasthenia is strongly suspected but the titer is negative, it can be valuable to repeat the titer as they sometimes seroconvert later. You cannot perform an edrophonium response test to diagnose localized myasthenia. Myasthenia gravis will sometimes spontaneously resolve. Treatment for myasthenia gravis that does not spontaneously resolve may include anti-acetylcholinesterase drugs and/or cytotoxic agents. Azathioprine and mycophenolate seem to be effective drugs for this purpose. In general, we try to avoid steroids as they seem to be associated with more problems. In really severe cases, we can place a percutaneous gastrostomy tube to support the patient and lessen aspiration while waiting for the drugs to have an effect. However, a gastrostomy tube will not prevent all aspiration as the dog is still swallowing saliva which can be regurgitated and aspirated.

Hypoadrenocorticism may be responsible for causing esophageal weakness, even when the serum electrolytes are normal. This is especially true in standard sized, black poodles, but it can occur in any breed. Treatment for hypoadrenocorticism is steroids, which can make the esophagus start functioning again. However, if your diagnosis is wrong and you give steroids because you suspect the dog may have hypoadrenocorticism, all you are doing is making aspiration pneumonia and subsequent death that much more likely. Therefore, testing is much preferred to steroid trials.

Idiopathic megaesophagus (i.e., either congenital megaesophagus or acquired megaesophagus for which a cause cannot be found) can only be treated with symptomatic therapy, which usually consists of feeding the animal 3-4 meals of gruel from an elevated platform and making the pet remain in the near vertical position from 5-10 minutes after eating. Near-vertical means just that. It is useless for the dog to just lift its head up while eating; it should be standing on its back legs. The Bailey chair is a very useful device. You can find out more about it on the web (http://www.caninemegaesophagus.org/support.htm). If necessary, use a portable ladder or put the dog in a large trash can to help it remain vertical during this time. This approach is a time-honored treatment, but it does not always work. Some animals with idiopathic esophageal weakness are controlled as well (or better) if they are fed free-choice dry food from an elevated platform. Some can even be fed from the floor. Free-choice feeding encourages the pet to eat small amounts of food throughout the day, thus avoiding intermittent large meals which are more likely to be retained and further dilate the esophagus. If there is any esophageal motility remaining, the dry food may be easier for the esophagus to propel then gruel. It is difficult to predict which feeding regime will work best for a particular patient, and both of these feeding regimes may need to be tried. While most dogs with idiopathic megaesophagus die from aspiration, there are enough of them that respond well that it is very much worth trying. A reasonable percentage of dogs with idiopathic, congenital megaesophagus will spontaneously improve and have normal or near normal function. You cannot predict response to therapy or spontaneous remission; all you can do is support the patient and see what happens.

Some individuals have tried using cisapride in selected patients with idiopathic esophageal weakness that do not respond well to nutritional modification. Theoretically, cisapride would not be expected to work in these animals because cisapride primarily works on smooth muscle and canine esophagus is striated muscle. Furthermore, cisapride is expected to tighten up the lower esophageal sphincter, thus making it harder for food to pass out of the esophagus

and into the stomach. Perhaps cisapride helps patients when gastroesophageal reflux is part of the problem.

More recently, achalasia-like disease has been diagnosed in some dogs with megaesophagus. Diagnosis requires fluoroscopy. If diagnosed, it can be treated with balloon dilation or injection with Botox. Sildenafil might (?) be helpful.

Esophagitis

Esophagitis is much more common than many clinicians are aware. The difficult partly arises from the fact that esophagitis can present with clinical signs that lead one to believe the dog is vomiting instead of regurgitating. Furthermore, mild esophagitis may only cause minor signs (mild regurgitation of mucus and phlegm) while severe esophagitis can cause so much pain that patients refuse to swallow water or even saliva. Because there can be so wide a range of clinical signs, it is easy to forget that esophagitis is a differential for a patient. It is critical to identify that esophagitis is present as delayed diagnosis can have serious clinical repercussions. Substantial inflammation of the esophageal mucosa causes muscular weakness by interrupting the reflex arcs within the esophagus and/or between the esophagus and the brain. However, this weakness is not always reflected by finding megaesophagus. Most patients have very minor esophageal distention and yet can have major signs. Likewise, barium exophoras can have relatively minor changes and not reflect the severity of the esophagitis. Esophagoscopy typically shows an edematous, reddened, bleeding esophageal mucosa, + structure formation, making it the diagnostic method of choice to find esophagitis. However, in rare cases, there may be more subtle changes with thickening and discoloration (especially at the lower esophageal sphincter of cats).

Adding to this problem is the fact that there is such a wide range of causes of esophagitis. Severe esophagitis may be caused by anesthetic procedures in which animals are placed in dorsal recumbency and then have gastric acid pool in their esophagus for relatively long periods of time. However, gastroesophageal reflux from any cause can be responsible. Hiatal hernias occasionally are responsible for such reflux. Rare animals ingest caustic substances (e.g., lye), and some cats will like caustic disinfectants off their fur. However, a surprisingly large number of animals are administered caustic substances by veterinarians. In particular, tetracyclines, NSAIDs, ciprofloxacin and clindamycin are recognized as having substantial potential to cause esophagitis. Pills and capsules are notorious for lodging in the esophagus of cats, and it is therefore not surprising that doxycycline is a recognized cause of esophageal stricture in cats. Esophagitis may also be secondary to any cause of protracted vomiting. In particular, parvovirus enteritis may cause such intense vomiting that esophagitis results. If a vomiting animal has the character of its vomitus change, which seems to suggest regurgitation, consider the possibility that esophagitis has occurred secondary to the persistent vomiting. Gastrinomas (a tumor which secretes gastrin and results in massive gastric acid secretion) also causes esophagitis because of the vast and unending amounts of acid the esophagus is exposed to as the dog continually vomits. Gastroesophageal reflux may be potentiated by or even caused by esophagitis (which may be caused by reflux in the first place). Thus, there may be a positive feedback loop which can be hard to break (i.e., esophagitis causes more reflux which causes more esophagitis which causes more reflux which causes ...). Rarely there can be spontaneous inflammation, as seen with eosinophilic esophagitis in dogs. Brachycephalic dogs seem to have an increased incidence of gastroesophageal reflux, esophagitis and perhaps hiatal hernia. Finally, esophageal foreign bodies typically cause varying degrees of esophagitis. The esophagus is far more susceptible to pressure necrosis from a foreign body than are the stomach or intestines.

You should seek to prevent further gastroesophageal reflux by keeping the stomach as empty as possible by using prokinetics such as metoclopramide or, preferably, cisapride. Studies in people show that cisapride is clearly more effective than metoclopramide. The only real advantage of metoclopramide is that it can be given by injection; a useful fact in animals that are regurgitating profusely. Most importantly, gastric acid secretion should be abolished. H-2 receptor antagonists are poor drugs for achieving this goal. Omeprazole, lanosprazole, pantoprazole and esomeprazole are non-competitive inhibitors of gastric acid secretion. Therefore, these drugs can be noticeably more effective and for much longer than the H-2 blockers. Omeprazole is given at 1 mg/kg PO bid. Giving it twice daily is particularly important.

Sucralfate is of uncertain value in patients with esophagitis. Unless there is some gastric acid reflux into the esophagus (which you are desperately trying to stop in the first place), it is doubtful that the sucralfate is of much use in healing the esophagitis. However, it can help alleviate pain. Sucralfate should be administered as a slurry. In patients with severe pain that refuse to even swallow their saliva can receive viscous lidocaine (OTC).

A combination of omeprazole and cisapride seems to be the most effective medical treatment regime. Glucocorticoids have been thought to help retard fibrous connective tissue proliferation and cicatrix, but their effectiveness is uncertain (and they might predispose to infection). Placing a PEG tube seems to have some real advantages in patients with very severe disease such that they will not eat or cannot refrain from regurgitating. First, we will then know that the cisapride and omeprazole tablets will reach the stomach. Second, we will also know that the animal will receive its caloric and protein needs, and hopefully with less irritation to the esophagus than would have occurred otherwise.

Esophageal Stricture

If there is severe esophagitis, cicatrix may form and obstruction develop subsequently. Diagnosis of stricture is best accomplished by esophagoscopy IF the operator is familiar with such obstructions. It is surprisingly easy to pass a slender endoscope through a stricture and never recognize the stricture. It is also surprisingly easy to miss a partial obstruction due to a stricture with a barium esophagram. If you suspect a stricture and must use a barium esophagram

to make the diagnosis, use barium mixed with solid food. Balloon-dilatation or bougienage is recommended if a stricture has occurred. Many animals need to have 2-6 dilatation procedures (all the while being treated for esophagitis), although some only need one procedure and some need more than 15. Do not try to resect the stricture unless you have had prior dilatation procedures fail.

Cicatrix (i.e., scarring) may occur after an episode of severe esophagitis from any cause (including foreign objects). It is particularly easy to miss this problem on a barium swallow if only liquid barium is used. If radiographs using liquid barium are nonrevealing, repeat the study using barium mixed with food, which is more likely to stop at a partial obstruction. Endoscopy is very good at finding these lesions; however, you must keep in mind the size of the patient as you evaluate the esophageal lumen. A partial stricture will be very obvious in a 10 lb dog or cat but may not be apparent in an 85 lb animal. Balloon-dilatation or bougienage is usually effective; it is also more likely to be successful than surgery and resection of the affected area.

For particularly difficult cases, stents may be placed in the esophagus. These must be sutured in place. The major point to remember is that if an animal starts to have problems days to weeks after anesthesia, consider strongly the possibility that an esophageal stricture has developed secondary to esophagitis. BE-tubes are the latest technique used for difficult strictures. In this technique, the owners balloon the stricture twice daily at home with an indwelling tube that doubles as a balloon and a feeding tube.

Hiatal Hernias

Hiatal hernias may be more common than suspected. Shar Pei's seem to have a relatively high incidence of hiatal hernias. They can be difficult to diagnose unless you know how to look for them. Sometimes seen on plain radiographs and simple barium contrast radiographs, the more occult cases sometimes need more aggressive diagnostics. Sometimes one must manually put pressure on the abdomen during film exposure to try to push the stomach through the hernia and into the chest so that it can be diagnosed radiographically. Endoscopic diagnosis is not always straightforward. You may need to put the endoscope into the stomach and retroflex it in order to see the abnormality. Even when found, the big question is whether the hiatal hernia is causing a problem or is an "innocent bystander". In particular, if you have an older dog or cat (i.e., > 1-2 years old) that just started having clinical signs, you should strongly consider that the hiatal hernia is a fortuitous finding that is not responsible for the clinical signs.

Esophageal Foreign Bodies

Esophageal foreign bodies usually consist of bones but may be rawhide treats, food, dental chew toys, toys, balls, rocks, wood, etc. They usually lodge at the thoracic inlet, base of the heart, or lower esophageal sphincter. A history of a patient that begins to regurgitate (as opposed to vomit) acutely is very suggestive of acquired esophageal obstruction due to a foreign object. These patients may continue to drink water, but they typically refuse solid food because the food bolus cannot pass by a partial esophageal obstruction and causes pain whenever it tries to. A casual, careless history that fails to raise the suspicion of regurgitation will typically lead the clinician to suspect an acute gastritis. However, the realization that the patient is regurgitating (as opposed to vomiting) should be a "red flag". Too often, a pet which has ingested a foreign object is treated conservatively while we wait and see if the supposed gastritis spontaneously resolves. This is problematic because foreign bodies can erode and perforate the esophagus much quicker than they would stomach or intestines.

Plain radiographs should be performed first. Bones are a common cause of obstruction, and plain films that are made with proper technique and then carefully evaluated are diagnostic in most cases. Remember that poultry bones are not as radiodense as the patient's bones, which means that excellent radiographic technique is required to see them. Foreign bodies in the esophagus can perfectly mimic pulmonary or mediastinal masses; you often cannot tell the difference with plain radiographs. If poor contrast in the region of the esophagus, pleural effusion or pneumothorax are seen, one must seriously consider esophageal perforation and mediastinitis. If plain films are not diagnostic, then contrast films can be performed. Barium provides better contrast, but iodide is safer if there is an unsuspected perforation. Esophageal perforation may occur at variable times after ingestion of a foreign object. Even a blunt object, if tightly lodged in the esophagus, can cause ischemia and perforation in 2-3 days. The prognosis for animals with esophageal perforation and severe mediastinitis is guarded to poor, depending upon their condition at the time of diagnosis.

Endoscopy is almost always the preferred method of removing foreign objects, but fluoroscopic and surgical techniques can be effective if the operator is well trained. Rigid endoscopes allow much more control of the foreign object and are preferred to flexible scopes for removal of these foreign objects. It is especially useful to be able to pull the object into a rigid endoscope and then withdraw it and the scope as a unit, thus protecting the esophagus. The main disadvantage of rigid endoscopes is that they are often not long enough in larger dogs. Finesse is required; brut force can easily lacerate/perforate the esophagus. If a large object or a bone cannot be easily dislodged, do not force it lest you perforate a previously intact esophagus; instead, you can use rigid equipment to "chew" it up and hopefully dislodge it. If that fails, passing a large Foley catheter behind the foreign object and inflating the balloon often helps; it distends the esophagus (thus freeing the foreign object) and then is used to pull the object out. If you cannot pull a foreign object out of the esophagus, you can try to push it into the stomach. However, do not push bones or other foreign objects into the stomach unless you are sure that it is smooth on the aborad side and will not further damage the mucosa. Finally, be careful if you insufflate the esophagus lest you rupture a weakened area in the mucosa and/or cause a fatal tension pneumothorax.

GI tract bleeding, ulcers and erosions (more common than most people realize)

Michael D Willard, DVM, MS, DACVIM

Hematemesis necessitates a slightly different approach than we take with other vomiting cases because some rule-outs become more likely while others become much less likely. We will be including upper gastrointestinal bleeding of any cause in this discussion. For starters, we will not be discussing vomiting that produces "flecks" of blood because this can be seen in any dog (and perhaps cat) with vigorous vomiting in which the gastric mucosa is traumatized by the physical act of vomiting. It is easy to identify fresh blood in the vomited material as long as the patient is not eating something that is red or that produces a pink color to the vomited material simple secondary to pigment leaching out of the food material. Most of the time, hematemesis is denoted by a "coffee-grounds"-like material that most clients (and some veterinarians) do not recognize as blood. A common mistake is being concerned over "dark stools". Noting that a patient has dark stools is generally useless. Lots of dogs have dark stools and no problems or GI blood loss at all. The color of the stool is not an issue until the stool is pitch-tar-coal-asphalt black. Then it may be melena (if it is not due to Bismuth or a lot of green bile giving it a near-black appearance). If in doubt, just place some fresh feces on absorbent white paper and see if a reddish color diffuses out from the feces, confirming that there is blood present. Melena is only seen if there is acute loss of a lot of blood into the upper GI tract. Most dogs losing blood in the upper GI tract do not have any important changes in the color of the feces. Rather, you might see anemia and hypoalbuminemia. Also remember, you may or may not see hypoglobulinemia; it all depends upon what the serum globulin concentration was before you started losing blood. Sometimes the BUN is higher than expected based upon the serum creatinine, but again this is only expected if there is a lot of blood being lost in a short period of time. Fecal occult blood tests are seldom that helpful or necessary, but can occasionally be informative in confusing cases. However, you need to use a test for which the laboratory has substantial experience in dogs so that the results can be meaningfully interpreted. Some fecal blood tests will routinely give a positive reaction when used on canine feces.

When there is a substantial amount of blood being ejected from the mouth, there tend to be 3 major reasons: coagulopathy, swallowing blood from elsewhere and gastrointestinal ulceration/erosion (GUE).

Ulcers And Erosions

Drugs are still a very important cause of GUE in the dog, despite all the newer, "safe" NSAIDs. High doses of dexamethasone also have substantial potential for significant GUE. Prednisolone by itself is generally not ulcerogenic unless it is used in very high doses (e.g., > 2-3 mg/lb/day) or is administered to a patient with other "ulcerogenic" risk factors (e.g., hypoxia, poor perfusion), and even then it is not particularly bad. Combining steroids and non-steroidal drugs can be devastating. You can use ultra-low dose aspirin (0.5 mg/kg once daily) when treating IMHA dogs with steroids.

There continues to be a substantial problem with the use of nonsteroidal anti-inflammatory drugs (NSAIDs) in dogs. All NSAIDs have the potential to cause devastating GUE, and some of these non-steroidal drugs are renowned for their toxic effects (i.e., indomethacin, naproxen, flunixin). Ibuprofen is also particularly ulcerogenic in the dog because it undergoes an enterohepatic circulation. Flunixin is a particularly dangerous drug from the standpoint of causing GUE. It is extremely potent and can be devastating if combined with steroids like dexamethasone. While able to cause significant ulceration and bleeding all by themselves, the ulcerogenic potential of NSAIDs is particularly augmented by other factors, especially concurrent administration of another NSAID or a corticosteroid, and hypoperfusion of the alimentary tract. Even though many dogs seemingly tolerate such combination therapy, you need to realize that you are "walking on thin ice" (see comments above on use of ultra-low dose aspirin). Many to most of the dogs treated with NSAIDs have endoscopically visible erosions, hemorrhages and/or ulcers, depending upon the drug used and the dose administered. It is important to note that most dogs with GUE due to NSAIDs may be completely asymptomatic. Finally, there is tremendous between-dog variation regarding the alimentary tract response to NSAID's; some dogs may almost bleed to death because of a small dose of aspirin while most dogs would tolerate a much larger dose with relative impunity.

While the newer Cox-2 NSAIDs (e.g., carprofen, etogesic, deracoxib, meloxicam, etc) have much less potential for causing GUE than the older NSAIDs, you can still see GUE (and even perforation) due to these drugs. Part of the problem is that these "safe" drugs are being used so extensively and casually. The problem often revolves around using inappropriately high doses (after all, the drug is so safe that ...), using the drug at the wrong time (e.g., when the patient is experiencing shock or has poor perfusion to the alimentary tract), and possible using the drug too soon after stopping some other NSAID. The concept of a "washout" period when changing from one NSAID to another is extremely controversial. There is published literature to the contrary, but the fact is that nobody really knows at this time.

Clinical Approach To The Patient With Hematemesis Or GI Bleeding

There is often something in the history that is suggestive of the cause of the bleeding (e.g., use of NSAIDs, shock, etc). If that is the case, then it is often reasonable to begin appropriate therapy after requesting basic laboratory testing (e.g., CBC, serum chemistry panel) to determine the severity of the bleeding and if there are other diseases (e.g., hepatic disease, renal disease) present. Imaging (especially ultrasound) is typically appropriate but not necessarily imperative at this time. If the cause of the GI bleeding or hematemesis is not obvious, if the patient has not responded to 5-7 days of appropriate therapy, or if the bleeding is severe, then additional diagnostics are important and should be performed promptly.

Medical management: If the patient is not exsanguinating, the cause is known or strongly suspected, and the patient has not had 5-7 days of appropriate medical therapy, then medical therapy is often reasonable as opposed to doing a major diagnostic work up. In distinction, if the patient is exsanguinating or if the patient has not shown any appreciable response to 5-7 days of appropriate medical therapy for the ulceration, then it is usually reasonable to surgically resect the ulcerated area. Note – when I say "response", I am not referring to the patient being cured; I am referring to clear evidence of improvement. If surgery will be considered, it is usually very wise to perform gastroduodenoscopy before the surgery to be sure that you find all of the sites of ulceration. It is very easy to fail to detect an ulcer at surgery, and endoscopy usually allows one to easily find all areas of ulceration. Sometimes intraoperative endoscopy is necessary to help the surgeon find the ulcer(s).

If medical management is elected, first be sure to remove the cause of the GUE. If the cause is not removed, medical management tends to be far less successful. Next, be sure that the patient is well hydrated; healing of the gut requires or is at least benefitted by adequate perfusion. If there is significant gastroduodenal reflux of bile, metoclopramide or cisapride may be helpful in preventing bile from entering and/or staying in the stomach and augmenting the ulcerogenic process.

H-2 receptor antagonists are commonly used but are very ineffective. Cimetidine, ranitidine, and famotidine are very poor medications for decreasing the gastric hydrogen ion concentration. These drugs cause tachyphylaxis (i.e., the become progressively less and less effective).

Proton pump inhibitors are the most effective antacid drugs we have. Omeprazole, lansoprazole and pantoprazole are the most effective inhibitors of gastric acid secretion we currently have available. Omeprazole is available OTC as Prilosec®. The H-2 receptor antagonists seem quite adequate for GUE except in some animals with gastrinomas and those with esophagitis due to gastroesophageal reflux: these seem to be the main reason for using the PPI's. The dose of omeprazole is 1-2 mg/kg bid. The dose of lansoprazole (Previcid), pantoprazole (Protonix), and esomeprazole (Nexium) is 1 mg/kg IV (not approved for use in dogs). It generally takes 2-5 days for a PPI to have maximal efficacy; but, the immediate effects on gastric acid secretion is often still better than that obtained by high dose H-2 receptor blockade.

Misoprostol (Cytotec®) is a prostaglandin E analog which was primarily designed to be a prophylactic drug used to prevent GUE due to NSAIDs. It is also useful in treating existing ulcers, but its higher cost and more plentiful side effects usually make it undesirable as a first line therapy for GUE. It is typically used at a dose of 2-5 ug/kg, 3-4 times daily. It can cause abdominal cramping and diarrhea, but the drug seems relatively safe in dogs. The main disadvantage is that it must be given orally, which is not possible in some vomiting animals. Because it is a prostaglandin analog, it should not be used in pregnant females for fear of causing abortion or miscarriage. It is the best drug available that can be used to prevent NSAID-induced ulceration, but it is not uniformly effective in dogs. The main indications to use it appear to be a) the patient that must have NSAID's to function, but which evidences side-effects from them (e.g., anorexia, vomiting) and b) the patient that seemingly needs to receive NSAID's that have substantial potential for such side-effects (e.g., piroxicam).

Sucralfate seems to be extremely effective in protecting those areas which are already ulcerated and helping them heal. The only common side-effect is constipation. There is minimal absorption from the intestines, but it does have the capacity for adsorbing other drugs (e.g., enrofloxacin). While carafate is effective in treating ulcers, it is not always effective in preventing ulceration. In patients with severe hematemesis and anemia, we sometimes us a large "loading" dose (e.g., 3-6 grams) initially and then decreasing the dose to 1 gram tid to qid. No body know if theloading dose is beneficial or not. My major problem with this drug is that it must be given orally, which does not always work in vomiting dogs. Sometimes you may dissolve the table in water or buy the suspension and have less problem with that being vomited.

Canine acute pancreatitis: it does whatever it wants to do

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Diagnosis

History and physical examination are, as always, critically important; but, they are not that helpful for diagnosing pancreatitis. Rather, they are more useful for finding other problems that may be mimicking pancreatitis. Regarding signalment, Schnauzers and Yorkies are famous for acute pancreatitis, but these breeds get a lot of other diseases that cause vomiting. Furthermore, acute pancreatitis can be found in any breed of dog. Canine pancreatitis is classically considered to present with acute vomiting and anorexia. Abdominal pain is frequently present, but it is easy to miss during physical examination, and fever is occasionally seen. However, we are recognizing more and more and more cases in which a) vomiting is not as severe as we have come to expect, and b) in which we are initially strongly drawn to other diagnoses. To some extent, many of us are no longer sure what a "typical" case of canine pancreatitis is. Some dogs (especially those with pancreatic abscesses) may have relatively mild, intermittent, unimpressive vomiting and continue to eat a reasonable amount of food. Many of the severely ill patients may present in classic systemic inflammatory response syndrome (SIRS) which is what used to be called septic shock (until we found out that you can have the same thing occur with any cause of massive inflammation). Many dogs with very severe acute pancreatitis present as though they had an acute, septic abdomen. Some have substantial amounts of abdominal fluid. If acute pancreatitis is associated with or due to pancreatic carcinoma (rare), you may rarely see a dog that has widespread subcutaneous fat necrosis causing sterile abscesses that are typically painful and cause cutaneous discoloration. Most cases of canine pancreatitis seem to be temporally related to either ingestion of fat or lipemia associated with diabetic ketoacidosis. Trauma and drugs can also cause canine pancreatitis. Drugs that are suspected of causing pancreatitis in people and animals include azathioprine, sulfonamides, tetracycline, and potassium bromide.

CBC's often show an inflammatory leukogram, but 1) this is a very nonspecific finding and may be due to any number of problems and 2) not all animals with acute pancreatitis have a notable leukocytosis. Degenerative left shifts and substantial toxicity of circulating WBCs can be seen if the patient is in SIRS. Likewise, thrombocytopenia due to DIC is often found in severely affected patients. However, some animals with clinically severe pancreatitis have absolutely normal leukograms. There are no findings on CBC that definitively diagnose or definitively eliminate pancreatitis

Serum biochemical panels are not as helpful as we would like. Serum lipase and amylase activities are insensitive (each is about 50%) and nonspecific (again, about 50%) for pancreatitis. We no longer request them in dogs or cats. Dogs with acute pancreatitis and even pancreatic abscesses have had normal serum lipase activities. We have also identified dogs with drastically increased serum lipase activities that have intestinal foreign objects or gastritis, but no gross evidence of acute pancreatitis. Lipase is produced by the canine gastric mucosa which explains why inflammation or damage to the stomach can result in excessive serum lipase activity. Canine TLI is slightly more specific than amylase and lipase, but it is still not a sensitive test (approximately 35%). Therefore, it too has very poor negative predictive value. We have seen plenty of dogs with pancreatitis that had normal serum TLI's.

The immunoreactive canine pancreatic lipase assay (i.e., cPLI or Spec cPL) appears to be the most sensitive (approximately 80-85%) test for pancreatitis available. There are a few false negative results with this test, but it is clearly much more sensitive than any other blood test available. The real question is how specific it is for clinically important disease (i.e., lesions of the pancreas that are causing clinical disease as opposed to microscopic lesions that are clinically silent). To some extent, you can best think about cPLI like "ALT for the pancreas". The biggest advantage is that if the cPLI test is negative, it is much less likely that pancreatitis is the real problem and you need to look very hard for extra-pancreatic disease in the dog.

Blockage of the main pancreatic duct due to swelling due to generalized pancreatitis, an intrapancreatic granuloma, or an abscess that subsequently blocks the pancreatic duct may cause extrahepatic biliary tract obstruction (EHBO) with a notable increase in serum alkaline phosphatase and serum bilirubin. Pancreatitis is probably the most common cause of EHBO in the dog. Thus, while EHBO is very suggestive of acute pancreatitis (assuming that the patient does not have a mucocoele, which is usually easy to detect with ultrasound), relatively few dogs with acute pancreatitis develop EHBO. Furthermore, there are reasons for this triad of signs besides acute pancreatitis and extrahepatic biliary tract obstruction (e.g., cholangitis-cholangiohepatitis). Ultrasonographic evaluation of the abdomen (discussed below) is particularly helpful in these patients.

Plain abdominal radiographs help eliminate other diseases which may mimic acute pancreatitis. Not finding evidence of other abdominal disease (e.g., foreign object) is helpful in eliminating obstruction and narrowing the list of differential diagnoses. Occasionally, one finds radiographic signs which specifically suggest acute pancreatitis. A sentinel loop (i.e., a dilated, air-filled segment) in the descending duodenum, and/or lack of serosal detail in the upper right abdominal quadrant, and/or lateral displacement of the descending duodenum on the ventro-dorsal projection, and/or a mass medial to the descending duodenum (on the ventro-dorsal projection) and/or a mass just behind the liver and just below the pylorus (on the lateral projection) are somewhat suggestive of acute pancreatitis. These findings are only meaningful if present; many (probably most) dogs and cats with acute pancreatitis do not have any of these

radiographic findings. Probably the most greatest value of abdominal radiographs is that they help eliminate other diseases that could be causing signs similar to those caused by pancreatitis.

Abdominal ultrasonography often finds abnormalities that suggest or are consistent with pancreatitis as well as eliminate other potential causes of vomiting and abdominal pain. Ultrasonography has been suggested to be about 40-70% sensitive in finding canine pancreatitis. One may sometimes detect hypoechogenicity surrounded by hyperechoic fat in the region of the pancreas that is due to pancreatitis. At other times, a markedly thickened pancreas may be found. Both findings are very specific evidence of pancreatitis. Evidence of EHBO (i.e., dilated bile ducts, not just a big gall bladder) is very suggestive of pancreatitis. Rarely, you will find dilated bile ducts due to inflammatory biliary tract disease, but this is not nearly as common a cause as is biliary tract obstruction. Any dog with extra-hepatic biliary tract obstruction (that does not have a mucocoele) and that is vomiting/anorexic should be assumed to have pancreatitis until proven otherwise. It is very important to note that the ultrasonographic appearance of the pancreas can change dramatically within a few hours, so repeating abdominal ultrasound later on the same day or early the next day can sometimes be most revealing.

Diagnosing pancreatitis during laparotomy is the least desirable method of diagnosis. Some patients present exactly like acute septic peritonitis but are ultimately diagnosed as having non-septic pancreatitis. There is nothing wrong with doing an exploratory laparotomy in a patient in which septic abdomen is a major consideration, only to find out that the patient has non-septic pancreatitis. We very rarely have reason to biopsy a normal appearing canine pancreas, and what grossly appears to obviously be pancreatitis in the dog seldom requires a biopsy unless carcinoma is a concern. However, you should never simply look at what appears to be an obviously neoplastic mass in the pancreas and make a diagnosis of carcinoma without biopsying it, no matter how extremely terrible it appears. Pancreatitis is much more common in dogs than pancreatic carcinoma, no matter how bad the pancreas looks or how many adhesions are present. If you biopsy the pancreas, it is important to obtain a biopsy that goes deeper than the superficial necrotic surface or adhesions. Cytology can be useful for making a presumptive diagnosis; however, I have seen at least one case in which cytology of a pancreatic mass was read out as carcinoma by two accomplished cytologists and yet multiple biopsies all came back as necrotic pancreatitis. Anecdotally, there appears to be more risk of causing iatrogenic pancreatitis with surgery in the dog than in the cat. Maintaining excellent mesenteric perfusion during anesthesia and performing the surgical biopsy with reasonable care and good technique minimizes the risks. Laparoscopic biopsy of the pancreas might be safer than surgical biopsy, but that is just anecdotal at this time.

Chronic pancreatitis (i.e., chronic pancreatitis with intermittent, relatively mild recurrences) can be challenging to diagnose. Dogs with episodic vomiting due to recurrent bouts of pancreatitis may not have any other signs of disease, and they invariably are admitted to your clinic for a work up after the last bout has run its course or is on the mend. Episodes of vomiting and anorexia due to recurrent pancreatitis can be random and unpredictable. In such patients, the previously mentioned diagnostics may be attempted, especially when acute exacerbations occur. Very rarely, upper gastrointestinal barium contrast radiographs may rarely reveal duodenal abnormalities (e.g., dilatation, stricture) which suggest that recurrent bouts of acute pancreatitis have caused scarring of the pancreas which in turn have compromised the maximum size of the duodenal lumen. Ultrasonographic changes are nice if they are present, but they can be minor making it difficult to accurately interpret them. Feeding an ultra-low fat diet for 3-4 times longer than what was previously the longest interval between episodes may sometimes be helpful in making a presumptive diagnosis. If episodic vomiting/anorexia does not recur while feeding such an ultra-low fat diet for an interval so long that you would have been sure to experience another episode, then we can often assume (rightly or wrongly) that the signs were due to pancreatitis (or perhaps some other dietary-responsive disease). Anytime you find exocrine pancreatic insufficiency (diagnosed with TLI) in a breed that is not commonly affected with pancreatic acinar atrophy (e.g., German shepherd, rough-coated Collie), then chronic pancreatitis becomes a major concern.

Pancreatic abscesses in dogs (as opposed to cats) are almost invariably sterile. Affected dogs typically can have a much more chronic, smoldering course (e.g., vomiting for a month or more, mild loss of appetite) than most dogs with more typical acute pancreatitis. We have even found a few dogs which had pancreatic abscesses that were completely asymptomatic. Abdominal pain may be present or absent. CBC and serum biochemistry findings are unpredictable. Diagnosis requires ultrasound. Treatment may be surgical marsupialization, percutaneous ultrasonographic drainage or just observation.

Therapy

As of this writing, there is not a single, well-designed, robust, prospective, stratified study on the treatment of canine acute pancreatitis. Therefore, all any of us has is opinions, period.

Nothing per os (NPO) has been the classic therapy for pancreatitis for many years. While it is true that they feed people with pancreatitis earlier than we feed dogs, you must remember that human pancreatitis is unassociated with dietary fat. People get pancreatitis from alcohol, trauma, gall stones and MOF (multiple organ failure). Canine pancreatitis is associated with dietary fat (as well as surgical trauma when poor technique is used around the pancreas). An initial study in Australia suggests that it is safe and perhaps beneficial to feed dogs with acute pancreatitis per os or with an esophagoscopy tube as soon as they can tolerate it (i.e., they do not get worse, even if they are still vomiting). I recommend that a) you feed a diet with as low a fat content as possible, and b) if the feeding is associated with worsening of the vomiting, that you stop it and either try again in a day or two, or go to jejunostomy feeding. Do not try to get full caloric intake into the patient; rather, start with small amounts to see if the patient will hold down the food. Obviously, if feeding is associated with worsening of the vomiting or general condition, stop the feeding. I generally start feeding potato or rice (i.e., no fat) and gradually work my way up to commercial diets with low fat content. Try hard to avoid parenteral nutrition.

Fluid therapy is critical, and subcutaneous administration of fluids is clearly inferior to IV fluids for all but mildly affected animals. IV fluid administration is often sufficient, even in dogs in which a pancreatic granuloma has temporarily blocked the main bile duct. Adequate pancreatic circulation is probably crucial for healing damaged pancreatic tissue; therefore, it is probably better to provide a little too much fluid rather than a little too little fluid unless the patient has congestive heart failure or oliguric renal failure. The abdominal viscera is not "first in line" to receive circulation when the patient is dehydrated (which most dogs with pancreatitis are when they come to your office). Obese and fat dogs (which describes a lot of dogs with pancreatitis) do not necessarily have skin tenting when they are dehydrated. Likewise, although you might expect dry, tacky oral mucus membranes, a nauseated animal may be salivating enough to make the mucus membranes moist even though it is dehydrated. If a vomiting dog is not eating or drinking, then it is dehydrated regardless of how well hydrated it appears on physical examination. However, if you give substantially too much crystalloid and dilute the serum protein concentrations, this could be detrimental.

One should monitor the serum albumin concentration during fluid therapy in these patients. If the serum albumin concentration decreases significantly (i.e., to < 2.0 gm/dl), then the plasma oncotic pressure likewise decreases which diminishes the effective perfusion at the capillary level. Since perfusion is so critical to treating dogs with pancreatitis, one should probably become concerned whenever the serum albumin concentration falls below 2.0 gm/dl. It is very hard to administer enough plasma to significantly raise the plasma albumin concentration. Half of the albumin in the plasma that you administer will end up in the extravascular compartment instead of the intravascular compartment. Hetastarch is a better choice because it will stay in the circulation and raise the plasma oncotic pressure for much longer than plasma. Be careful with hetastarch; it occasionally is associated with worsening of clinical signs. It is best to give small amounts repeatedly than just give a large amount. Human albumin can be used effectively, but it occasionally causes anaphylactoid reactions that can kill the patient; therefore, it is not recommended. Canine albumin is safer, but it does not last as long as hetastarch. Plasma might be more effective than hetastarch because plasma might also restore circulating protease inhibitors and replenish AT III (which is a treatment for DIC). This is a very contentious point. One retrospective study has shown that plasma did not help treat dogs with pancreatitis; however, this study suffers from the problems inherent in all retrospective studies.

If the patient cannot tolerate early refeeding (i.e., the vomiting becomes worse), then jejunostomy feeding is another option. It is safer, less expensive, and less dangerous than parenteral nutrition, and has been associated with a better prognosis. In particular, it should be considered if an exploratory laparotomy was performed when the pancreatitis was diagnosed because a J-tube can be placed at that time. Alternatively, one can place a jejunostomy tube via laparoscopy, through a G-tube, and via the nose (naso-jejunostomy).

Antiemetics are useful in patients that are vomiting repeatedly or that feel so nauseated that they feel terrible. I prefer to only use antiemetics for short periods of time because I want to see if the patient is improving enough so that it no longer needs the antiemetic to stop vomiting. However, if the patient is vomiting multiple times per day or obvious feels terrible due to the nausea, then maropitant (1 mg/kg SQ) appears to be very useful. Maropitant might also have the advantage of providing some analgesia because it blocks Substance P binding. Dolasetron (0.3-1.0 mg/kg qd) and ondansetron (0.25 mg/kg qd) can also be effective.

H-2 receptor antagonists have been used to "prevent gastric ulceration and erosion". It is doubtful that ulceration/erosion is a common problem in all but the sickest patients. Furthermore, if one desires to protect the gastric mucosa, the proton pump inhibitors are far superior to the H-2 receptor antagonists. Pantoprazole (1 mg/kg IV qd) or omeprazole (1-2 mg/kg PO bid) are the most commonly used drugs. I suspect that they provide more benefit by being antidyspepsic in nature (thereby making the patient feel better) than they do by preventing ulcers. Currently, there is no clear evidence that they are indicated in dogs with acute pancreatitis.

Antibiotics have been used to "prevent" secondary bacterial infection of the inflamed pancreas, which is supposed to be "fertile ground" for infection. However, there is minimal evidence that bacterial infection is of any significance in routine canine pancreatitis. Antibiotics do not hurt these patients, but it is very questionable how helpful they are. However, dogs in SIRS due to pancreatitis may be a different story. Any dog in SIRS from any reason is potentially at increased risk of infection due to severely compromised mesenteric circulation.

Currently, glucocorticoids are very controversial in the treatment of pancreatitis. While they increase serum amylase and lipase activities, they do not cause pancreatitis. It is possible (this is controversial) that they may be useful in treating patients that are in Systemic Inflammatory Response Syndrome (i.e., SIRS, which used to be called "septic shock") due to the pancreatitis. At this time, there are good data showing that it is probably reasonable to give physiologic doses because dogs in SIRS typically can have what has been termed "Critical illness related corticosteroid insufficiency" (CIRCI), that is to say that they are relatively hypoadrenal. However, this is a very controversial statement. If steroid therapy for pancreatitis is contemplated, it should probably be reserved for the severely ill dog which is not responding to appropriate fluid resuscitation.

If DIC appears to be a major problem, aggressive administration of fresh frozen plasma to replace clotting factors and anti-thrombin III concentrations is probably more effective than heparin.

Analgesics are critically important. One must remember that dogs are clearly much "tougher" than people, and they often hide their pain well. Unless there is some good reason to the contrary, it is best to routinely assume that dogs with acute pancreatitis are in pain and will benefit from analgesic. In the very mildest of cases, butorphanol might be sufficient. In moderate cases, methodone is reasonable. As the pain becomes more severe, we progress to constant rate infusions of fentanyl. Is the most severe cases, we administer a constant rate infusion of fentanyl, lidocaine and ketamine.

Chronic small bowel diarrhea: IBD is not the most common cause

Michael D Willard, DVM, MS, DACVIM

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD), depending upon how you define it, is not the most common cause of chronic small or large bowel diarrhea in dogs and may not be as common in cats as was once believed. In this discussion, we will define IBD as "idiopathic inflammation of the intestines". This means that you cannot diagnose IBD just by histopathology. You diagnose IBD by finding intestinal inflammation and showing that it is idiopathic by eliminating diet, parasites, bacteria and fungal agents as the cause. You cannot eliminate dietary causes and bacterial causes by histopathology or blood tests; therapeutic trials are necessary. This is very important because diagnosing IBD generally results in anti-inflammatory or immunosuppressive drugs being used. However, if the patient has dietary-responsive or antibiotic-responsive disease, then these drugs are generally unnecessary. I stress this point because many patients have been erroneously diagnosed, improperly treated, and significantly harmed because IBD is a "fashionable" or "trendy" diagnosis. IBD is a real syndrome and is important for the veterinary practitioner to understand. However, it often degenerates into an excuse of convenience rather than a real diagnosis. More and more evidence is accumulating that shows that bacteria are probably a major source of the inflammation in dogs and cats with this disease. See below, under Antibiotic-responsive enteropathy.

Dogs With Chronic Small Bowel Diarrhea (Not Ple)

Once parasites, protein-losing enteropathy, and maldigestion are eliminated (i.e., you have determined that the patient has a non-PLE malabsorptive disease), the question is whether to recommend therapeutic trials or a major diagnostic work up. If the patient can tolerate a possible delay of 4-8 weeks without undue risk, then therapeutic trials are reasonable. If therapeutic trials are performed, they must be designed such that even if they fail, useful information is obtained and the clinician is further ahead than previously. Always ask yourself: "If this therapy fails, will I really know more about what the patient probably has, or will I be as confused as I was before treating it?".

An elimination diet for dietary responsive disease is often useful for non-protein-losing malabsorptive disease. There is no such thing as a commercial diet which is an appropriate elimination diet (i.e., is hypoallergenic and appropriate to look for non-allergic intolerance) for all dogs. We often see cases in which the right thing was done (i.e., an elimination diet was used); but, it was done in such a poorly planned or implemented fashion that the effort was wasted. One must carefully investigate the history and see what the patient has eaten in the past. However, even when you have determined what dietary ingredients the patient has previously been exposed to, it is sometimes difficult to find a diet that works for that particular patient. In some cases, all of our well-planned hypoallergenic diets fail but a chance try at some commercial brand works.

When starting the patient on an elimination diet, one may use a homemade diet or a commercial diet. There are many excellent commercial diets, and they usually work. Home-made elimination diets sometimes work when commercial diets do not; however, this is very uncommon. Therefore, you will have to decide which is most appropriate in the patient that you are treating. The hydrolyzed diets are usually good but are not always the best choice for every patient. Some animals respond better to a novel protein diet than a hydrolyzed diet, and vice-verse. Which ever elimination diet is used, one must be prepared to feed it and it alone for an absolute minimum of 3-4 weeks before its efficacy can be accurately determined. Rare cases need to be feed a diet for 6-8 weeks before they respond, but this is probably well less than 5% of cases. If a diet seems to be effective (i.e., weight gain plus resolution of diarrhea) then continue it for at least another 3-4 weeks to be sure that it was the diet that made a difference as opposed to the patient having some transient improvement due to any number of causes.

Antibiotic-responsive enteropathy (ARE) seems to be a relatively common problem in dogs. It can best be described as a syndrome in which there are substantial numbers of bacteria in the upper small intestines AND the host responds to them in such a manner as to cause intestinal dysfunction. These bacteria are not usually obligate pathogens. Rather, they can be of any species, and *E. coli, Staph, Strep*, and *Corynebacterium* are particularly common aerobic/facultative anaerobic bacteria found in the upper small intestines, while *Clostridium* and *Bacterioides* are especially common anaerobic bacteria. These bacteria are probably commensals or they may represent contamination from ingested material which is not eliminated by normal host defense mechanisms. The signs they produce, if any, seemingly depend upon at least two factors: a) which bacteria are present and b) how the host responds to them. The relationship of ARE to IBD is unclear, but it seems very possible that bacteria could be responsible for either initiating and/or perpetuating the intestinal inflammation we call IBD. The term "dysbiosis" has been suggested as the bridge between ARE and IBD – that is to say that having bacteria that are somewhat prone to cause problems (i.e., usually enterics such as E. coli) as opposed to having overt pathogens.

Antibiotic-responsive enteropathy is hard to definitively diagnose with laboratory tests. Histopathology and cytology of the intestinal mucosa are extremely insensitive at detecting ARE. Serum cobalamin and folate concentrations have

been used for diagnosis, and finding both a low serum cobalamin and an increased serum folate concentration has been considered to be relatively specific for ARE. Measuring serum cobalamin and folate concentrations is relatively insensitive and non-specific for detecting ARE. There are many dogs with chronic GI disease that respond to antibiotic administration but which have normal cobalamin and/or normal folate concentrations. Finding hypocobalaminemia or low serum folate levels is beneficial when looking for otherwise occult gastrointestinal disease. Supplementing cobalamin can clearly make cats feel better and diarrhea diminish. In fact, it is almost getting to the point where it is never wrong to give any sick cat cobalamin injections, regardless of blood values of the vitamin. Severe hypocobalaminemia has been suggested to be a poor prognostic signs. While the value of supplementing cobalamin to cats is clear (in fact, it is almost never wrong to give any sick cat supplemental cobalamin), the clinical value of administering cobalamin to dogs with low serum cobalamin concentrations is very uncertain.

Culture of the small bowel was once considered the "gold standard", but this test is fraught with problems. First, it is technically hard to do it correctly. Samples must be obtained without contaminating them with oral secretions. Then they must be processed correctly in an expedient manner so as not to lose any anaerobic bacteria while not allowing the numbers of aerobes to increase. Many investigators have snap frozen fluid samples to culture them later, but such freezing appears to kill large numbers of bacteria, especially anaerobic bacteria. We now know that culture only detects about 30% of the bacteria in the gut; the other 70% cannot be cultured. This makes one seriously question the value of culture unless one is searching for a specific pathogen, and even then there are culture-less methods (e.g., PCR) that may be better. Finally, as has already been said, just culturing bacteria from the small bowel does not allow one to make a diagnosis of a bacterial disease of the small intestines. Large numbers of bacteria (i.e., $> 10^7$ CFU/ml) can be present in dogs without any evidence of any clinical disease. For these reasons, we very rarely culture the small intestine of dogs with chronic GI disease. However, there are rare patients that appear to have ARE and yet are resistant to treatment with commonly used antibiotics. Seemingly, these dogs may have one or two very resistant bacteria in their GI tracts, and culture may be required to determine what antibiotic will be effective. However, we have only seen this scenario 2 or 3 times, and we believe it to be very rare.

Because of the apparent difficulty in diagnosing ARE with lab tests, empirical antibiotic therapy is often chosen as a means to diagnosis instead of laboratory tests. There are obvious drawbacks to this approach. First, the most obvious drawback is that we (i.e., pretty much everybody in human and veterinary medicine) are trying to minimize the use of antibiotics to help decrease the emergence of antibiotic-resistant strains of bacteria. Beyond this major disadvantage, there are also the following drawbacks: a) clinical "response" of the patient to the administered antibiotics may be due to the antibiotics or may be due to something else, b) if the patient did not respond to the antibiotic, it may be that you used the wrong antibiotics, and c) even if the patient does have ARE, there may be yet another disease present (e.g., a tumor causing a partial intestinal obstruction) which predisposed the patient to the ARE. Tylosin powder has been useful and is revered by many clinicians. Some clinicians like metronidazole; however, I have not been impressed with the efficacy of metronidazole for chronic ARE. Metronidazole for a long time has been the main treatment of many acute diarrheas, and that approach is increasingly being called into question.

Regardless of which antibiotic is used, such a therapeutic trial for ARE should be performed for at least 3 weeks before the treatment is considered ineffective. It may prove effective early, but it can take 3 full weeks to see a beneficial effect in some patients. Remember, you must not only suppress the numbers of bacteria, but you must also allow the intestinal mucosa time to heal. Finally, it appears that concurrently feeding a high quality elimination diet can substantially enhance the efficacy of the antibiotic therapy. Therefore, we now routinely use both in our therapeutic trials.

If the patient appears to respond to this therapeutic trial of elimination diet and tylosin, then it appears best to continue everything unchanged for an additional 2-3 weeks to be sure that the patient responded to this therapy (as opposed to the patient having some fortuitous, transient response to who-knows-what). If the patient is still doing well after the additional 2-3 weeks, then we typically stop the antibiotics and see if they diet alone is sufficient to control signs. It often is. If the diarrhea reoccurs every 2+ months, then it makes sense to only treat when the patient is symptomatic. If the signs consistently recur within a few days of stopping the antibiotics, then you are probably stuck with treating almost constantly. In some cases, the patient will breakthrough and re-develop clinical signs after several weeks or months, and a different antibiotic must be used. If the decision is made to stop administering the antibiotics, then the owners should be warned that it is possible that the signs are likely to recur at some point. For ARE to occur, there is probably some defect in host defense mechanisms that allowed the commensal bacteria to cause the clinical signs, and this defect is unlikely to disappear. The question is how severe is the defect (i.e., is the dog likely to have problems continually or only once in a while)?. You should warn the clients that they are likely to have to deal with this problem repeatedly and you need to explain the difference between "cure" and "control".

Other options that are becoming increasing more interesting are prebiotic and probiotic therapy as well as fecal transplantation. These therapies are being looked at as possible alternatives to protracted antibiotic therapy.

High quality probiotics are clearly beneficial in acute diarrheas. Their place in chronic diarrheas is somewhat controversial. Probiotic therapy seldom resolves chronic small bowel diarrhea, and when it does, it may require 2-6 weeks of therapy before a beneficial result is seen. Furthermore, if the patient responds to probiotic therapy, it may require ongoing probiotic therapy, which can be expensive if you are using a high quality product.

Fecal transplantation seems to be very helpful in some patients. However, at present, there really is no consensus as to the best way to perform fecal transplantation or how many times to perform it before deciding that it will not be effective. When fecal transplantation is effective, it seems to be obvious within 1-2 weeks. Personally, I'd prefer to try this approach before performing a 3 week antibiotic trial.

If the patient did not respond to well designed and well implemented therapeutic trials, or if the patgient is so sick that you cannot chance a 3 week therapeutic trial that may fail; or if the owners insist upon obtaining a histologic diagnosis, then tests are the next step. If, based upon history, physical examination, laboratory data (including basal serum cortisol concentations), fecal examination and/or abdominal ultrasonography you are sure that the small intestine is involved, then the best next step is usually intestinal biopsy.

Intestinal biopsy may be accomplished two ways: endoscopy and surgery. CBC, serum chemistry profile, and urinalysis are useful and may point out systemic manifestations of the disease which will aid in correctly diagnosing and prognosing the problem (e.g., hypoalbuminemia due to histoplasmosis), but are also useful as a preanesthetic work up before endoscopy. Ultrasound is useful to look for enlarged mesenteric lymph nodes, focal intestinal/gastric lesions, and loss of mucosal layering. Focal enlargements may suggest a tumor (e.g., alimentary lymphoma or carcinoma), as may lymphadenopathy. However, animals with severe IBD may also have mesenteric lymphadenopathy (as may dogs with histoplasmosis or pythiosis). If the lymph nodes are enlarged, it is reasonable to aspirate them percutaneously with ultrasound guidance. Mesenteric lymph nodes are typically reactive, making it more difficult to interpret cytology from them. However, finding obvious sheets of lymphoblasts or fungal organisms (e.g., histoplasmosis) allows diagnosis. Sonographic examination of the intestines is important (i.e., you may make a diagnosis), but it does not detect intestinal mucosal disease in many patients that are afflicted with such disease. If loss of mucosal layering is seen, then severe infiltration is likely (either inflammatory or neoplastic), but normal-appearing mucosa may have marked disease present. Most of the time, ultrasound's major use is to help you decide whether to perform intestinal biopsy using endoscopy or laparotomy. If there is an obvious lesion where an endoscope cannot reach, it is best to perform laparotomy instead of endoscopy.

Protein-losing enteropathies (low albumin is not necessarily a death sentence)

Michael D Willard, DVM, MS, DACVIM

Basic Approach To Hypoalbuminemia

When concerned with protein loss of any cause, one should measure serum albumin concentrations as opposed to the serum total protein concentration. Do not use human clinical pathology laboratories because their technology sometimes does not detect canine albumin; this means that they routinely report serum albumin concentrations of < 1.5 gm/dl in clinically normal dogs. If the patient has hypoalbuminemia (especially less than 2.0 gm/dl), the next step is to examine the skin for obvious lesions which can cause protein loss. Cutaneous lesions sufficient cause such hypoalbuminemia are obvious; you should be able to just look at the patient and know if this is the problem or not. Next, hepatic function testing (e.g., resting and post-prandial serum bile acid concentrations) and a urinalysis are requested. Never consider "panhypoproteinemia" as a good criteria to determine if protein-losing enteropathy is or is not present. It is insensitive and non-specific. If there is any doubt regarding the amount of protein being lost in the urine, then a urine protein:creatinine ratio will quantify the magnitude of urinary protein loss. Severe hypoalbuminemia (i.e., < 2 gm/dl) in an animal with diarrhea suggests a protein-losing enteropathy (PLE); however, diarrhea (even when severe) in no way is sufficient to eliminate hepatic disease as the cause of the hypoalbuminemia. Hepatic disease can at times cause such profuse diarrhea that it perfectly mimics intestinal disease. To further complicate matters, a very substantial number of dogs and cats with protein-losing enteropathy do not have vomiting or diarrhea; remember the diarrhea is nothing more than excess water in the feces. As long as the colon can absorb the excess water, the feces appear normal. That is why some dogs with PLE are asymptomatic while others (maybe 10-15%) have ascites as the only sign of a protein-losing enteropathy. This seems to be especially true of dogs with primary intestinal lymphangiectasia.

In general, once severe, exudative cutaneous disease, protein-losing nephropathy, and hepatic insufficiency are eliminated, then PLE is becomes a diagnosis of exclusion in patients with a serum albumin < 2.0 gm/dl. Fecal examinations for parasites are obviously appropriate in all such patients. Although parasites are an uncommon cause of PLE in adult animals, pets in select environments (e.g., confined areas where patients can reinfect themselves) may incur substantial parasitic loads. In the southern US, we have seen adult large breed dogs literally exsanguinated by hookworms.

Hypocholesterolemia

The serum cholesterol can be very helpful in determining the cause of hypoalbuminemia. Most dogs with either protein-losing enteropathy or hepatic insufficiency sufficient to cause hypoalbuminemia also have hypocholesterolemia. In contrast, most dogs with protein-losing nephropathies sufficient to cause marked hypoalbuminemia typically also have hypercholesterolemia. In patients with low urine specific gravities and large amounts of proteinuria, it is not hard to figure out what is happening. However, a patient with a 1.034 urine specific gravity and a 1+ protein and a urine protein:creatinine ratio of 1.34 may be confusing.

Fecal Alpha-1 Protease Inhibitor Testing

Fecal concentrations of alpha-1 protease inhibitor can be used as a means of confirming PLE if there is confusion because of concurrent hepatic or renal disease. The major use for this test in clinical medicine seems to be the hypoalbuminemic patient in which you strongly suspect PLE (e.g., based upon it having severe diarrhea or having hypocholesterolemia), but which also has PLN and/or hepatic disease. However, there are several nuances about this test, especially collecting samples, that make it potentially difficult to interpret. We seldom need this test in clinical practice. Finally, contrary to what the textbooks say, PLE may be associated with a low, normal or increased serum globulin concentration – personally, finding "panhypoproteinemia" is not very helpful in my patients.

Diagnostic Approach To The Dog With Protein-Losing Enteropathy

Hypoalbuminemia has been reported to be a poor prognostic sign in patients with chronic GI disease; however, there may be one or more subset(s) of patients that respond well to appropriate therapy if diagnosed in a timely fashion. Therefore, diagnosing PLE is not necessarily cause for despair. Aggressive diagnostics are typically an appropriate recommendation in PLE patients. Although therapeutic trials can be chosen in place of classic diagnostic tests in many of the more common alimentary tract diseases (e.g., dietary allergy, dietary intolerance, antibiotic-responsive enteropathy, parasites), such an approach is generally ill-advised if the serum albumin concentration is less than 2.0 g/dl. This is true because hypoalbuminemic patients tend to be more ill, and perform an antibiotic and/or dietary therapeutic trial for 3-6 weeks in order to ascertain if it is being effective may allow the patient to become markedly

worse if the serum albumin concentration is falling rapidly. Furthermore, failure to respond to a dietary trial for lymphangiectasia does not eliminate it. And, if you live where histoplasmosis or heterobilharzia or pythiosis exists, doing therapeutic trials with anti-inflammatories or immunosuppressive drugs may be very ill advised.

Any GI disease can cause protein-losing enteropathy if it is severe enough. Many acute GI diseases cause protein-losing enteropathy (e.g., parvoviral enteritis); however, these diseases typically are comparatively easier to treat than the chronic GI disease causing protein-losing enteropathy. Therefore, the focus in this lecture is PLE in animals with chronic GI disease. The major causes of protein-losing enteropathy in adult dogs tend to be intestinal lymphangiectasia, alimentary tract lymphoma (LSA), intestinal fungal infections (i.e., histoplasmosis and pythiosis), and severe inflammatory bowel disease (IBD. Other causes include alimentary tract ulceration/erosion, severe disease of intestinal crypts, antibiotic-responsive enteropathy, and parasites. The major causes of protein-losing enteropathy in juvenile dogs tend to be parasites and chronic intussusception. Cats with protein-losing enteropathy usually have IBD or alimentary tract lymphoma.

Diagnosis Of Cause of Protein-Losing Enteropathy

Once protein-losing enteropathy has been diagnosed, intestinal biopsy is usually the ultimate means of establishing a diagnosis. Biopsy can be done via laparotomy, laparoscopy, or endoscopy. Feeding a small, fatty meal (use canned food, not dry, and add in cream or corn oil) the night before the procedure might (?) make it easier to diagnose lymphangiectasia. Flexible endoscopy, when done by someone who is trained in how to take diagnostic tissue samples and submit them, is usually more than adequate to obtain diagnostic samples. However, if endoscopy will be used to biopsy the small intestines, it is preferable to first ultrasound the abdomen to make sure that there are no focal infiltrates that are out of reach of the endoscope, or which might be more easily diagnosed by ultrasound-guided fine needle aspiration. Furthermore, there are ultrasonographic changes (streaks in the submucosa) that can be nearly diagnostic for lymphangiectasia (i.e., about 95% confidence). Feeding fat the night before an ultrasound exam is clearly indicated as it has been shown to increase the sensitivity of ultrasound for making this diagnosis. Radiographs and barium series are seldom as sensitive as ultrasound. If flexible endoscopy will be done, one should biopsy the duodenum and ileum and, if at all possible, the proximal jejunum. There have been numerous cases in which lymphangiectasia, IBD or LSA were obvious in the ileum but not in the duodenum. It is not necessary to enter the ileum with the endoscope to obtain a good tissue sample of the ileal mucosa.

Laparotomy and laparoscopy are good means of obtaining diagnostic samples, but it is surprisingly easy to procure non-diagnostic samples with these techniques (i.e., "full-thickness sample" is not synonymous with "diagnostic sample"). Endoscopy does have the advantage of allowing one to visualize mucosal lesions that are "invisible" when looking at the serosa. In some cases, the diagnosis can only be obtained by biopsying these focal lesions. If full-thickness biopsies are obtained in severely hypoalbuminemic animals, then serosal patch grafting will minimize the risk of suture line leakage. A nonabsorbable or a poorly absorbable suture (PDS) should also be used.

Intestinal lymphangiectasia seems particularly common in Yorkshire terriers and Soft-Coated Wheaten terriers, but may occur in any breed. Sometimes these dogs have distinct ultrasonographic findings: "streaks" in the mucosa that represent dilated lymphatics. While histopathology is obviously the desired means of diagnosis, one can sometimes make a definitive diagnosis based upon grossly visible endoscopic findings (i.e., numerous, erratic, grossly engorged lacteals seen as large white blebs on the mucosa). These lesions are "fragile" and apparently may be destroyed by biopsying them (both endoscopically and surgically) if the endoscopist or surgeon is not careful. It is important to note that lymphangiectasia can be a relatively localized disease in the intestines, being present in only the ileum or only the jejunum or only the duodenum; therefore, it is important to biopsy as much of the intestinal tract as possible. Furthermore, if one biopsies the intestines and cannot find a cause of PLE, sometimes lymphangiectasia can be tentatively diagnosed by eliminating IBD, lymphoma, parasites, intussusception, fungal infections, etc.

Diagnosis by means of endoscopic biopsy is certainly possible if the endoscopist is trained in taking high quality tissue samples. However, recent work has demonstrated that poor quality mucosal biopsies (e.g., primarily villus tips or substantial "squash" artifact) makes is much more difficult or even impossible to find the lesions. If one is taking high quality tissue samples (i.e., total length of the villi plus subvillus mucosa down to the border of the mucosa and muscularis mucosa), it typically takes about 6-7 tissue samples to have 90-99% confidence in finding lymphangiectasia. However, it can take 5-7 times as many tissue samples to have the same assurance if you are obtaining poor quality tissue samples that primarily consist of villus tips.

When doing endoscopy, it is important that ileal biopsies be taken in addition to the typical duodenal biopsies. We are finding that ileal biopsies often reveal lesions not found on duodenal biopsies. This is true for lymphangiectasia as well as lymphoma and other lesions. With basic training, an endoscopist should be able to obtain ileal biopsies endoscopically at least 85%+ of the time. Typically, ileal biopsies are often of higher quality than duodenal biopsies.

Therapy For Lymphangiectasia – Ultralow Fat Diet

Therapy for intestinal lymphangiectasia revolves around an ultra-low fat diet. Please note that "low fat" is NOT acceptable; it needs to be ULTRALOW FAT (i.e., less than 2 grams fat/100 kcal). Feeding homemade diets that are highly digestible and ultra-low in fat (e.g., white turkey meat plus potato or rice) is fine, but now there are commercial ultralow fat diets that are often very successful in these patients. Dogs that are in the earlier stages of lymphangiectasia often show a marked increase in serum albumin concentration (i.e., an increase of 0.5 gm/dl or more) within 7-14 days

of starting such a diet. Dogs that are diagnosed later in the course of the disease may not have such a dramatic response, which is one reason why failure to respond to an ultralow fat diet is not grounds for eliminating lymphangiectasia as a diagnosis.

Supplementation with medium chain triglyceride oil (MCT) used to be recommended. Don't use it. It is unnecessary and expensive. Pancreatic enzymes were often added to the diet to ensure digestion of the medium chain triglyceride oil. It too is no longer recommended.

Therapy For Lymphangiectasia – Dealing With Lipogranulomas

Lipogranulomas in the intestinal wall and mesentery appear to be very important to the ultimate prognosis of the patient. We hypothesize that most patients that fail to respond to appropriate dietary therapy do so because of formation of very large or excessive numbers of lipogranulomas that so completely obstruct the intestinal lymphatics that even an ultra-low fat diet cannot prevent lacteal rupture. Therefore, once a diagnosis of lymphangiectasia is made (either by histology, grossly at endoscopy, or tentatively by response to an ultra-low fat diet), we routinely use anti-inflammatory therapy designed to prevent granuloma formation and/or enlargement. Prednisolone (NOT prednisone) is commonly used, but I do not like prednisolone simply because of all the side effects it has in these patients.

I like cyclosporine, but be aware that it is critical that you measure blood levels of the drug if the patient is not responding within 10 days. Not only is there a major difference between patients in how much cyclosporine they absorb, but the bioavailability of the same product may change as the intestine heals. Remember that hyporexia is the main sign of overdose.

Because cyclosporine is so expensive, many clinicians opt for prednisolone but add in chlorambucil or azathioprine. If you use azathioprine (2.2 mg/kg PO), be very careful not to overdose the patient lest hepatic failure, acute pancreatitis, and/or bone marrow suppression occurs. Be careful to give the correct dose, meaning that you should be willing to have the drug recompounded, if necessary. Most people give azathioprine daily for 7 days and then every other day. I often give azathioprine every other day from the start to lessen the chance for toxicity, but it takes 4-5 weeks for it to work if you start giving it every other day.

Chlorambucil is safer and probably more effective than azathioprine, and I recommend it instead. Given at 4-6 mg/M2 PO daily or every other day, it can take 3-5 weeks for it to take effect. Even though it is an alkylating agent, it seems to be much safer than azathioprine.

If the serum albumin is very low (e.g., < 1.3 gm/dl), one is often tempted to administer a plasma transfusion while waiting to see what effect the diet will have. However, it is exceedingly difficult to increase the serum albumin concentration by transfusing patients that are losing protein with plasma because so much of the albumin is quickly lost out the gut. You would probably have to give at least two and possibly three units of plasma to a 15 lb dog in order to raise the serum albumin from 1.0 gm/dl to 1.6 gm/dl, and sometimes you would have to give more. However, any benefit will probably be so short lived that it is not cost-effective. If it is critical to raise the plasma oncotic pressure, then administering hetastarch may be preferred because it costs less than plasma, and it stays in the intravascular compartment longer than albumin.

These patients may be a increased risk for hypomagnesemia which may potentiate the problem of hypocalcemia. At this time, we do not know how important it is to supplement magnesium to patients, but severe hypomagnesemia can be resolved by a constant rate infusion of magnesium sulfate.

Intestinal Crypt Lesions

Lesions of the intestinal crypts have been recognized as being associated with PLE in dogs. We have identified two different lesions of the small intestinal crypts that can cause PLE. One type is characterized by crypts (usually duodenal) that are filled and somewhat distended with proteinaceous fluid and necrotic inflammatory cells. While such dilated crypts can be found in many animals, including clinically normal dogs, finding large numbers of them in multiple tissue samples seems to be consistently associated with PLE. We do not know if this is a cause-and-effect relationship, or if the dilated crypts are simply a marker for some other process but are not causing the protein loss themselves. Several of these patients have responded to therapy with elemental diets, total parenteral nutrition, prednisolone, azathioprine, and/or metronidazole. We have seen this lesion associated with IBD as well as lymphangiectasia (especially in Yorkshire terriers).

A second type of crypt lesion that appears to be less common than the first, is characterized by focal accumulations of mucus causing massive distention of the intestinal crypts. This has been reported once before, and we have seen a few such cases. The most important aspect of diagnosis seems to be the fact that the lesion may be very focal, almost appearing as ulcers when looking at the intestinal mucosa through an endoscope. Therapy similar to that used on animals with the other form of crypt lesion may be helpful. We have used cyclosporine, but do not know if it is helpful, or if the clinical response is due to the other drugs that the patient is receiving.

These lesions have not been commonly reported. Recent work has shown that these lesions are extremely easy to miss if poor quality endoscopic biopsies are performed. While 7-12 high quality tissue samples (i.e., full length of villi plus subvillus mucosa down to the level of the muscularis mucosa) will find these lesions 90-99% of the time, about 7 times as many tissue samples will be needed if poor quality samples primarily consisting of villus tips are submitted.

Chronic Intussusception And Other Causes Of Protein-Losing Enteropathy

Chronic intussusception is a relatively important, and often missed cause of PLE in juvenile animals. The classic history is one of acute enteritis (e.g., parvoviral enteritis) which does not resolve as expected. The patient feels somewhat better, but continues to have diarrhea, and the serum albumin concentration gradually diminishes. It can be very hard to palpate an ileo-colic intussusception; abdominal ultrasound is clearly the preferred way to diagnose intussusception. Therapy is surgical.

Although uncommon, nematodes may cause PLE in adult animals if there are large numbers of them. Whipworms and hookworms in particular may occasionally be responsible for PLE in older dogs. However, giardiasis has been reported to cause PLE in people.

We believe that we are starting to recognize antibiotic responsive enteropathy (now commonly called dysbiosis) as a cause of protein-losing enteropathy in dogs. We now have several patients that appeared to have marked increases in their serum albumin concentration associated with antibiotic therapy. However, because dietary change is often performed simultaneously with antibiotic therapy in these patients, cause-and-effect is not clearly established. However, since we believe that bacteria (i.e., ARE or dysbiosis) is probably the ultimate cause of IBD, it makes sense that treating ARE may resolve some cases of protein-losing enteropathy.

Chronic large bowel diarrheas

Michael D Willard, DVM, MS, DACVIM

Distinguishing Small Bowel Diarrhea From Large Bowel Diarrhea

The first question in a patient with diarrhea is whether it is acute or chronic disease. Most acute diarrheas are self limiting and only need supportive therapy to help them resolve faster. If the diarrhea becomes chronic, then you know that this is not a self resolving disease; therefore, diagnosis is necessary in order to resolve the problem. When faced with a chronic diarrhea, the next question is whether the patient has large intestinal disease or small intestinal disease. It is important to realize that diarrhea is simply increased fecal water. Severe, life-threatening small bowel disease may cause minimal or no diarrhea if the colon can absorb enough water to make the feces firm or solid by the time they are evacuated. In particular, if the patient has been in a cage and unable to exercise (a potent stimulus for defecation), the feces may be normal despite significant intestinal disease. It is only when the colon's water absorbing capacity is exceeded that diarrhea occurs. Even when small bowel disease does cause diarrhea, the weight loss from nutrient malabsorption may precede diarrhea by months.

Use the history to help differentiate large bowel from small bowel disease. Weight loss, especially in the face of a reasonable appetite, strongly suggests nutrient loss from the small intestine. Hepatic disease can closely mimic intestinal disease in this regard, but the intestines are usually a better place to start looking. Weight loss (or loss of body condition as reflected in the hair coat) is probably the most important area to look at in differentiating large bowel from small bowel disease. Any animal with chronic small intestinal disease that is clinically significant should have weight loss or loss of condition. Any animal with chronic diarrhea and no loss of weight or condition has large bowel disease until proven otherwise. Some animals with severe large bowel disease will have weight loss, but these have more severe causes (usually infiltrative) of diarrhea and therefore usually also have hematochezia, mucus, hypoalbuminemia and/or marked tenesmus.

Red blood in the feces (hematochezia) comes from the large bowel or the ileum. This finding is specific but insensitive for large bowel diarrhea. Mucus in the feces comes from the large intestine or ileum. This finding is specific but insensitive for large bowel diarrhea. Tenesmus and dyschezia suggest large bowel disease; however, any animal with chronic diarrhea can have anal irritation causing mild tenesmus. Vomiting can occur with either large or small bowel disease.

Causes Of Large Bowel Diarrhea

The most commonly diagnosed chronic large bowel diseases causing diarrhea in dogs in our practice are so-called irritable bowel syndrome (IBS) (which is NOT the same as irritable bowel disease in people), fiber-responsive colonic dysfunction (which is probably a subset of irritable bowel syndrome), dietary intolerance (by which I am referring to allergic as well as non-allergic dietary problems), clostridial colitis (which might be better called "tylosin-responsive colitis"), parasites, fungal infections (i.e., histoplasmosis and pythiosis) and schistosomiasis (i.e., heterobilharzia). The most commonly diagnosed large bowel diseases in cats in our practice are fiber-responsive disease, dietary intolerance, antibiotic-responsive colitis and inflammatory bowel disease (IBD), especially lymphocytic-plasmacytic infiltrates. Fortunately, colonic histoplasmosis is much less common in cats than it is in dogs.

Parasites

The first concern in a diagnostic work up is parasites. Whipworms can be very difficult to demonstrate on fecal flotation. Direct fecal examination will be more useful than fecal flotation if the flotation solution is not dense enough to ensure that the whipworm ova will float. Also, remember that whipworms can be periodic egg shedders. Whipworms can be very easily missed by fecal flotation; therefore, it is appropriate to treat any dog with chronic large bowel disease with fenbendazole. I have seen several cases of whipworms that were diagnosed during colonoscopy because fecal examinations were non-diagnostic. Tritrichomonas is primarily a problem of cats, but very, very rarely will be seen in dogs.

If the diarrhea persists after eliminating parasites from consideration, the next question is whether to try a therapeutic trial or perform tests. If the patient is hypoalbuminemic, lost substantial weight, or is a Boxer or a French Bulldog, then extensive diagnostics aimed at infiltrative diseases, especially histoplasmosis, pythiosis, heterobilharzia, histiocytic ulcerative colitis, and cancer are indicated. Otherwise, a therapeutic trial (e.g., dietary therapy or empirical antibiotic therapy) plus modest diagnostics (e.g., fecal examination) may be particularly helpful. It is worth noting that many of the more common diseases affecting the colon are better diagnosed with a therapeutic trial than with an extensive diagnostic work up that includes blood tests and endoscopy/biopsy. The main therapeutic trials are usually a fiber-supplemented diet, an elimination diet, anthelmintics, and/or antibiotics (e.g., tylosin or amoxicillin). Good therapeutic

trials are better at diagnosing some of the more common large bowel disorders of dogs than are endoscopic examinations and biopsies.

Clostridial Colitis

Clostridial colitis might better be called "antibiotic-responsive colitis". It is a very important disease in the dog, but we are not sure how important or common it is in the cat. We think that it is caused by toxigenic strains of *Clostridium perfringens*. However, even when a toxigenic strain of *Clostridium perfringens* is established in the colon, it does not generally produce disease unless there is sufficient toxin being produced due to upregulation of toxin production in the bacteria. Toxigenic strains upregulate the amount of enterotoxin produced when they sporulate, and it is this toxin which damages the colonic epithelium and produces diarrhea.

Diagnosing clostridial colitis is not as "easy" as it was a few years ago. One cannot reliably diagnose clostridial colitis by finding spores in the feces on fecal cytology, performing quantitative cultures for *Clostridium perfringens*, or assaying for clostridial enterotoxin in the feces. Looking for fecal spores is an especially easy screening procedure, and the spores can be detected with a variety of stains. However, just as the disease can wax and wane unexpectedly, the presence and number of spores may likewise vary. Biopsy is not that helpful; there may or may not be histologic changes in the colonic mucosa in animals with clostridial colitis. Besides, the histologic lesions seen with clostridial colitis are nonspecific, and cannot be reliably differentiated from IBD or dietary allergy/intolerance. We used to think that the most definitive method of diagnosing clostridial colitis was to assay the feces for the presence of toxin; however, this is relatively expensive and is no more sensitive or specific than other tests.

Many of us currently just treat for the disease and observe the clinical response. Typically, the patients are treated with tylosin and a high fiber diet simultaneously (even if they have been shown to not respond to a high fiber diet in the past). While this approach can cause a problem when there are two things happening concurrently (e.g., clostridial colitis PLUS dietary intolerance), it seems to currently be one of the better ways to diagnose clostridial colitis. Response to amoxicillin or tylosin may be one of the best ways to presumptively diagnose clostridial colitis. Many patients with clostridial colitis do not respond to metronidazole.

Tylosin is an antibiotic that seems to be consistently effective against *Clostridium perfringens*. This is a wettable powder that is used to treat poultry. Animals that respond to tylosin and a high fiber diet usually do so within 3-7 days. The initial dose of Tylan is 10-40 mg/kg bid (20 mg/kg seems to be a good place to start). Most patients that respond can be slowly weaned off the drug and maintained on a high fiber diet alone. It is important to note that you will not eliminate Clostridium perfringens from the patient, and very rarely, some patients seem to need to be tylosin for life. Tylosin tends to have an unpleasant taste and needs to be mixed into the food, and sometimes it is better to put it into capsules and give it that way instead of putting it on the food. Amoxicillin is also effective in almost all animals with clostridial colitis. Many animals with chronic clostridial colitis that cannot be completely removed from tylosin therapy can be well controlled with one treatment of amoxicillin or tylosin every 2-3 days.

Metronidazole is very effective against anaerobic bacteria in general, but metronidazole is inconsistently effective in animals with clostridial colitis, possibly because metronidazole does not reliably achieve therapeutic levels throughout the feces.

Some dogs that are tylosin responsive also respond to fiber supplementation, which makes sense because fiber will usually remain relatively intact until it reaches the colon where it may have profound effects on the microenvironment of the colonic bacterial flora. The goal is not necessarily to eradicate *Clostridium perfringens* from the animal (you probably can't do that even if you wanted to); rather, it is to prevent the bacteria from elaborating and releasing its toxins. The preferred long term therapy of clostridial colitis is to maintain the animal on a high fiber diet which controls signs and not have to give antibiotics; however, not all animals can achieve this level of control.

Fecal Transplantation

Fecal transplantation has seemingly been beneficial in some cases of clostridial colitis. It is reasonable to try, although at this time there is not a consensus as to the best way to perform this procedure.

Dietary-Responsive

We will use the term "dietary-responsive" to include both dietary allergy (an immune process) and dietary intolerance (a non-immune process). Dietary-responsive disease is more common than many suspect, especially in cats with chronic large bowel disease. You cannot count on finding eosinophils in the blood or the colonic mucosa of animals with dietary allergies; most patients with dietary intolerance have minimal histologic changes or have nonspecific lymphocytic and/or plasmacytic and/or eosinophilic infiltrates. Because the histologic findings are nonspecific, it is typically preferable to try elimination diets prior to performing colonoscopy. The biggest problem in these patients is finding an effective diet. We often see cases in which the right thing was done (i.e., an elimination diet was used), but was so poorly planned or implemented that the effort was wasted. Hydrolyzed diets are a good place to start; many (not all) dogs with dietary hypersensitivity respond to hydrolyzed diets. If the patient does not respond to a hydrolyzed diet, then a novel protein diet should be tried. It is critically important to carefully investigate the history and see what the patient has eaten in the past. However, sometimes it is difficult to find a diet that is "right" for a particular patient. This might be because you do not know if the problem is an allergy or an non-allergic intolerance. In some cases, all

of our well-planned hypoallergenic diets failed but a chance try at some commercial brand works. It is easy to do a poor job of feeding a "hypoallergenic" diet and thereby make the client so discouraged with dietary therapy that they end up requesting costly work ups when a good dietary trial done at the beginning would have worked. Also, if you do a thorough work up and do not find a reasonable cause of the diarrhea, it is probably a dietary intolerance or allergy, and you will have to simply try diet after diet until you finally find the right one.

Histiocytic Ulcerative Colitis

Histiocytic ulcerative colitis, also known as "Boxer colitis" is being seen more commonly now than it was 5-10 years ago. First described about 30 years ago, it was a horrible, progressive disease of young Boxers (and sometimes related breeds, such as the French Bulldog) that invariably had a terrible prognosis. The signs are those of severe large bowel disease (lots of hematochezia and fecal mucus) plus weight loss. Diagnosis is made histologically by finding PAS-filled macrophages in the mucosa. Recently, it has been discovered that this is an antibiotic-responsive disease caused by enteroadherent strains of *E. coli*. Initially, enrofloxacin seemed to be particularly effective but any number of antibiotics would work. Unfortunately, there has been an upsurge in antibiotic resistance of the *E. coli* responsible for this disease. Most strains are no longer sensitive to enrofloxacin. Therefore, it is recommended that mucosal samples (not fecal samples) be taken for bacterial culture and sensitivity analysis. The biggest problems are that a) many people (clients and veterinarians) are reluctant to biopsy the dogs because they assume that any disease so severe must have a bad prognosis, and b) many pathologists have never seen it and miss it, even when it is fairly obvious to the experienced eye. It is best to biopsy the dog instead of giving empirical enrofloxacin therapy since other treatable diseases may be present (e.g., histoplasmosis) that also can be successfully treated if therapy is begun in a timely fashion. If antibiotics are given, it is important to treat for several weeks (at least 8) to ensure eradication of the bacteria lest resistant strains be selected for and allowed to cause a relapse that is more difficult to control than the initial presentation. Unlike some diseases, failure to eradicate the infection with the first choice of antibiotics is almost uniformly associated with subsequent resistance to the antibiotic(s) used initially.

New Or Less Common But Important Diseases

Recently, we have seen miniature Dachshunds with what is initially diagnosed as multifocal inflammatory polyps. However, FISH analysis shows that these are bacterial in origin (something now shown by special histologic stains). At least some of them respond exceedingly well to aggressive antibiotic therapy. However, relatively few have been seen so far, so broad-sweeping statements are not appropriate.

Histoplasmosis can be a very important cause of large bowel diarrhea in dogs (and rarely in cats). The urine antigen test is reasonably sensitive and specific, but I have seen false negative and false positive results. It is safest to perform a colonic biopsy to rule this out. Be aware that in its early stages, it can closely mimic more mild colonic diseases such as dietary-responsive, fiber-responsive, and clostridial colitis.

Protothecosis seems to be recognized more frequently over the last several years. It typically causes a severe colitis, but it is easy for pathologists to miss it as many have not seen it before. I've even seen cases where it was erroneously diagnosed as "coccidiosis".

Chronic hepatic diseases

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Chronic Inflammatory/Necrotic Diseases

Adverse drug reactions may cause mild to fatal hepatic disease. They can be due to almost any drug (e.g., cimetidine, amoxicillin, clindamycin, etc, etc, etc); however, some drugs are clearly more likely to cause hepatic disease than others. Whenever there is any doubt as to whether a particular drug might be responsible for hepatic disease in a patient, stop administering it and observe the results. Again, as for cats, the healthier the patient is, the more inclined we are to wait and see what happens after stopping the drugs. The sicker the patient is, the quicker we are to biopsy, just in case there is something more significant that we need to eliminate now.

Doxycycline occasionally causes increased ALT and even icterus. Although this is not a commonly recognized problem, we use so much doxycycline for suspected rickettsial diseases that it is very important to recognize the possibility. I have seen a few dogs that appeared to have substantial hepatic side effects (including icterus) from doxycycline administration.

Sulfa drugs are famous for causing severe hepatic disease (as well as bone marrow, cutaneous, joint, ocular and renal problems). Furthermore, the hepatic disease caused by sulfa drugs may not occur for 1-2 weeks after starting the drug, even if the patient has not received the drug for over a week. The hepatic lesions caused by sulfa drugs can look a lot like idiopathic chronic hepatitis. Doberman pincers and Rottweilers appear to be especially sensitive to sulfa drugs.

Carprofen (i.e., Rimadyl) causes hepatotoxicity in dogs, especially Labrador retrievers. The histologic changes seen in carprofen hepatotoxicity can resemble chronic hepatitis, so be sure that you have an adequate history. Also, be aware that hepatotoxicity may not be seen until 1-2 weeks after starting a drug; in fact, the patient may have stopped taking the medication several days before clinical signs of toxicity occur.

Lomustine is a chemotherapeutic used as rescue therapy when treating lymphoma. It will reliably cause severe hepatic disease if used inappropriately.

Amiodarone is an anti-arrhythmic drug that can cause substantial hepatotoxicity, and patients receiving this drug should be monitored closely. Some breeds appear to be excessively prone to adverse effects from specific drugs.

Itraconazole can cause icterus, but the signs usually regress quickly after withdrawing the drug.

Anticonvulsants (i.e., phenobarbital and Primidone) are famous for causing severe hepatic disease, eventually resulting in cirrhosis. This is why it is so important to perform therapeutic blood monitoring and measure the serum phenobarbital levels in patients receiving these drugs.

Azathioprine can cause severe, acute hepatocellular necrosis in some patients. This may be due to different rates of metabolism of the drug in different patients. I have not seen this problem when the patient was receiving azathioprine on an every-other-day basis as opposed to receiving it daily.

Acetaminophen is toxic and fatal when overdosed. You need to be very careful if you decide to use this drug in a dog.

Vacuolar hepatopathy (hydropic change) is probably the most common histologic change seen in hepatic biopsy of canine livers. In general, this lesion seldom causes any clinical signs. I did not say it never caused clinical disease; rather, it very seldom causes clinical disease itself. There are some suggestions that severe change is sometimes responsible for hepatic failure. Vacuolar hepatopathy is best known for being associated with steroids. Both exogenous or endogenous steroids can be involved. Furthermore, it appears that vacuolar hepatopathy can be due to hyperadrenocorticism or to dogs with excessive steroid release associated with significant illnesses (e.g., tumors, infections). Classically, these dogs have a high SAP with a relatively minor (or no) increase in ALT. The GGT may be increased.

Chronic hepatitis is probably one of the main reasons it is a good idea to biopsy dogs' livers. It is a reasonably common disease, and a lot can often be done for the dog if you diagnose it before the hepatitis causes cirrhosis. Chronic hepatitis can be found in almost any breed of dog, although Doberman pinchers (especially young to middle-aged females) seem to have a very high incidence of the disease. There are several clinical presentations of this disease. First, one may see a chronically ill dog with high ALT and SAP. Second, one may be presented with a dog that was normal until it was stressed (e.g., underwent surgery or anesthesia). Third, one may see a dog that was normal until a few days ago but that now suddenly presents with signs of hepatic failure and is found to have an absolutely end stage cirrhotic liver (see discussion under cirrhosis) even though the clinical signs have only been present for 1-3 days. Finally, one may see a clinically normal dog that has an increased ALT that was fortuitously found during routine health screening or during a preanesthetic work up for a dental. The ALT typically remains increased despite the dog acting and appearing fine. Chronic hepatitis is more common than many people realize and is one reason why it is better to biopsy clinically normal dogs with persistent increases in ALT rather than wait until clinical signs occur.

Treatment of chronic hepatitis usually centers around a) removing the cause, if possible, b) administration of anti-inflammatory therapy (i.e., steroids, azathioprine), and c) administration of supportive therapy (i.e., ursodeoxycholic acid and anti-oxidants). Two causes of chronic hepatitis that you might be able to remove are drugs and copper. Copper is a bit confusing in that it can be the cause of chronic hepatitis, it can be secondary to chronic hepatitis but not causing a clinical problem, and we think that it can sometimes be secondary to chronic hepatitis and yet be severe enough to cause disease in and of itself. There has been one report that seemed to show that removing copper from the liver of dogs with chronic hepatitis in which the copper accumulation clearly appeared to be secondary to the hepatic disease was clinically beneficial to the dogs. You can measure copper levels in biopsies, or you can do special stains on hepatic biopsies. If you are in doubt as to how significant the hepatocellular copper is, it is probably best to just remove it. If the decision is made to remove copper, then one may elect oral zinc therapy before meals or copper chelation with d-Penicillamine. Feeding a copper restricted diet is reasonable; but, feeding a copper restricted diet by itself often will not lower hepatic copper concentrations sufficiently. D-Penicillamine (10-15 mg/kg bid) is the drug typically used to lower hepatic copper concentrations. This drug occasionally causes vomiting, and administering it with food seems to lessen that problem. Trientine is another copper chelator (Cuprimine) that is also effective (10-15 mg/kg bid) and seems to have fewer side effects than d-penicillamine. If the dog is clearly being intoxicated by very large concentrations of hepatic copper, chelators should be used.

Zinc can be used to prevent copper accumulation, but it can also act as an antifibrotic agent. Various forms can be given, but the idea is to administer approximately 100 mg of elemental zinc daily for 3-6 months and then decrease it to about 50 mg daily. Zinc should be administered on an empty stomach, and generally should not be given with copper chelators. Be aware that zinc administration can rarely cause hemolytic anemia, and periodic blood zinc measurements are not a bad idea in patients receiving zinc therapy.

Dogs with chronic hepatitis not due to copper accumulation or drugs often need anti-inflammatories, and this usually includes glucocorticoids. However, it seems important to use the lowest effective dose of the corticosteroid. If you give too much corticosteroid to a dog with steroid-resistant hepatic disease, you may create a vacuolar hepatopathy in addition to the preexisting hepatic disease. When corticosteroids are used for this disorder, they should typically be used at an anti-inflammatory dose (1 mg prednisolone/kg/day) and then tapered quickly. The steroid treatment should be for relatively short periods of time (i.e., until a week or two after clinical signs substantially diminish or disappear). Severely affected patients and patients that require excessive amounts of corticosteroids may benefit from azathioprine or cyclosporine therapy. Azathioprine may cause severe hepatic disease, but this appears to be an idiosyncratic reaction, possibly due to differences in the rate of metabolism of the drug in different dogs. I do not hesitate to use azathioprine when it seems like it may be helpful. Indications seem to be when steroids are insufficient to control signs, when excessive doses of steroids are required to control signs but cause substantial side effects, and when very severe hepatic disease is found on the initial biopsy. While 1 mg/lb daily is a commonly quoted dose, I typically give azathioprine at the same dose but only every other day, which seems to be much safer.

Patients with hepatic disease may also benefit from supportive therapy, especially those drugs and neutroceuticals that are antioxidants. Antioxidants (i.e., s-adenosyl-L-methionine, silymarin, phosphatidylcholine, N-acetylcystine) and ursodeoxycholic acid are what should be called "hepatosupportive" therapy. These drugs will generally not cure severe disease all by themselves, but they can substantially help the patient if appropriate therapy is being directed at the primary cause. In general, antioxidants are poorly effective if used as single drugs. Rather, antioxidant therapy is best accomplished if multiple drugs are used simultaneously.

S-adenosyl-L-methionine (20 mg/kg sid) is a neutroceutical that appears to have benefit in some patients with hepatic disease. It increases hepatic glutathione concentrations as well as enabling a variety of important, intermediary metabolism reactions. The drug appears to have no adverse effects, and there is good evidence that it helps protect against alcoholic hepatitis in people. It should be given on an empty stomach, and the patient should not be feed for 30 minutes. It comes in foil-wrapped, enteric coated tablets. Milk thistle (silymarin) (4-8 mg/kg/day OR 50-250 mg/day) is a herbal treatment that has proven efficacy in some diseases (e.g. Amanita mushroom poisoning). There are different active fractions, and silybin seems to be the most active. There is one preparation in which silymarin is complexed with phosphatidylcholine complex (i.e., Marin by Nutramax) which seems to have increased uptake and bioavailability. N-acetylcysteine can be obtained from the health food store. It is an anti-oxidant, and has been given to dogs and cats at a dose of 70 mg/kg tid. It seems to be safe, but should be given on an empty stomach. It seems that s-adenosyl-L-methionine is probably effective in promoting intracellular glutathione concentrations. It is important to note that administering glutathione orally is ineffective; the orally administered drug will not increase intracellular glutathione concentrations. Ursodeoxycholic acid (15 mg/kg/day) is beneficial because of its ability to displace more toxic hydrophobic bile acids from the hepatocyte membrane. Like the antioxidants, it generally should not be used as sole supportive therapy. It seems to work best if combined with anti-oxidants.

Copper storage is reported in Bedlington terriers, where it commonly causes chronic hepatitis that progresses to cirrhosis. West Highland White terriers often have excessive hepatic copper accumulation, but it is different than what is found in Bedlington terriers and seldom causes clinically significant hepatic disease. Dalmatians, Labrador retrievers and Skye terriers have recently been reported to have a copper-associated hepatic disease in which accumulation of copper by the liver may be the cause of the clinical disease. Recently, there is increased concern that many dog foods have increased amounts copper that is more bioavailable than before, making it easier for some breeds (e.g., Labrador retrievers) to accumulate toxic amounts and develop chronic hepatitis. Biopsy with special stains or preferably quantitated copper analysis performed on frozen hepatic tissue is required for diagnosis.

Cirrhosis is an end-stage hepatic disease that may be caused by various problems, especially chronic hepatitis. In

particular, Cocker spaniels seem to have a distinct genetic predisposition to having cirrhosis at inordinately young ages (i.e., < 5 years of age). This may be due to an inherited problem in which they accumulate alpha-1 protease inhibitor in their hepatocytes, which eventually results in cellular death. In general, these dogs are clinically normal until they have completely exhausted all of their hepatic compensatory mechanisms. This means that there is usually little or nothing that can be done when they start showing clinical signs. Unfortunately, many of these dogs have normal serum ALT and SAP activities when they are approaching end stage. Serum albumin and BUN are often decreased, and serum bile acids, if measured, are typically markedly increased (e.g., > 90 umol/L). However serum bile acids are not as sensitive or specific as desired. If blood ammonia is increased, that is very specific for hepatic insufficiency, but we are not sure how sensitive it is. Chronic hepatitis may cause the identical scenario in other breeds (especially but in no way limited to the Doberman pincher). There may be ascites due to portal hypertension and salt accumulation in cirrhotic animals. In such animals there is usually acquired hepatic portal shunting with many tortuous shunts seen in the abdomen, especially around the kidneys. Hypoalbuminemia can make the ascites more likely and more severe if it occurs.

Although controversial, I believe it is usually appropriate to biopsy dogs that you strongly suspect of having cirrhosis, unless the anesthesia risks are too great. I say this because I hope to find other disease in the liver (e.g., inflammation that caused the cirrhosis in the first place) that can be treated. By treating the apparent primary hepatic disease, you may a) prevent further cirrhosis, and b) allow the remaining hepatocytes to heal and recompensate the patient. However, remember that a dog with cirrhosis may have exhausted all of its compensatory mechanisms, and even minimal anesthesia may result in acute decompensation and death. This is not common or likely, but it is devastating when it happens. Most patients with hepatic cirrhosis die shortly after diagnosis. However, some can live for months or even over a year with aggressive supportive therapy. It is hard to know which dogs will respond in which way. All you can do is treat and hope.

You must be very careful about diagnosing cirrhosis based upon clinical appearance. There are several diseases that look like cirrhosis but that are not cirrhosis.

Hepatic lobular collapse looks much like cirrhosis when viewed grossly, laparoscopically, or by ultrasound. However, there is no fibrosis, just loss of hepatocytes. Therefore, there is no need to use potentially dangerous drugs (e.g., azathioprine, colchicine) or even prednisolone. This disease can be associated with dermatohepatopathy, which sometimes responds to amino acid infusions. However, we have also seen improvement with more conservative management aimed as protecting the hepatocytes.

Noncirrhotic portal hypertension closely mimics cirrhosis in its clinical appearance, but is easily distinguished from cirrhosis by biopsy. This disease in particular is an important reason why you need to biopsy the liver of dogs with "obvious" cirrhosis; they might have a very different disease. Noncirrhotic portal hypertension generally has a much better prognosis than cirrhosis. It is now believed that this disease might be a manifestation of portal vein hypoplasia (discussed under congenital portosystemic shunts and microvascular dysplasia). The dog can have a small liver, polyuria-polydipsia, acquired portosystemic shunting, massive ascites, and still have a much better prognosis than seen in animals with cirrhosis. Animals with noncirrhotic portal hypertension often respond well to conservative, symptomatic and supportive therapy to alleviate ascites. They may be successfully controlled for months or years. It is sometimes important to combine diuretic therapy with low salt diets so as to enhance the effectiveness of the diuretic therapy. If the patient stops eating, it becomes very important to monitor serum potassium and magnesium concentrations.

Lobular dissecting hepatitis is another disease that mimics cirrhosis. It is a "chronic hepatitis/cirrhosis"-like disease in which there is fibrous connective tissue infiltrating between hepatocytes. It typically occurs in younger dogs, causing ascites and signs of hepatic failure. Diagnosis requires biopsy, and the prognosis is much worse than that of chronic hepatitis or non-cirrhotic portal hypertension or lobular collapse.

Congenital portosystemic shunts: the textbooks are all wrong and you see them more frequently than you realize

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Congenital portosystemic shunts (pss) are much more common and certainly much more confusing than we ever imagined. At Texas A&M, we infrequently see the "classic" congenital PSS with the relatively straight forward presentation (i.e., young Yorkie with post prandial hepatic encephalopathy), probably because those cases are efficiently filtered out and never referred to us. Some breeds are more commonly affected (i.e., Yorkshire terriers, Pugs, Maltese, Schnauzers, Poodles, Shih Tzus, Havanese, Irish Wolfhound, Golden Retrievers, and Labrador Retrievers), but any dog may have a congenital PSS. We infrequently see classic post-prandial hepatic encephalopathy; rather, we more commonly see a young dog (e.g., one of the above breeds that is less than a year old) that is a "poor doer" who is not as big or as strong as the litter mates with very intermittent vomiting (i.e., "he or she has always had a sensitive stomach") and subtle signs of encephalopathy. Therefore, it is important to eliminate intestinal parasites and hypoglycemia in animals with suspected congenital PSS since the signs may be very similar. Polyuria-polydipsia can be a major clinical sign. In fact, in our practice, most young animals referred for possible central diabetes insipidus turn out to have hepatic disease, especially congenital PSS.

Classic hepatic encephalopathy consists of post-prandial seizures, coma, somnolence, blindness, head pressing and/or aggression. However, we are seeing more and more animals in which hepatic encephalopathy is manifested simply by their laying around a lot, acting tired or lethargic, or just not being interested in anything. In many cases, there is no obvious relationship between eating the signs. In some cases, about all you can say is that he patient has always been a "calm" dog and never really caused a lot of trouble by getting into things. In older dogs, the only comment by the owner may be that they dog is "getting older and slowing down a bit". To make matters more confusing, we are finding dogs that have hepatic encephalopathy that do not respond to medical management with lactulose or metronidazole. Some of these patients only quit having signs of hepatic encephalopathy when the shunt is surgically corrected. Therefore, you cannot allow lack of response to medical therapy help you decide whether or not a dog has hepatic encephalopathy due to a congenital PSS. Cats with hepatic encephalopathy due to congenital portosystemic shunting often have drooling as a major presenting complaint.

We sometimes see hematuria due to ammonium urate urolithiasis, but this usually often happens in older dogs (especially Schnauzers) that have had chronic hyperammonemia. Many times, this is the only clinical sign in the affected patient. Contrary to what is often described in textbooks, you can sometimes see major increases in ALT and SAP. We occasionally see patients with major increases in ALT (i.e., > 1,000 U/L) that appear to have acquired hepatic disease, probably toxic in nature. The ALT waxes and wanes with clinical signs. Our guess is that these dogs only have signs when they develop liver disease secondary to exposure to "toxins" that the atrophied liver cannot process because it is insufficient.

To further complicate the situation, we are seeing more and more dogs with congenital PSS that are being diagnosed for the first time when they are 7 or even > 10 years old. This appears to be especially common in Schnauzers, although other breeds may also be affected. Many times these patients have relatively minor signs that have been considered as normal for the particular patient (i.e., has always been a quiet dog, has always been a smallish dog, etc).

Ascites is exceedingly rare in animals with congenital portosystemic shunts. This is in distinction to dog with congenital hepatic AV fistula, which is another congenital vascular abnormality but which is entirely different from the standpoint of signs, diagnosis, and treatment. Ascites is relatively common in dogs with acquired portosystemic shunting. Therefore, if ascites is seen, one should first look for other hepatic diseases. In like manner, icterus is very seldom caused by congenital portosystemic shunts, and finding hyperbilirubinemia is an indication to first look for other diseases. In summary, congenital PSS present in a variety of ways, many of which are not the "classic" presentation that is described in textbooks.

The major criteria for presumptive diagnosis of congenital portosystemic shunts has classically consisted of an appropriate history and physical examination as well as obvious microhepatia and very increased serum bile acid concentrations. It was generally anticipated that dogs with congenital PSS would have serum bile acid concentrations > 90 mmol/L. Hypoalbuminemia, hypocholesterolemia, and/or decreased BUN are common findings on clinical pathology, but they are not invariable; some patients with congenital PSS do not have any abnormalities on the serum biochemistry panel. Ammonium biurate crystals in the urine are useful if they are present; but, most of the cases of dogs with congenital portosystemic shunts that we see do not have ammonium biurate crystals in the urine.

It now appears that serum bile acid concentrations are not as easy to interpret or as definitive as many people think. First, you must always measure both resting and post-prandial concentrations because about 20% of dogs have a resting serum bile acid concentration that is higher than the post-prandial serum bile acid concentrations. Second, there can be marked variation in serum bile acid concentrations from day to day. It is easy to see a two-fold difference in values taken a few days apart, and we have seen a three-fold increase in samples that were taken 72 hours apart.

Third, some dogs with congenital portosystemic shunts have surprisingly low serum bile acid concentrations. We have found dogs with congenital PSS that have what we would consider relatively modest increases in serum bile acids (e.g., 55-65 mmol/L, which is a value found in many animals with clinically insignificant hepatic disease), and rare cases have completely normal serum bile acid concentrations. In distinction, some dogs without any demonstrable hepatic pathology other than vacuolar hepatopathy have values in excess of 200 mmol/L. This major overlap in the values of serum bile acid concentrations in dogs with and without clinically significant hepatic disease leads to diagnostic confusion in some cases.

Hyperammonemia is very specific for hepatic insufficiency, especially congenital PSS. However, it is easy to have laboratory artifacts that falsely increase these values. This test can only be run in house, and the instructions must be followed to the letter to avoid artifactual results. Measuring only fasting blood ammonia concentrations is approximately 80% sensitive for congenital PSS (and lower for diseases causing acquired hepatic insufficiency). The ammonia tolerance test is an excellent test with very high sensitivity and specificity, but it is a royal pain to do (e.g., would you like to drink ammonia chloride or have it infused into your rectum?) and consequently is seldom performed. Measuring blood ammonia concentrations 4-8 hours post-prandially seems to enhance the sensitivity for congenital PSS up to about 90%.

Imaging can be helpful, but one must recognize the limitations of these techniques. We expect to see microhepatia in dogs with PSS, although sometimes the change is very modest. Sometimes there is a marked difference in the apparent size of the liver on the left lateral versus the right lateral projection. Radiographs are a much more sensitive way to find microhepatia than ultrasound. If there is any doubt about the size of the liver, one can administer a few mls of barium sulfate to help outline the stomach, allowing one to easily ascertain the cranial border of the stomach. The area between the cranial border of the stomach and the diaphragm is usually the liver. However, occasional animals will appear to have a small liver when in fact they have a normal sized liver. Fortunately, this situation appears to be unusual and should be picked up if lateral and DV views are obtained.

Ultrasound is commonly employed when looking for congenital portosystemic shunts. A good ultrasonographer can find a congenital PSS about 50-75% of the time, if they are accomplished and can take their time and look. Truly exceptional ultrasonographers seem to find congenital PSS about 90% of the time. Therefore, you must remember that failing to find a congenital PSS on ultrasound does not eliminate it. Furthermore, one cannot look at the liver to see if there are apparently normal portal areas as a means of deciding if a congenital shunt is more or less likely. We have seen animals with congenital PSS that appeared to have normal portal vasculature on ultrasound, to the point that the conclusion was that a congenital shunt was very unlikely. Ultrasonography is a very good way to check for an intrahepatic shunt, which is much harder to correct than an extrahepatic shunt.

Other imaging techniques may include operative or percutaneous portograms, nuclear scintigraphy, and MR or helical CT. These latter techniques should primarily be done for one of two reasons. First, the case is "atypical" and it is important to absolutely confirm the presence of a congenital PSS before going to surgery. The second reason is that the surgeon is unable to find the shunt during an exploratory laparotomy. In general, it is not always necessary to definitively "see" the shunt via some imaging modality before going to surgery. If the case is classic in that it is a young animal with appropriate signs and an obviously small liver and obviously high serum bile acids or ammonia, then one is justified in going to surgery even if the shunt has not been visualized. If the shunt cannot be found during surgery, then an intraoperative portogram can be performed. However, if any of those three criteria are not met (i.e., "classic" history, obviously small liver, obviously increased serum bile acids or ammonia), then confirmation by portography, scintigraphy, CT or MR is appropriate.

Retrograde portography is often preferred when an intrahepatic shunt is believed likely because we prefer to fix these with catheters (i.e., putting in a stent and then coils). Nuclear scintigraphy is also very nice, but requires special facilities. One advantage of portography is that one may place the catheter in the shunt and leave it there in order to help the surgeon find the shunt if they are having a very difficult time finding it.

Lastly, it is important to do a full work up (i.e., CBC, serum chemistry panel, abdominal radiographs, abdominal ultrasound, serum bile acids or blood ammonia) on all dogs with suspected congenital PSS. These dogs may have other, concurrent diseases. In fact, dogs with previously well compensated congenital portosystemic shunts may not become symptomatic until another disease process causes the patient to start showing signs due to the shunt. Furthermore, a reasonable number of affected dogs have cystic calculi that can be removed during the surgery to correct the congenital shunt.

Surgical correction is usually preferred for younger animals and for those that have signs of encephalopathy that are not controlled with medical therapy. But, surgery is not without risks. The Ameroid constrictor makes the surgery much easier and quicker than before. However, about 15-20% of dogs that have surgery to correct a PSS will have some post-operative complications (usually something minor like ascites). This is usually not a major problem, but the owner needs to be warned ahead of time. Some dogs develop enough portal hypertension to cause acquired PSS, and a few (i.e., 5-7%) have major, life-threatening problems (e.g., post-ligation seizures, portal hypertension) and die. Not every dog with a congenital PSS is benefitted by Ameroid constrictors.

A major concern centers around dogs (especially those 5 years old and older) with congenital PSS that are clinically normal and that have minimal changes on serum biochemistry panel and a liver that is not too small on radiographs. We are finding these dogs because awareness of congenital PSS has substantially grown, and more and more people are looking for them and diagnosing them in animals with minimal or even no clinical signs. If the liver is not too small on radiographs, the serum albumin is > 2.0 gm/dl, and there are minimal to no clinical signs, then we might decide to

watch them to see if they will ever need surgery. Dogs with congenital PSS causing hepatic encephalopathy typically benefit from corrective surgery. There is concern that dogs > 5 years of age are more likely to have severe complications from corrective surgery. While this might be the case, many dogs have benefitted from surgery despite being > 5 years of age. This entire area is currently very controversial. We see some dogs with congenital PSS that seemingly live a normal life and never need corrective surgery. Therefore, if you are considering surgery in an older dog (e.g., > 6 years old) without any major clinical signs, you should probably have a long talk with the owners about how the dog could be worse after the surgery than it was before.

If post-ligations seizures occur, you must first be sure that the dog is not hypoglycemic. The cause of this problem is uncertain, but some suggest it might be due to cerebral edema. We have not treated for cerebral edema in these patients; rather, we typically anesthetize them with a constant rate infusion of propofol until the seizures have stopped. Do not use diazepam or phenobarbital. Some people recommend treating dogs with potassium bromide or Keppra and cats with phenobarbital before surgery for congenital portosystemic shunts, in an effort to avoid this problem. This approach is contentious, and time will tell if it is correct or not. In general, cats with congenital portosystemic shunts do seem to have more post-operative problems than dogs.

Dogs with intrahepatic shunts have a worse prognosis because the surgery is technically much more difficult to perform. If you can refer the dog to a center which can place coils in the shunt via intravenous catheters used with fluoroscopy, that might be a much safer way to try to correct the problem.

The medical treatment for hepatic encephalopathy is relatively straightforward; lactulose, metronidazole, and a low protein diet. However, the concept of low protein must be revisited. Giving too little protein is extremely detrimental to the liver. The goal is to give as much protein as the liver can tolerate. In particular, it is best to give milk and vegetable proteins instead of meat proteins.

Biliary tract disorders in dogs and cats

Michael D Willard, DVM, MS, DACVIM

Cholecystitis

Cholecystitis is much more common than many people realize. Dogs that have evidence of antibiotic responsive hepatobiliary tract disease may have a bacterial cholecystitis. Typically, both the ALT and SAP are increased, and icterus is common. Most dogs with cholecystitis do not have discernable gall stones. Many (maybe most) gall stones found in dogs and cats are clinically insignificant and only serve to confuse veterinarians. Ultrasound findings in dogs with bacterial cholecystitis are non-specific: finding "sludge" in the gall bladder can also occur in clinically normal dogs.

At this time, aspirating bile via ultrasound-guided, percutaneous puncture with a 22-25 gauge needle may be the best diagnostic test we have. You are much more likely to find bacteria in the bile than you are to find them in hepatic parenchyma (this applies for cytology/histopathology as well as culture). Rarely, such percutaneous aspiration techniques will cause a vagal response that will cause extreme bradycardia (this is rare, but it is more likely in cats than in dogs); however, if this happens all that is usually needed is an injection of a parasympatholytic such as glycopyrrolate. If you use ultrasound guidance to insert the needle through the quadrate lobe of the liver (which is adherent to the gall bladder), then there is no risk or concern with leakage of bile into the abdomen. In this case, if bile leaks from the gall bladder, it will simply leak into the liver lobe which is harmless.

Finding WBCs and/or bacteria in the bile seems to be very specific, but we are not really sure how sensitive this test is for cholecystitis. It is important to note that normal dogs and cats can have a very few bacteria in the bile. This is because there is a normal entero-hepatic-biliary circulation of bacteria in bacteria go from the intestines to the liver (probably due to translocation across the intestinal mucosa) where they are excreted into the bile and then ejected with the bile back into the intestinal lumen. Therefore, you need to find more than just one or two bacteria in the bile before you make this diagnosis.

Therapy of infectious cholecystitis usually involves chronic (i.e., > 6-8 weeks) antibiotic therapy. If I can see lots of bacteria but cannot culture the bacteria and obtain a sensitivity assay (which happens surprisingly often), I prefer to use a combination of amoxicillin and enrofloxacin. If that approach is unsuccessful, then cholecystectomy is usually the next step. Do not do a cholecystotomy or an incisional biopsy of gall bladder wall; dehiscence appears to be a major cause of morbidity and mortality after such surgery. Rather, remove the entire gall bladder and submit it for histopathology and microbiology. Be sure that you do not ligate or transect the common bile duct, or you may kill the dogs. Remember that cholecystectomy may be required to cure a patient with cholecystitis.

Emphysematous cholecystitis is classically associated with diabetes mellitus or hyperadrenocorticism, but it probably occurs just as often in non-diabetic animals. This malady is diagnosed radiographically: gas in the wall of the gall bladder or gas within the gall bladder lumen. Both lesions are typically are very obvious on abdominal radiographs, but care must be taken to not off-handedly attribute any gas seen in the cranial abdomen to gastric or intestinal gas. Treatment with antibiotics that are effective against gas-producing anaerobic bacteria (e.g., penicillin, metronidazole, chloramphenicol, or clindamycin) is indicated. If that approach is unsuccessful, then cholecystectomy will be required.

Necrotizing cholecystitis is typically the result of long standing bacterial cholecystitis or mucocoele (see below). The three most important things to remember about this problem are that a) necrotizing cholecystitis can be clinically obvious or clinically occult, b) abdominal ultrasound can be relatively specific for cholecystitis, but it is insensitive, and c) if the gall bladder ruptures, the prognosis is grave.

Sometimes during surgery or laparoscopy, the gall bladder obviously looks like it may be necrotic. However, some dogs with severe necrotizing cholecystitis have a gall bladder that visually appears normal. It is critical to realize that a gall bladder can look and feel normal and yet have transmural necrosis and be about to spontaneously rupture. This lack of obvious gross changes in affected animals is one of the major reasons why cholecystotomy is such a bad idea. If you try to suture diseased (often necrotic) tissue together, perforation is almost expected.

Ultrasound might reveal changes that are very suggestive of necrotizing cholecystitis (e.g., discontinuous wall, markedly thickened wall, trilaminate wall), mildly suggestive of necrotizing cholecystitis (e.g., pericholecystic edema or hyperechoic fat), or nothing at all. Aspirate cytology is still the most reliable diagnostic test.

If rupture of the gall bladder is suspected, immediate surgery is indicated. Rupture of a gall bladder with necrotizing cholecystitis releases bacteria as well as bile into the abdomen. Such patients can almost literally melt in front of your eyes in a matter of hours. This is a genuine surgical emergency.

Mucocoeles

Sometimes excessive mucus is secreted into the gall bladder and becomes so thick and inspisated that it essentially becomes a solid mass. This is referred to as a biliary mucocoele. Endocrinopathies (e.g., hyperadrenocorticism, diabetes mellitus, excessive androgens as are suspected to occur in Scottish Terriers) and animals with problem of lipid metabolism (e.g., Schnauzers) seem to be at increased risk, but the cause is probably multifactorial. Poor emptying of the gall bladder seems to be important, but its cause is uncertain. Biliary mucocoeles are essentially unknown in cats. For reasons that are not clear, the incidence of this disease appears to have substantially increased compared to 15 years ago.

As mucus fails to be evacuated from the gall bladder, it accumulates and becomes thicker, similar to the consistency of extra-thick jell-O. Initially, the gall bladder expands as it becomes more and more filled. Eventually, as the gall bladder becomes more filled, the mucus will be pushed into the cystic duct, causing occlusion and extra-hepatic biliary tract obstruction (EHBO). Diagnosis is typically accomplished by abdominal ultrasound. You are not looking for gravity-dependent sludge; rather, you are looking for a "stellate" appearance to the gall bladder (the so-called "kiwi fruit" appearance). Cholecystectomy appears to be the only appropriate therapy. Many of these patients have necrosis of the wall of the gall bladder due to the pressure exerted by the lumen of mucus. Because the gall bladder is typically a very thin-walled structure, this intraluminal pressure can result in avascular necrosis with eventual rupture causing peritonitis. Prognosis is good, as long as you do surgery before the gall bladder ruptures and there are no post-surgical complications such as pancreatitis.

A couple of very controversial points are what constitutes the ultrasonographic diagnosis of an immature biliary mucocoele, and whether gall bladders with non-gravity dependent "sludge" need to be removed or not. Some animals with "immature" mucocoeles seemingly resolve if treated with choleretics such as ursodeoxycholic acid.

Gallstones

Gall stones, as mentioned are usually there simply to distract the veterinarian. I am not saying that they never cause disease. I am saying that they are usually innocent of causing disease. If you find gall stones, you should first look elsewhere for the cause of the patient's illness. If you can find nothing else that seems likely to be responsible for causing hepatobiliary tract disease in the patient, only then should you allow yourself to focus on the gall stones. Of course, if there are bacteria in the bile, then the gall stones are likely to be very important and should be removed so as to prevent recrudescence of the infection.

Extrahepatic biliary tract obstruction from other causes

Pancreatitis is the most important cause of extrahepatic biliary tract obstruction (EHBO) in the dog. If EHBO is present in a sick dog and appears to be idiopathic, it should generally be assumed to probably be due to pancreatitis until there is evidence to the contrary. History and physical examination are helpful in diagnosing pancreatitis, but not as useful as we'd like. Schnauzers and Yorkies are famous for pancreatitis, but these breeds get a lot of other diseases that cause vomiting, and pancreatitis can be found in any breed of dog. Canine pancreatitis is classically considered to present with acute vomiting and anorexia. Abdominal pain is frequently present, but it is easy to miss during physical examination, and fever is occasionally seen. However, we are recognizing more and more "atypical" cases to the point that we are no longer sure what a "typical" case of canine pancreatitis is. We are now recognizing more and more cases of severe disease which present in shock due to systemic inflammatory response syndrome (what used to be called septic shock, until we found out that you can have the same thing occur with any cause of massive inflammation); such patients may die very suddenly. We are also recognizing more and more dogs with acute pancreatitis that present as though they had an acute, septic abdomen. Some have substantial amounts of abdominal fluid. If acute pancreatitis is associated with or due to pancreatic carcinoma (rare), you may also see a dog that has widespread subcutaneous fat necrosis causing sterile abscesses that are typically painful and cause cutaneous discoloration. Most cases of canine pancreatitis are related to either ingestion of fat or lipemia associated with diabetic ketoacidosis. Trauma and drugs can also cause canine pancreatitis. Drugs that are suspected of causing pancreatitis in people and animals include azathioprine, sulfonamides, tetracycline, and potassium bromide.

Imaging

Pete Mantis (UK)

DVM, DipECVDI, FHEA, MRCVS

(Diagnostic Imaging)

Panagiotis (Pete) Mantis graduated from the Faculty of Veterinary Medicine of the Aristotle University of Thessaloniki, Greece. Pete completed his veterinary diagnostic imaging residency at the Royal Veterinary College. After completing his residency, Pete worked in first opinion practices and referral hospitals in the United Kingdom providing an emergency and diagnostic imaging consultancy service.

In 2000, he joined the Department of Veterinary Clinical Sciences at the Royal Veterinary College and currently he is Senior Lecturer in Radiology. Pete is a European and RCVS Recognized Specialist in Veterinary Diagnostic Imaging and a Fellow of the Higher Education Academy. Pete is a regular author, speaker and CPD tutor on the subjects of small animal radiology, ultrasonography, computed tomography and magnetic resonance imaging.

Computed tomography: the basics

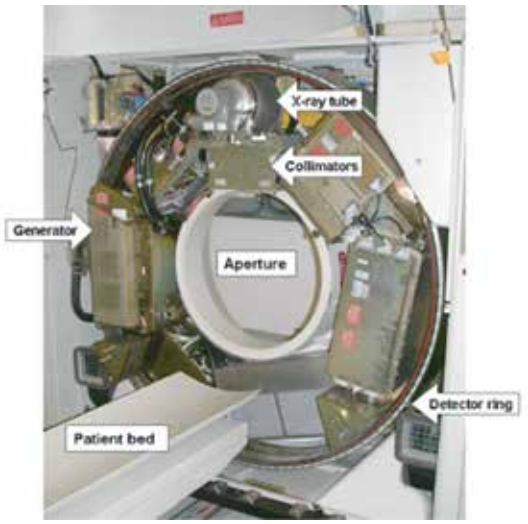
Panagiotis Mantis DVM, DipECVDI, FHEA, MRCVS
Consultant Radiologist, Dick White Referrals

Computed Tomography (CT) was invented in 1972 by Godfrey Hounsfield. The first veterinary use was reported about 10 years after the introduction of CT. The first units were dedicated to head imaging however whole-body systems with large openings were introduced in 1976.

The first scanner took several hours to acquire the data and days to reconstruct a single image. The multi-slice CT systems available now can collect multiple slices of data in milliseconds and reconstruct a 512 x 512-matrix image from millions of data points in less than a second. An entire body can be scanned in a few seconds using the most advanced multi-slice CT system.

The initial systems used in veterinary medicine were single detector units while now multidetector units are available for veterinary patients in academic and private hospitals and practices.

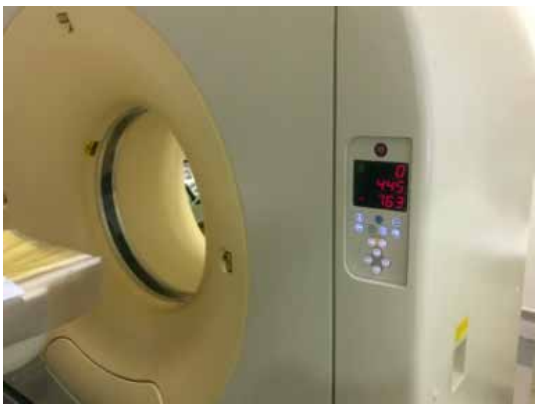
Basic components of a CT unit



Basic parts of a CT unit

- Moving table (patient bed).
- A gantry where the x-ray tube and detectors are mounted. The CT x-ray tube is mounted on a rotating gantry and revolves around the patient during the exam.
- Lasers mounted at the gantry indicating the horizontal and the vertical axis.

Lasers indicating the horizontal and vertical axis



- Numerical display.
- CT user control where the patient details are entered, and the examination is planned. The control station is connected to the computer that will handle the image reconstructions of the raw data.

CT user control screen from a 16-slice system. On the left the patients details screen is visible. On the right the examination planning screen is visible.

Different to the beam geometry used in conventional radiography, the CT x-ray beam is collimated thinly in the Z-direction. In single detector units the slice thickness is controlled by this collimation. In multi detector units the slice thickness is controlled by the detectors used.

Benefits of CT

CT can differentiate between 4096 shades of grey providing higher contrast resolution in comparison to radiography.

The cross-sectional nature of CT allows the elimination of superimposition.

Generations of CT

The CT technology has evolved through several generations.

In early generations of CT, the tube and detectors would rotate once around the patient and the patient table would move a pre-determined distance, before the next rotation of the tube and detectors (step and shoot approach). The scan mode using this approach is called axial scanning. In third generation CT units the slip-ring technology was introduced, and the helical scan mode was possible. Depending on how fast the table is moving in one rotation, the helix of the scan will stretch or compress. This is expressed as the pitch and it is set by the user.

Acquiring a CT examination

- Enter the patient details.
- Select the body part.
- Tube rotation time: is usually set low to 0.5-1sec. In some units the mA setting is automatically coupled to the tube rotation time to generate the same mAs.
- mAs (mA): between 100-200mAs for the thorax and abdomen and 200-250mAs for the head and musculoskeletal system are used in small animal patients.
- kV: Generally high kV settings are used in CT. Usually 120kV are adequate for small animal patients. For larger patients, the mA is adjusted rather than the kV.
- Scan field of view: this parameter is commonly not user-adjustable but set to the maximum scan field of view available. It is paramount to place the patient in the centre of the scanner within the scan field of view, using the lasers for alignment.

- Display field of view: it is the same or smaller than the scan field of view. The choice of display field of view will determine the pixel size (large display FOV will result in large pixel size and small display FOV will result in small pixel size). It is advisable to set the display FOV closely around the anatomic area of interest.
- Gantry tilt: the gantry can be tilted to allow optimal alignment.
- Slice thickness:
  – Thorax and abdomen: 1-3mm slice thickness provides good anatomical image quality.
  – Musculoskeletal: thin slice thickness, less than1mm, is preferred.
  The thinner the slice thickness the higher the number of images generated, and more accurate anatomical depiction will be evident. However, the final number of generated images can become very high delaying image reconstruction and increasing the time of transfer and therefore needing more time to read and interpret the study.
- Slice interval: is the interval the images are acquired in axial mode or reconstructed in helical mode. It is commonly set up the same as the slice thickness so there would be no gap between the slices.

Axial vs helical scanning

As a rule of the thumb, axial scanning will result in increased image quality in up to 16-slice-scanners. There is no benefit in using axial scanning in more than 16-slice scanners.

Spatial image reconstruction algorithms

Low frequency reconstruction algorithms are used to produce a smooth image. They are used for body areas with inherently low contrast such as the abdomen, brain and all post-contrast studies.

High frequency reconstruction algorithms are used for body parts with an inherent wide object contrast such as the lungs, bones and nasal cavity. The application of these algorithms is performed when planning the examination. Multiple reconstructions of the scanned body area are commonly obtained.

Hounsfield units

Each pixel in the image is displayed according to the mean attenuation of the tissue(s) that it contains. This is represented on a scale (Hounsfield scale) from +3071 (most attenuating) to –1024 (least attenuating). Water is set as 0(zero) on the scale. Tissues with a density lower than water displayed as less than 0 and any tissue with a density higher than water is displayed as more than 0.

Air -1000 HU
Lung -500 to -700 HU
Fat – 100 to -50 HU
Water 0 HU
CSF 15 HU
Soft tissues 30-50 HU
Bone 700-3000 HU

Window Width and Window length

Although the CT technology differentiates 4096 shades of grey the human eye can detect far less. Window width (how many shades of grey) and window length (the centre of these shades of grey) are set to highlight the tissue of interest (bone, soft tissue, lung, brain etc).

Examples of setting (WW: window width and WL: window length):

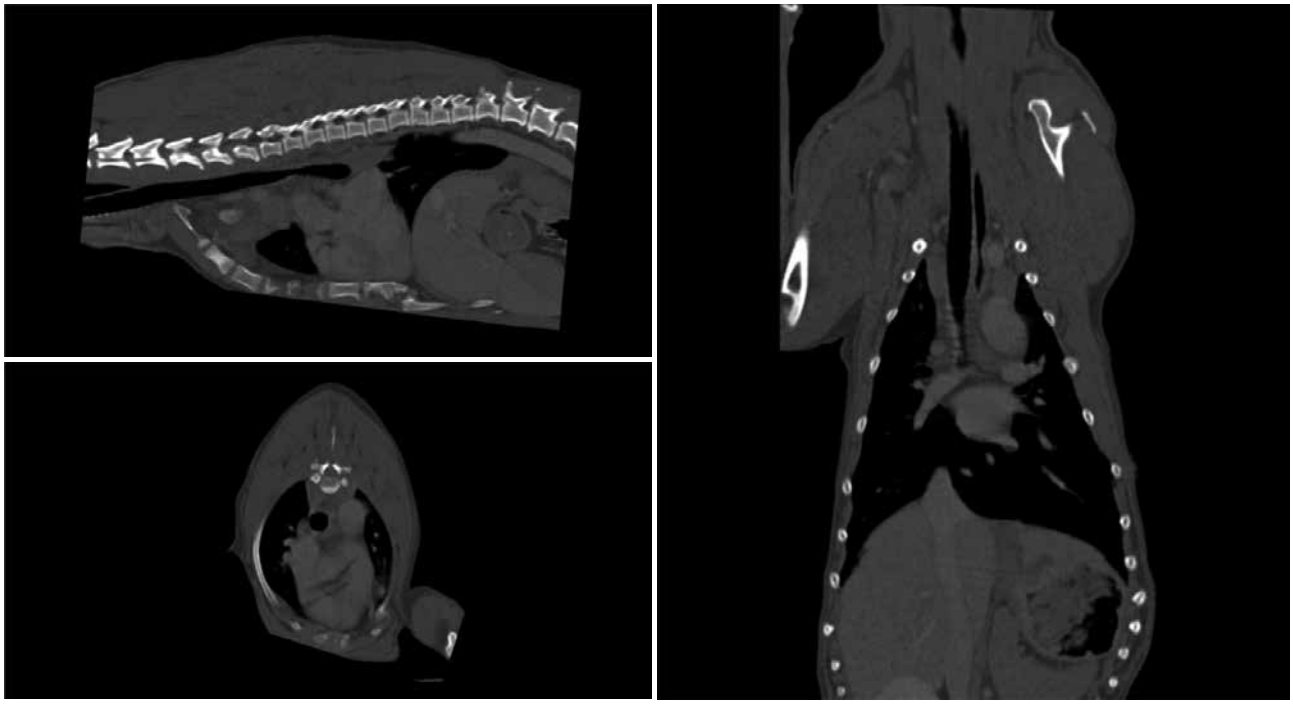
Brain WW 50 WL 100
Abdomen/mediastinum WW 50 WL 350
Bone WW 300 WL 1400
Lung WW – 500 WL 1500

The windowing can be modified at any time after the end of the examination using DICOM viewing software. The reconstruction algorithm previously mentioned (low or high frequency algorithm) needs to be planned at the time of the acquisition or reconstructed later from the raw data.

Optimal visualisation of the different obtained series will need the correct combination of algorithm and window.

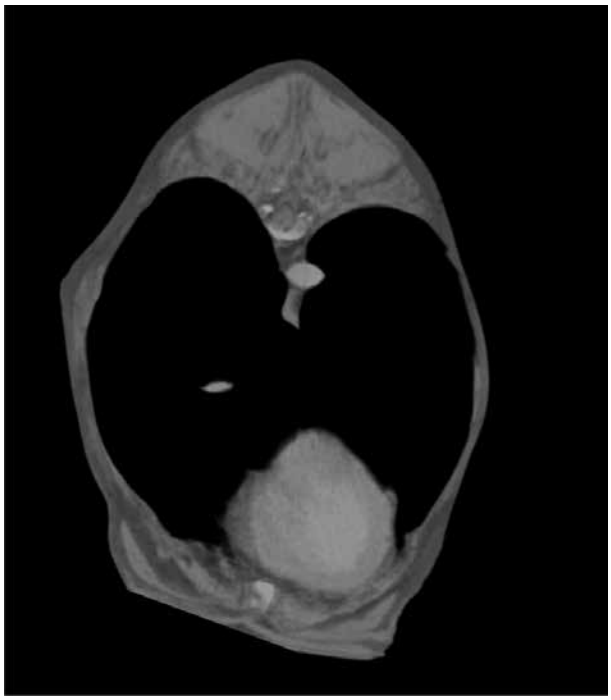
Multiplanar reconstruction (MPR)

A scan acquired in transverse plane can also be displayed in dorsal or sagittal plane, and the user is able to scroll through these planes

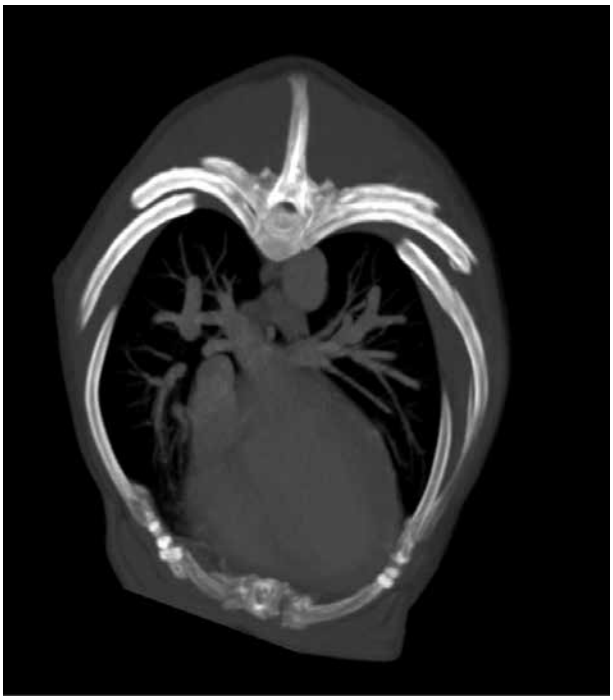


Maximum intensity projection (MIP)

Thin slices are summed into thicker slices on the viewing station.



Minimum intensity projection



Maximum intensity projection

Minimum intensity projection (MinIP)

Like MIP with all the dense structures subtracted. MIP is a data visualization method that enables detection of low-density structures in a given volume.

3D rendering

Works better with thin slices. It provides 3D reconstructions.

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Thoracic CT of the dog and cat

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Protocol

- Sternal recumbency
- Margins of scan: thoracic inlet to caudal tip of lung. Scan from caudal to cranial.
- Pre-scan hyperventilation, if the animal is under general anesthesia, would allow respiratory pause for a motion free examination.
- kVp= 120
- mAs=160 (for high resolution 200-300)
- Slice thickness= 1-3m
- Scan mode: helical
- Spatial reconstruction algorithm: Medium frequency (soft tissue) pre and post contrast, high frequency (lung) pre-contrast.
- Contrast: 600-800 mg I / kg

Reading thoracic CT studies

- Evaluation pre and post contrast studies in soft tissue windows side by side.
- Evaluate high resolution lung window study and
- Evaluate pre and post contrast studies in bone window.
- MPR, MIP and MinIP can be employed to assist with the anatomic localisation and identification of specific diseases.

Systematic evaluation

Make sure you evaluate all visible structures. A list for example is:

- Lungs
- Bronchi
- Pleural space
- Vessels
- Any visible thrombi
- Heart
- Mediastinum (including lymph nodes, thymus, trachea, oesophagus)
- Chest wall, lower neck, extra-thoracic structures
- Cranial abdomen included
- Skeletal structures

You can create your own list making sure you include everything that you can see or possible see.

Lungs

On CT you can identify the lung lobes: 4 on the right (cranial, middle, caudal and accessory) and 2 on the left (cranial and caudal).

In cases of pneumonia, the lungs become more soft tissue attenuated. Peribronchial thickening can be seen in allergic or parasitic pneumonia. Pulmonary nodules, masses, abscesses and granulomas may be identified and characterised based on the pre and post contrast findings. Idiopathic pulmonary fibrosis (reported in terriers and cats) appears as diffuse ground glass soft tissue attenuation with peribronchial and subpleural soft tissue attenuating areas and possible mild bronchiectasis. Lung lobe torsion (Fig 1) appears as collapsed or swollen lung with accumulation of small air pockets (called vesicular pattern), pointing in the wrong direction with abruptly interrupted bronchus. Pulmonary oedema

appears as areas of soft tissue attenuation in the lung and enlarged pulmonary veins (if cardiogenic). Pulmonary neoplasms appear as soft tissue attenuating masses with possible mineralisation. Cavity(ies) or gas in larger masses may be also seen. Metastatic lung neoplasia usually appears as multiple soft tissue attenuating nodules and masses (Fig 2).

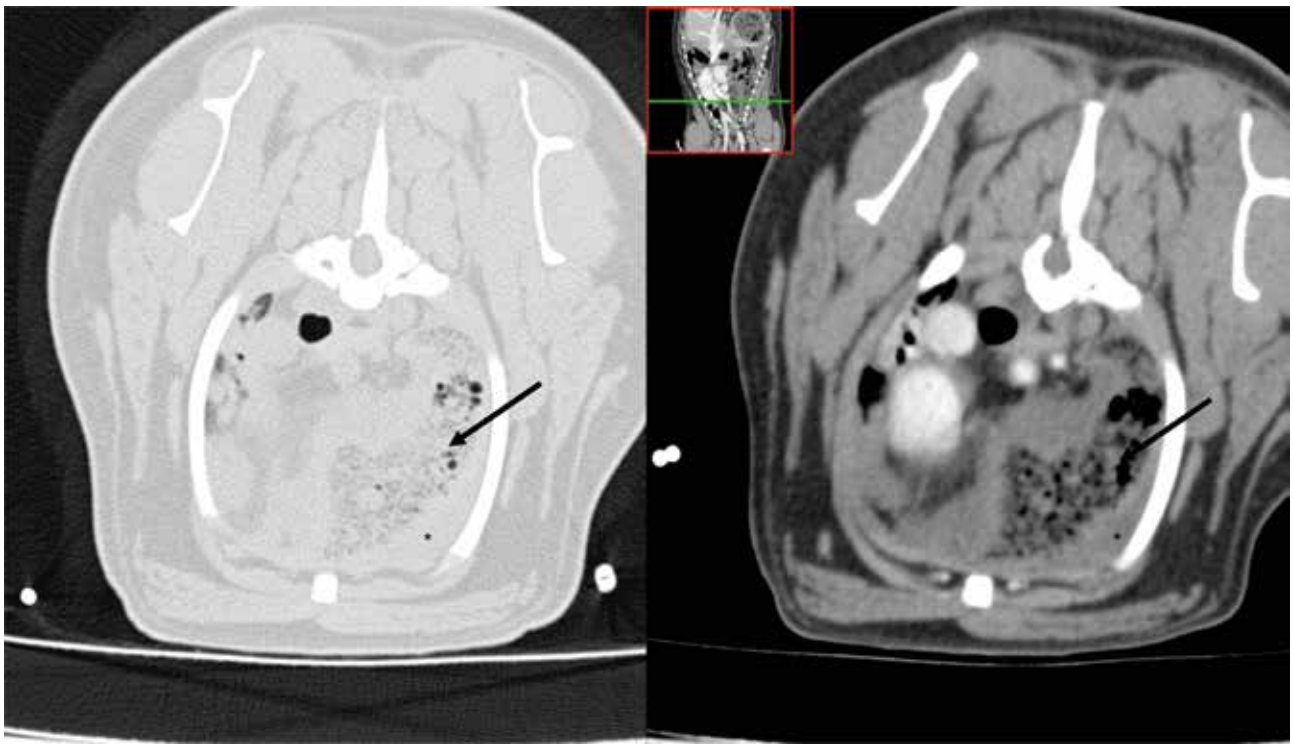

Figure 1. Male pug 4 years old. Lung window image (left) and soft tissue post contrast images (right). There is moderate pleural effusion distributed in the dependent part of the pleural space (*) and an enlarged, left cranial lung lobe with CT features consistent with lobar torsion and evident vesicular pattern (arrow).

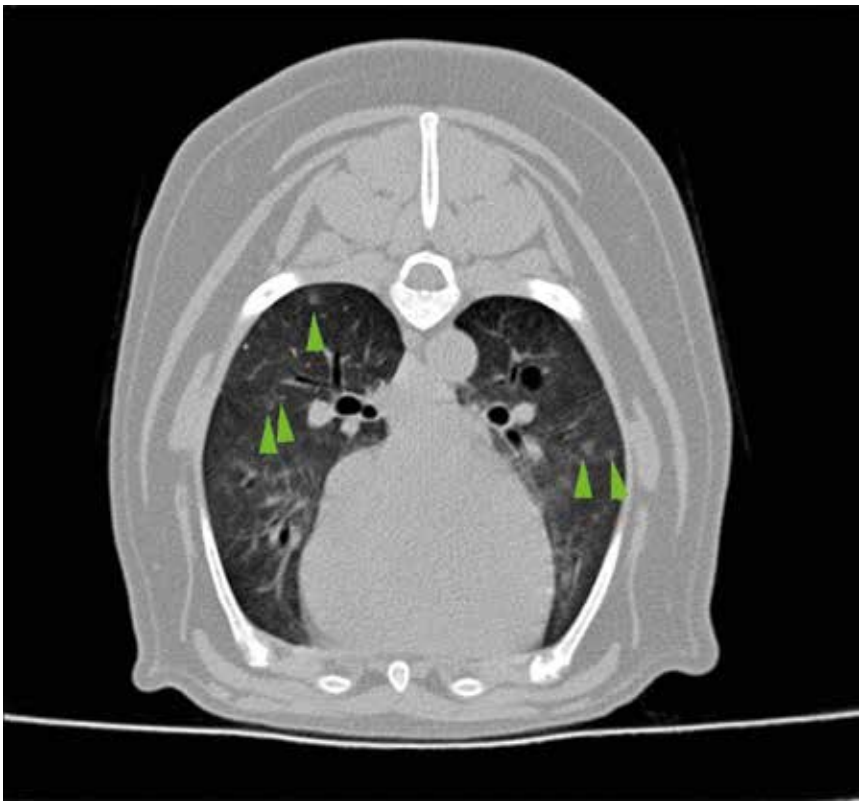

Figure 2. Female neutered JRT 13 years old. Lung window image Multiple lung nodules compatible with metastatic neoplasia (arrowheads).

Bronchi have thin walls and taper towards the periphery. They can be dilated in cases in bronchiectasis or be collapsed or narrowed. They can be thickened in cases of bronchitis with soft tissue attenuating material in the lumen. Bronchial foreign bodies can be identified on CT and focal pneumonia or abscessation can be seen concurrently.

Pleura

- Pneumothorax appears as space with lack of attenuation between the parietal and visceral pleura.
- Pleural effusion appears as hyperattenuating (soft tissue density) tissue with no contrast uptake in the pleural space. It can be unilateral (more common with pyothorax) or bilateral.
- Pleural masses appear as irregular or nodular thickening of the pleura.

Heart and great vessels

Cardiovascular angiography allows more detailed assessment.

On routine thoracic CT, the size of the cardiac silhouette can be subjectively evaluated along with the heart location, presence of masses and pericardial effusion.

Cardiac CT angiography

Gated CT acquisition (scan acquisition is timed to the cardiac cycle; can be prospective or retrospective) is used because the heart is in motion continuously. This requires special software installed. Coronary angiography is used mainly to identify the presence of aberrant vessel that may be present in bulldogs with pulmonic stenosis. Functional cardiac CT angiography requires retrospective gated examinations. Non-gated CT angiography can help with the identification of a heart base mass or/ and pericardial effusion. Pulmonary CT angiography allow visualisation and evaluation of the pulmonary arteries and veins.

Mediastinum

The thymus is visible in young animals. The thymic remnant can be seen in older animals. Thymomas appear as ventral cranial mediastinal masses with often cystic components, displaying poor contrast enhancement (Fig 3). The lymph nodes can be seen and stand out more when enlarged or/ and rounded. The oesophagus may contain a small amount of gas if the animal is sedated or anesthetized. Oesophageal masses and foreign bodies can be identified. An oesophageal diverticulum can be seen as focal dilatation of the oesophagus in the cranial mediastinum. Megaoesophagus shows as extensive or complete oesophageal dilatation. In cases of oesophageal stricture the stricture is not usually visible, but the proximal distension is visible. The trachea extends to the bifurcation at the carina. The trachea contains gas and the tracheal rings do not overlap. Tracheal hypoplasia, tracheal collapse or masses can be identified in pre and post contrast studies. Tracheitis may not be seen since the examination may appear normal; however tracheal narrowing may be seen. Tracheal laceration or avulsion can be identified along with pneumomediastinum.

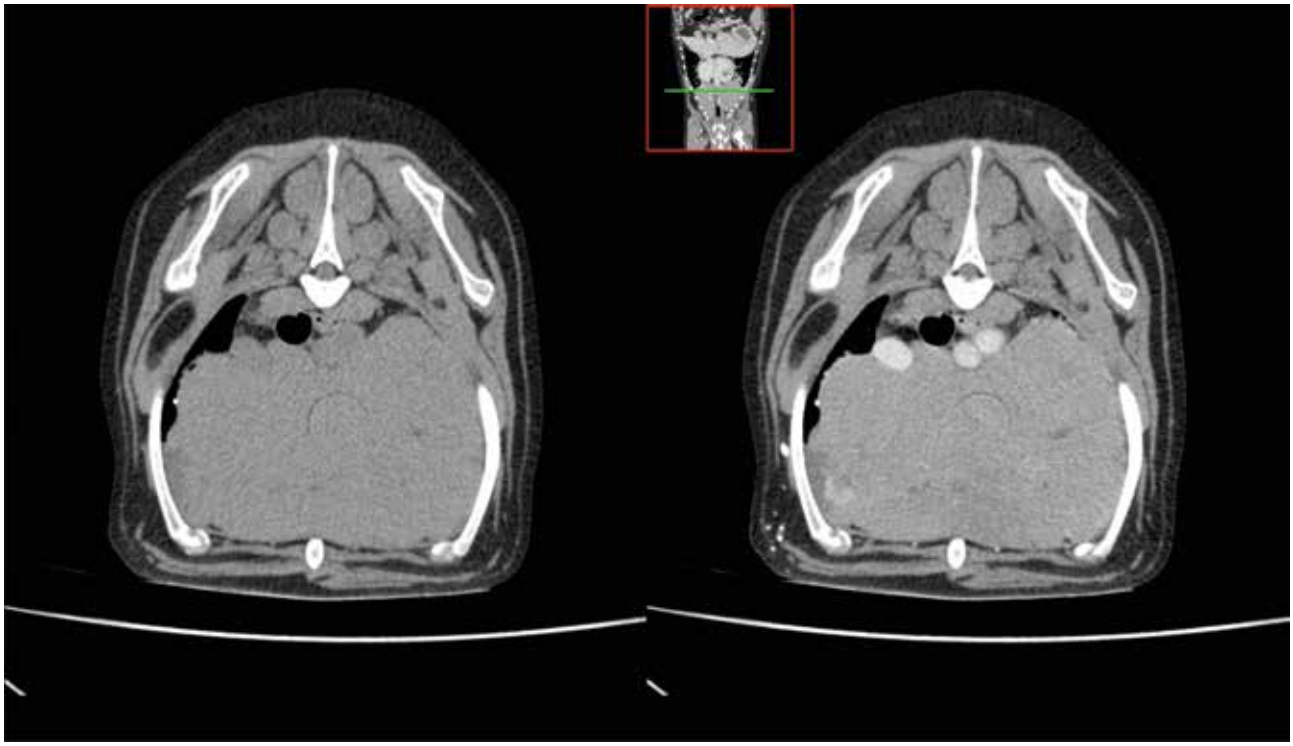

Figure 3. Male neutered Labrador 12 years old. Soft tissue window (pre-contrast (left) and post-contrast (right). A large, poorly contrast enhancing thymoma is visible.

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Canine and feline abdominal CT: clinical applications

Panagiotis Mantis DVM, DipECVDI, FHEA, MRCVS
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Protocol

- Ventral recumbency
- Margins of scan: cranial edge of diaphragm to perianal area
- Pre-scan hyperventilation, if the animal is under general anesthesia, would allow respiratory pause for a motion free examination.
- kVp= 120-140
- mAs=100-250
- Slice thickness= 1.25-3m
- Scan mode: helical
- Spatial reconstruction algorithm: Medium frequency (soft tissue) pre and post contrast, high frequency (bone) pre-contrast and possibly post contrast if musculoskeletal lesions are suspected.
- Contrast: 600-800 mg I / kg

Reading abdominal CT studies

- Evaluate pre and post contrast studies in soft tissue window.
- Evaluate pre (and post contrast) studies in bone window if musculoskeletal involvement is suspected.
- MPR, MIP and MinIP can be employed to assist with the anatomic localization and identification of specific diseases.

Systematic evaluation

Make sure you evaluate all visible structures. A list for example is:

- Liver
- Bile ducts
- Gallbladder
- Pancreas
- Spleen
- Adrenal glands
- Kidneys
- Reproductive organs
- Ureters
- Urinary bladder
- Urethra
- Stomach
- Small intestine
- Large intestine
- Lymph nodes
- Peritoneum
- Vessels
- Retroperitoneum
- Abdominal wall and extra-abdominal structures
- Skeletal structures

You can create your own list making sure you include everything that you can see or possible see.

Normal abdomen

- Liver: soft tissue attenuation. The hepatic and portal veins can be seen. Uniform post contrast enhancement.
- Gallbladder: thin wall with hypoattenuating to the wall and liver bile. Increased attenuation sludge can be seen on the dependent aspect. The common bile duct can usually be followed to the duodenal papilla.
- Pancreas: Can be seen caudal to the stomach. It displays uniform contrast enhancement in the venous phase.
- Spleen: The spleen can have variable size. It has uniform soft tissue attenuation and the splenic veins appear hypoattenuating.
- Adrenal glands: located at the craniomedial aspect of the kidneys. The left adrenal has a „monkey nut" shape

while the right is more rounded or elongated. They have a homogeneous soft tissue attenuation similar of that oft he kidneys. .
- Kidneys: The cortex is soft tissue attenuation with the medulla slightly hypoattenuating to the cortex. In post contrast studies, widening the window or even using bone window allows better evaluation of the kidneys.
- Reproductive organs: The vestibule, body and horns of the female genital tract can be seen. The uterine wall displays strong enhancement. The normal horns are small but can usually be followed to the ovaries which lie caudal to the kidneys. Depending on the timing with in the cycle, follicular cysts may be observed. The uterine stump in neutered female animals is small and may be difficult to see. The prostate displays uniform attenuation and contrast enhancement.
- Ureters: Can be seen, especially post contrast injection when they can be followed to the termination. It is important to check the ureters prior to contrast injection in case calculi are visible in the lumen. The ureteral jet can be observed at the ureterovescicular junction, though the scan may need to be repeated a couple of times.
- Urinary bladder: It is helpful if the urinary bladder is moderately full. The apparent wall thickness varies with filing level.
- Urethra: Can be identified and examined. Sagittal reconstruction help identifying normal anatomy in the region. The urethral lining displays contrast enhancement,
- Stomach: the fundus, body and pylorus can be distinguished and evaluated.
- Small intestine: The duodenum can be followed along the right abdominal wall. Although it can be difficult, the duodenum can be followed to the jejunum and ileum.
- Large intestine: the ileocecocolic junction can be identified and the colon ca be followed caudally with the descending colon more commonly in the left abdomen. The thin-walled rectum can be followed caudally and likely contains faecal material.
- Lymph nodes: display uniform attenuation. Fusiform shape and uniform contrast enhancement is common.

Abnormal abdomen

- Liver: Masses can be identified altering the margin of the liver (Fig 1). Cystic lesions or components will be recognised by the reduced attenuation and the rim (peripheral) contrast enhancement. Generalised lesions affect the attenuation of the liver parenchyma and may appear as increased, decreased or mixed attenuation. The differentiation of the type of mass or lesion in not typical and sampling is required for final diagnosis.

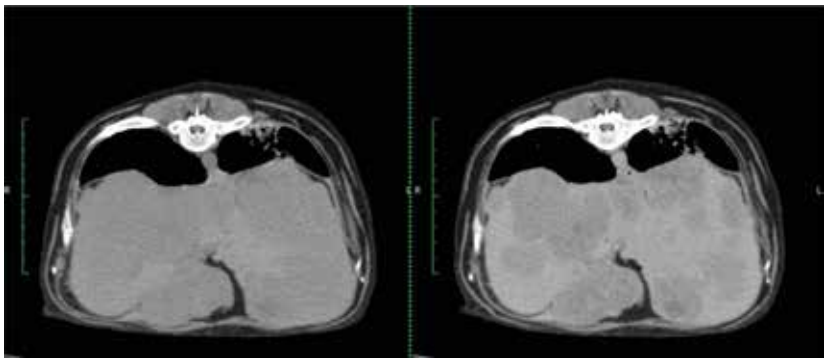

Figure 1. Basset hound, female neutered, 14 years old with hepatic carcinoma. Soft tissue window pre-contrast (left) and post-contrast (right).

- Gallbladder: calculi and wall thickening can be identified. Dilatation of the common bile duct and biliary masses can also be identified. Contrast accumulation in the gall bladder, biliary ducts and duodenum can be seen in patients with renal failure; however, it can also be seen incidentally.
- Pancreas: Pancreatitis usually appears as diffuse enlargement of the pancreas with increased attenuation of the peripancreatic fat representing peritonitis and focal effusion. Insulinomas have a characteristic strong contrast-enhancement pattern in the arterial phase of the exam
- Spleen: Benign and malignant neoplastic lesions can be seen. Myelolipomas appear hyperattenuating to the spleen pre and post contrast.
- Adrenal glands: alteration of the size of the adrenal gland while maintaing the shape indicates hyperplasia while shape alteration and enlargement indicates neoplasia. It is not always easy to distingusih hyperplasia from neoplasia. Pheochromocytomas and adenocarcinomas usually grow very large with heterogenous contrast-enhancement pattern.
- Kidneys: Alterations of the renal parenchyma can be the result of benign and aggressive lesions. Cysts, infarcts, masses, nephritis can be identified though histological confirmation is achieved by aspiration or biopsy of the lesion.
- Prostate: Benign prostatic hyperplasia appears as heterogenous parenchymal attenuation and contrast enhancement often with small cystic areas. Prostatic neoplasia deforms the prostatic parenchyma and also periprostatic changes may appear.
- Ureters: Ectopic ureters can be identified post excretory urogram, though may be seen pre-contrast. Ureteral dilatation due to obstruction or infection may also be identified.

- Urinary bladder: Thick wall and masses can be identified, especially post contrast. CT appearance and location is not pathognomonic to a mass. Ureteroceles can be seen as cystic structures at the level of the ureterovescicular junctions.
- Gastrointestinal tract: Foreign bodies may be found within the GI tract. They may lodge and cause obstruction or even perforation. In cases of gastrointestinal perforation (e.g. perforation from foreign body, ruptured ulcer) pockets of extraluminal gas may be seen with small amount of ascites. The gastric or intestinal wall may be thickened and the surrounding tissue may be inflamed with increased contrast uptake. A gastrointestinal mass may be seen on CT with variable homogeneity of attenuation and variable contrast enhancement. The appearance of the neoplastic tissue is not pathognomonic for the type of tissue.
- Lymph nodes: Reactive lymph nodes are enlarged and easily identified. They are usually enlarged and more rounded with possible cavities (if abscessation or cysts). In neoplastic lymph nodes the shape may be irregular or very rounded and often display heterogeneous attenuation pre and post contrast.

Abdominal CT angiography

- Common indications:
  - Portosystemic shunt detection (Fig 2)
  - Arteriovenous malformation detection
  - Identification of pancreatic insulinomas (Fig 3)
  - Aortic or caudal vena cava invasion by adrenal neoplasia.
  - Identification of arterial or venous thrombi.
- Bolus tracking or test bolus method
- Using a dual-phase exam allows separation of the arterial from the venous phase.

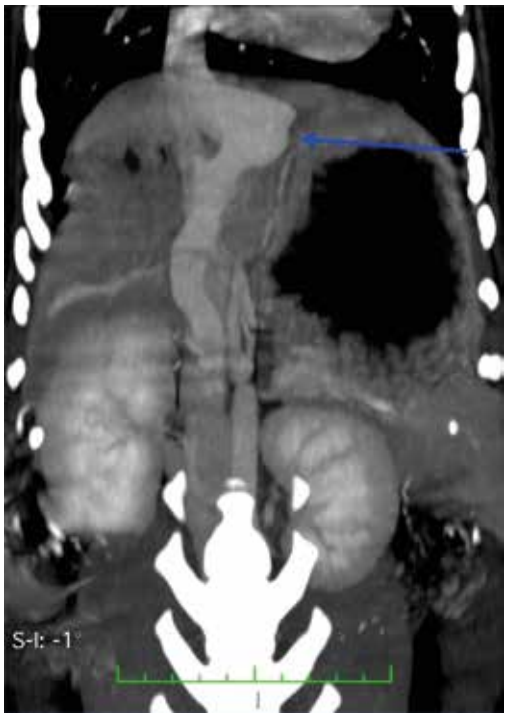

Figure 2. Left sided intrahepatic shunt (PDA) in a dog is visible with CT angiography.

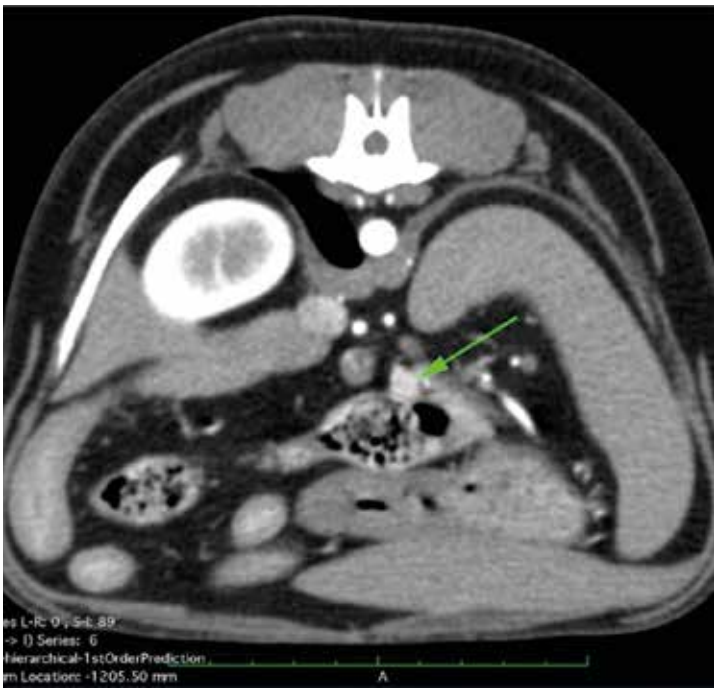

Figure 3. WHWT male neutered 9 years old dog. Soft tissue window post-contrast (arterial phase). A well demarcated, contrast- enhancing nodule is visible in the left pancreatic lobe.

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Clinical applications of musculoskeletal CT of the dog and cat

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Protocol

- Ventral recumbency is usually preferred. Both limbs should be positioned at the same level.
- Margins of scan: To include the area or joint in question. From joints, carpi and tarsi the distal part of the distal part of the long bone proximally and the proximal part of the long bone distally are included.
- kVp= 100-140
- mAs=100-250
- Slice thickness= 0.5-2mm
- Scan mode: Axial scan mode. For more than 16 slice-CT helical scan mode with low pitch.
- Spatial reconstruction algorithm: Medium frequency (soft tissue) pre and post contrast, high frequency (bone) pre-contrast and possibly post contrast.
- Contrast: 600-800 mg I / kg.
  For arthrography 30mg/ml contrast non-ionic or ionic iodinated, after pre-contrast examination. The injection rate should be approximately 0.5ml/sec. Repeat flexion and extension of the joint, for a minute or two minutes, will ensure adequate spread and mixture of the contrast.

Reading abdominal CT studies

- Display bone and soft tissue (pre and post contrast) images alongside to allow comparison during evaluation.
- Arthrograms are better displayed in bone algorithm though dynamic adjustment may be required deadening on the level of attenuation.
- MPR help with the identification of anatomic relationships.
- 3D reconstruction helps in displaying anatomic relationships between bones and provide a 3D visual representation of the lesion that may help with repair planning and explanation to the owner of the animal.

Systematic evaluation

- Be familiar with the anatomy. Anatomy books, surgical anatomy books, CT books and online resources can help with this.
- Musculoskeletal studies should be evaluated for:
  - Alignment of bones and joints,
  - Bone: cortical density and surface, medullary cavity appearance and the appearance of the corticomedullary junction, physis
  - Joints: synovium appearance and attenuation, articular surfaces, areas of attachment of ligaments and joint capsules.
  - Any Implants: location, integrity, stability, appearance of bone around implants
  - Soft tissues: thickness, integrity, lymphadenomegaly

  An easy way to remember is A (for alignment), B (for bone), C (cartilage for joints), D (device for implants is post operative study), S (for soft tissues) i.e. ABCDS

Normal

Bone and joint appearance on CT is similar to the radiographic appearance. Think CT as "radiographs in slices". The lack of superimposition on CT allows better definition of the medullary bone and endosteal cortical margins. Physes appear as lucencies of variable width. The physeal closure varies and timings of physeal closures are documented in the literature.

Abnormal

Bone

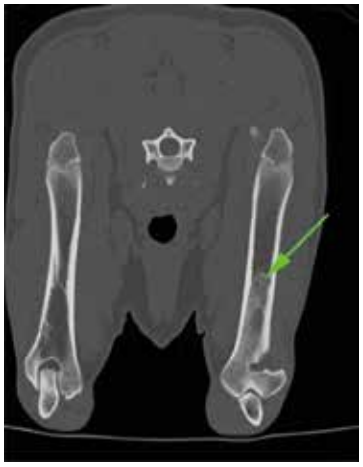
Trauma

- CT is useful at evaluating complex fractures that may be difficult to assess with radiography due to superimposition.

Angular limb deformities

ALD can result from trauma or developmental diseases and they have been associated with a variety of clinical disorders. CT, especially with the help of MPR and 3D reconstructions, can characterise the deformity.

Panosteitis



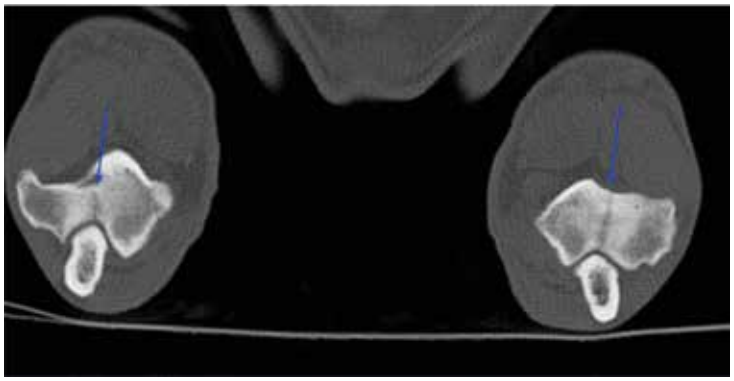
Labrador retriever, female, 1.5 years old. Bone window images showing increased medullary opacity in the left and slightly the right humerus.

- Large breed dogs usually immature.
- Lesions can be mono- or poly-ostotic.
- Ill-defined intramedullary opacities.
- Regional periosteal and endosteal new bone

Metaphyseal osteopathy (hypertrophic osteodystrophy)

- Swelling at the metaphyseal region of distal antebrachium and distal tibia and metacarpal/ metatarsal bones
- Double physeal line: metaphyseal radiolucent zone parallel to the physis.

Incomplete ossification of the humeral condyle



Cocker spaniel, male, 4 years old with incomplete ossification of the humeral condyle bilaterally (arrows). Bone window image.

- Vertical lucent line in the humeral condyle that can extend from the supratrochlear foramen to the elbow joint after 84 days of age.
- Sclerotic bone may be seen surrounding the lucent line.

Hypertrophic osteopathy

- Seen secondary to a mass or lesion in the thorax or abdomen.
- Palisading or columnar periosteal reaction along the long bones that usually starts at the metacarpal or metatarsal bones and progresses proximally.

Aseptic necrosis of the femoral head (Leg-Calve-Perthes disease)

- Toy or small breed dogs.
- Resorption of femoral head subchondral bone.
- Femoral head remodelling follows.
- Pathologic fracture of the femoral head may occur.

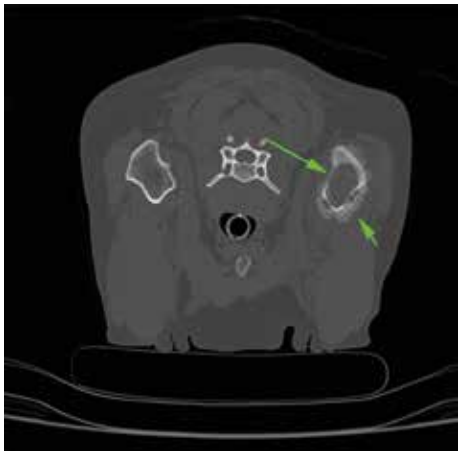
Osteomyelitis

- Bacterial or fungal.
- Marked bone destruction and variable periosteal reaction.
- Possible sequestrum formation.

Secondary hyperparathyroidism

- Generalised decreased bone density
- Thin cortices or double cortices
- Pathologic fractures (folding fractures)

Neoplasia



Cocker spaniel, male, 4 years old with left humeral osteosarcoma (arrows). Bone window image.

- Primary or metastatic
- Cortical bone destruction
- Aggressive periosteal reaction
- Ill-defined margin with normal bone
- Rapid rate of change.

Joints

Osteochondrosis

- Rapidly growing large or giant breeds of dogs 4-12 months old.
- Common sites in dogs: the caudal humeral head in the shoulder, the medial aspect of the humeral condyle in the elbow, the lateral femoral condyle in the stifle and the talar ridges in the tarsus.
- Flat or concave articular surface with subchondral sclerosis.
- Free osteochondral fragments (called osteochondrosis dissecans).
- Increased joint attenuation.
- Degenerative joint disease (DJD) changes.

Articular fracture

- CT allows: detection and detailed evaluation of the fracture, identification soft tissue changes and joint instability (stress positioning) and planning of treatment

DJD and luxation. Subluxation

- Similar findings to radiography, however the lack of superimposition allows a more detailed assessment.

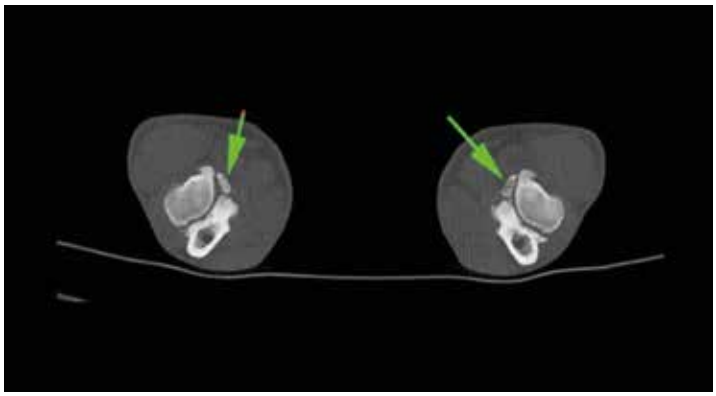
Septic arthritis

- Subchondral bone lysis and sclerosis.
- Thickening and increased intracapsular attenuation.
- Possible sequestrum formation.
- Synovial enhancement post contrast.

Neoplasia

- Synovial cell sarcoma and histiocytic cell sarcoma are the most common.
- Usually multiple bones of a joint are affected by lysis and a soft tissue mass is present.

Elbow dysplasia



Labrador retriever, male, 6 years old with bilateral fragmented medial coronoid processes (arrows), sclerotic medial coronoid processes and evidence of secondary degenerative joint disease. Bone window image.

- Fragmented medial coronoid process
- Ununited anconeal process
- Osteochondritis dissecans
- Elbow joint incongruity

Fragmented medial coronoid process

- Single or multiple fragments may be seen.
- Possible sclerosis of the medial coronoid process.
- Periarticular new bone formation, more marked on the medial aspect may be seen.
- Soft tissue swelling mainly medially.

Ununited anconeal process

- Anconeal process not fused with ulna beyond 22 weeks of age.
- Irregular gap between the anconeal process and humeral condyle.

Elbow incongruency

- Widened or diverging joint space at the level of the trochlear notch and anconeus.
- Step between radius and ulna on dorsal or sagittal reconstructions.

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Ultrasonography of the eye of the dog and cat

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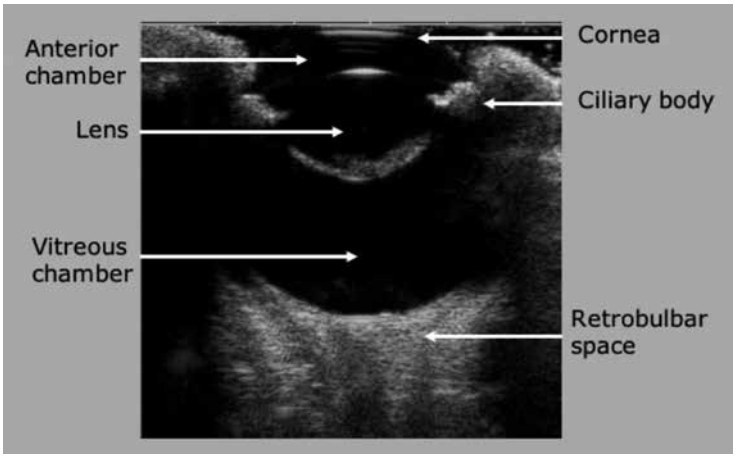
Ocular ultrasonography is helpful because it allows evaluation of the interior of the eye, that may be obscured from direct visualization and allows evaluation of the retrobulbar space.

Normal eye

The canine and feline eye is roughly spherical and measures approximately 2 -2.5cm in diameter. The eyeball is divided into three chambers, the anterior, posterior, and vitreous chambers.



Examination technique

- mode (amplitude mode
- Real time B-mode

Equipment

- High frequency transducers (7.5-15 MHz)
- Small contact surface is desirable

Scanning technique

- Corneal technique (requires topical ocular anaesthesia). This is the preferred method.
- Eyelid technique

Abnormal eye

Intraoccular masses

Intraoccular masses can be produced by:

- Neoplasia (primary or metastatic)
- Infectious and inflammatory disease
- Organized haemorrhage

Lens subluxation/ luxation

- Secondary to trauma, space occupying masses, glaucoma, or hereditary predisposition
- With complete luxation the lens can move anteriorly or posteriorly.
- Sometimes the lens may not be visible (displaced or aphakia).

Cataract

A cataract produces echoes in the normally anechoic lens.

Concurrent retinal detachment is more common with hypermature cataracts than with immature cataracts.

Glaucoma

- Ultrasonography useful in measuring the axial length of the globe to evaluate if enlarged.
- Optic disc cupping may also be seen.
- Ultrasound may identify the cause of glaucoma.

Intraoccular haemorrhage

- Vitreal haemorrhage can appear as a hyperechoic mass lesion and/ or echogenic foci in the vitreous.
- Clot formation can mimic mass lesions.
- Concurrent retinal detachment or other causes of haemorrhage may be seen.

Endophthalmitis

- May appear like vitreal haemorrhage.

Vitreal degeneration

- Appears as sparse, mildly reflective, point-like echoes lying mainly within the ventral aspect of the vitreal chamber that move with the eye movement.

Asteroid hyalosis

- Asteroid hyalosis is a degenerative condition of middle-aged and older dogs in which small foci of calcium lipid complex (up to 0.1 mm) are suspended within the vitreous body.
- They persist with reduction of the overall gain.

Retinal detachment

- Retinal detachment appears as a linear echo on a B-mode scan. Total detachment results in attachment only at the optic disc and the ora serrata giving the typical "seagull appearance".
- Partial retinal detachment appears ultrasonographically as a convex echogenic structure separated from the posterior ocular wall by a lucent zone. It may or may not be associated with the optic disc.
- Vitreal haemorrhage may also be seen.

Posterior vitreal detachment

- PVD appears as a linear or curvilinear convex echo in the posterior portion of the vitreous chamber. It may be confused with a detached retina, but PVD attaches anteriorly but not at the optic disc.
- Vitreal haemorrhage may also be seen.

Persistent Hyperplastic Primary Vitreous

- PHPV is a congenital condition characterized by retrolenticular fibrovascular tissue formation and possible retention of the hyaloid vasculature.
- A funnel-shaped retrolenticular echo is seen with a thin echogenic stalk emerging from the lens and extending to the optic disc.
- Blood flow within the stalk and posterior aspect of the lens may be visible with colour or power Doppler.

Foreign bodies

- Metallic or non-metallic foreign bodies within or around the eye can be imaged.
- Metallic FBs appear hyperechoic with comet -tail artefact,
- Small metallic and wooden FBs may appear as echogenic echoes.
- Wooden FBs appear as double linear echoes with distal acoustic shadowing.
- Fluid and cellulitis may be seen around if in the retrobulbar space.

Retrobulbar and optic nerve lesions

- Cellulitis is seen as interruption of the normal architecture. Diffuse thickening of the retrobulbar tissues with abnormal mixed echogenicity may be present
- Abscesses appear with well-defined echogenic wall and a hypoechoic to anechoic central area.
- Neoplastic lesions may be identified in the retrobulbar space, their appearance is not pathognomonic.
- Optic neuritis and optic nerve tumours can be identified.
- Aplasia, hypoplasia, and optic nerve atrophy may be suspected by an absent or small optic nerve.

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What lurks in the shadows: how to interpret abdominal radiographs

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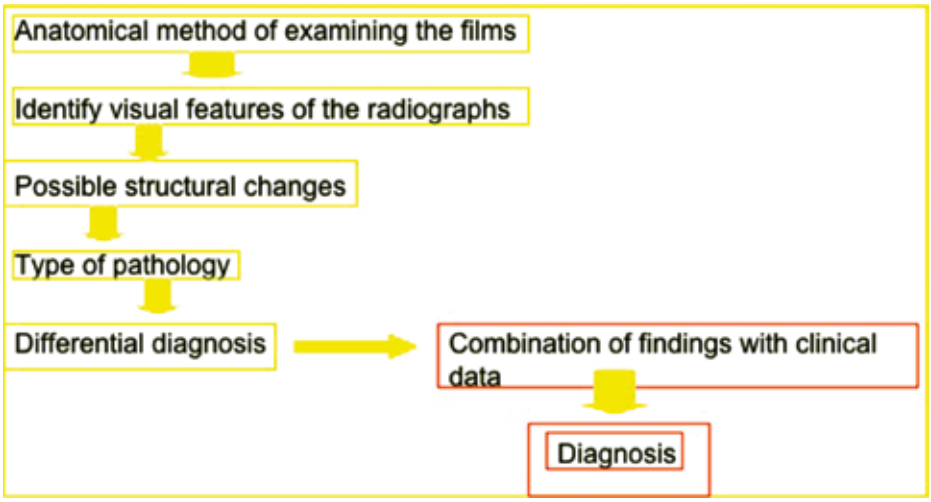
There is only one rule in radiography and that is to examine the entire radiograph. Sometimes radiologists will state that as "the lesion is situated at the corner of the radiograph".

This is not always the case, but is a reminder to ourselves to look at everything.

Why is it essential to examine the entire radiograph? First of all we cannot always predict the lesions based on the clinical signs. Furthermore some lesions may be suggested by

the history, however others may be unexpected and of more importance than the ones associated with the clinical signs. Finally many diseases have unpredictable patterns, e.g. trauma may appear as soft tissue swelling, fractured ribs, pleural effusion, ascites etc.

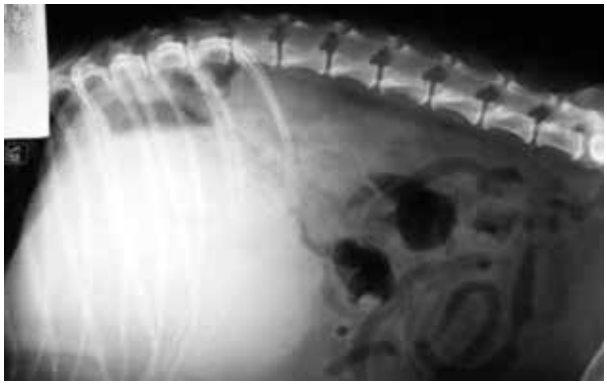
Radiographic interpretation



Liver

HEPATOMEGALY

- GENERAL
- Caudodorsal displacement of the gastric axis
- Rounded ventral liner margin
- FOCAL
  - Right (lateral and medial)
  - Right sided structures are displaced medially, caudally and dorsally
  - A portion of the mass may be behind the stomach displacing the gastric body cranially and dorsally
  - Left (lateral and medial)
  - Affected structures are displaced medially and dorsally
  - If part caudal to stomach may displace the gastric fundus cranially and dorsally



Dog with hepatomegaly (lateral abdominal radiograph). Observe the caudal extend of the liver, the rounded caudal liver margin and the caudodorsal displacement of the gastric axis.

MICROHEPATICA

- Commonly causes: cirrhosis and PSS
- Gastric axis displaced cranially
- Renal and cystic calculi may be seen in cases of PSS

HEPATIC MINERALISATION

- Branching
  - Biliary tree mineralisation–choledocholithiasis
  - Incidental hepatic mineralisation
- Focal unstructured/ shell-like
  - Gallstones
  - Chronic cholecystitis/ gallbladder neoplasia/ cystic hyperplasia of GB wall
  - Chronic hepatopathy
  - Neoplasia
  - Chronic abscess/ haematoma/ granuloma
  - Parasitic cysts

Spleen

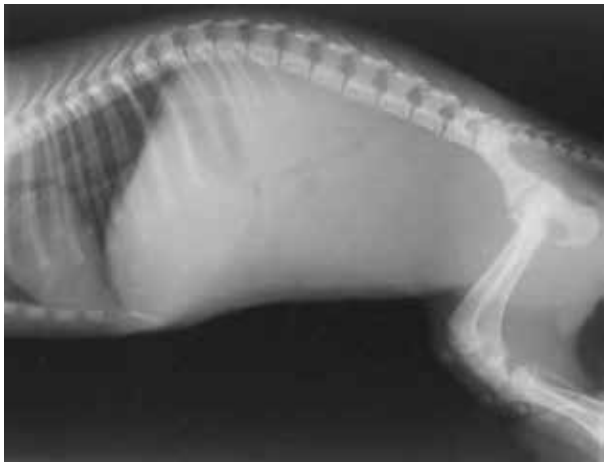
SPLENOMEGALY

- FOCAL
- HEAD
  - Adjacent small intestine displaced dorso-caudally and to the right
  - Indented gastric fundus?
- BODY + DISTAL EXTREMITY
  - Mass caudal to stomach
  - Small intestine displaced dorsally, cranially/ caudally and left/ right
- DIFFUSE
- Rounded splenic margins
- Displaced surrounding organs
- Displaced spleen (if torsion)
- In cats with normally do not see the spleen–if visible consider splenomegaly
- Occurs with conditions such as congestion and torsion (usually with gastric torsion)

Peritoneum

GENERAL LOSS OF SEROSAL DETAIL IN PERITONEUM

- Ascites
- Peritonitis
- Lack of fat
- Peritoneal carcinomaotsis



Lateral abdominal radiograph of a skeletally immature dog. Observe the loss of serosal detail in the abdomen due to lack of fat.

Masses

INTRA-ABDOMINAL MASSES

The organ containing the mass may be identified by the:

- Location of the mass
- Displacement of the surrounding structures

Stomach

THE STOMACH

The major areas of the stomach are : the cardia, the fundus, the body, the pyloric antrum and the pyloric canal.

The radiographic appearance of the stomach varies depending on how the animal is positioned because fluid moves

to the dependent aspect and gas to the non-dependent aspect. In the right lateral projection the gas is usually present in the fundus of the stomach. When more gas is in the stomach then gas is also present in the body, while the fluid and solids are located in the pylorus. In the left lateral projection the gas is usually located in the pyloric antrum while the fundus contains fluid and any solids.

In the dorsoventral projection the gas is visible in the fundus of the stomach while in the ventrodorsal projection the gas is visible in the pylorus of the stomach.

DISPLACEMENT OF THE STOMACH

CRANIAL DISPLACEMENT :

Cranial displacement of the stomach usually occurs if the liver is smaller in size or in cases of diaphragmatic hernia. If a mass is located caudal to and next to the stomach it may actually push the stomach cranially and then it may appear as though it is displaced.

CAUDAL DISPLACEMENT :

Usually caudal displacement of the stomach occurs due to hepatomegaly or hepatic masses. However, pulmonary over-inflation and pleural effusion can displace the diaphragm, liver and stomach caudally. The displacement of the stomach can be seen by identifying the axis of the stomach from the fundus and the pylorus. In the lateral projection the gastric axis shifts caudally from the normal orientation (axis parallel to the ribs up to vertical to the spine) while in cranial displacement of the stomach this axis shifts cranially more than normal. In the dorsoventral view the gastric axis is almost perpendicular to the spine in the dog.

GASTRIC ENLARGEMENT

Here we have to distinguish an abnormally dilated stomach from a full stomach.

The stomach may be filled with gas, food or fluid. But at which point do we start calling it dilated?

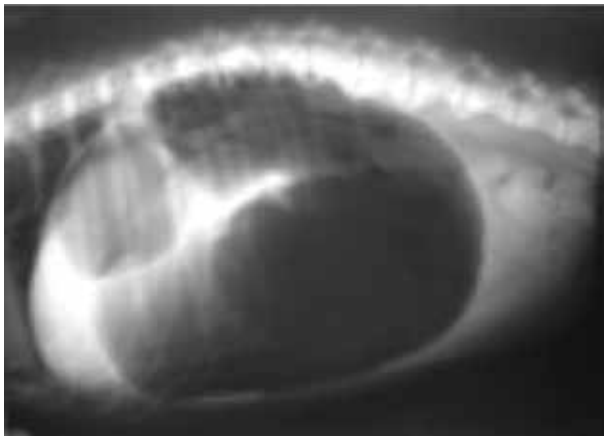
If the stomach extends up to the last rib then that is just normal size.

If it is full but extends beyond the last rib then the stomach is considered dilated.

OTHER

Other abnormalities that may be seen include:

- Gastric ulcers
- Gastric neoplasia
- Gastric foreign bodies
- Gastric dilatation volvulus



Lateral abdominal radiograph with markedly dilated , gas filled and rotated stomach (pylorus appears dorsally) in a dog with GDV.

Intestines

SMALL INTESTINE

The small intestine is divided into three portions: the duodenum, jejunum and ileum. Radiographs cannot differentiate the individual segments from one another except from their location when normal.

Intestines are easily displaced by organs and masses around them. The surface of the small intestine can be usually readily identified unless in cases of animals with very little fat (young, emaciated), peritonitis, ascites and/ or peritoneal carcinomatosis. It is always very dfficult to trust the radiographic appearance of the walls for intestinal wall thickness since this may silhouette with soft tissue material in the lumen and make the wall appear thicker.

As a "rule of thumb" the diameter of a small intestine in the dog should be equal or less than 2 widths of a rib. Or another rule of thumb states that the small bowel diameter in a normal dog should not exceed the height of the central portion of the body of a lumbar vertebra, while in the normal cat the small intestinal diameter should not exceed 12mm or twice the height of the central part of the vertebral body of the 4th lumbar vertebrae.

ENTERITIS

In survey radiographs, in animals with enteritis, the stomach and the intestines usually do not contain any food or faecal material. The small intestine could be fluid filled and small air bubbles (irregular gas pattern) may be seen within

the fluid filled loops of intestine. In the contrast studies we may see rapid transit time in acute enteritis while in chronic enteritis the transit time may be normal or mildly faster than normal.

INTESTINAL OBSTRUCTION

This can be caused by intraluminal, intramural or extramural causes like foreign bodies, intestinal wall tumours and compressing masses around the intestine, respectively.

Radiographically foreign bodies may be identified (even radiolucent ones) especially after contrast studies.

In case of complete obstruction we will have dilatation of the proximal part of the small intestine while in partial obstruction this dilatation may be mild.

With a contrast study we may see delayed transit time of the contrast proximal to the obstruction. If we have a partial obstruction the contrast can pass through the obstructed area and then the movement may be normal.

INTUSSUSCEPTION

This is more common in young dogs and cats. In older animals it may be secondary to intestinal stricture caused by neoplasm. What happens is that the proximal portion of the intestine intussuscepts into the more distal portion.

Radiographically this is a localised sausage shaped bowel mass in the abdomen usually mid or caudal. Gas and fluid dilated loops of intestine proximal to the obstruction may be seen and vary in severity.

With contrast administration the contrast will be seen proximal to the intussusception while a thin line of contrast may be seen extended to the intussuscepted segment sometimes having the appearance of a "coiled spring". In case of ileocolic intussusception barium enema may be more helpful and the intussuscepted bowel appears as a filling defect within the colon.

OTHER

Other abnormalities that may be seen include:

- Intestinal perforation
- Intestinal volvulus
- Mesenteric thrombosis

LARGE INTESTINE

On survey radiographs the normal colon can usually be seen because of gas and faecal material within the lumen.

The caecum in the dog usually contains some gas and has a "C" shape and is usually visible on the right of the midline at the level of the lumbar vertebrae.

The diameter of the normal colon should be less than the length of the 7th lumbar vertebrae.

DISPLACEMENT OF COLON

Ventral displacement of colon may be secondary due to: left kidney mass, left sublumbar mass, retrograde hernia, haemorrhage or urinary bladder displaced in the perineum (perineal hernia).

Dorsal displacement of colon may be secondary to: splenic mass, descending urinary bladder, uterine enlargement.

Right displacement of the colon may be secondary to: left uterine or ovarian mass, distended urinary bladder, left sublumbar mass.

Left displacement of the colon may be secondary to: distended urinary bladder, small bowel or mesenteric mass.

DISPLACEMENT OF RECTUM

Ventral displacement of the rectum may be secondary to enlarged medial iliac lymph nodes.

Dorsal displacement can be secondary to prostatomegaly, vaginal, cervical or uterine mass and urethral mass.

It can be displaced dorsally by a mesenteric or a small intestinal mass and also by a splenic masses.

It can be displaced ventrally by right sublumbar masses e.g. an abscess or haematoma, splenic mass and caecocolic lymphadenopathy.

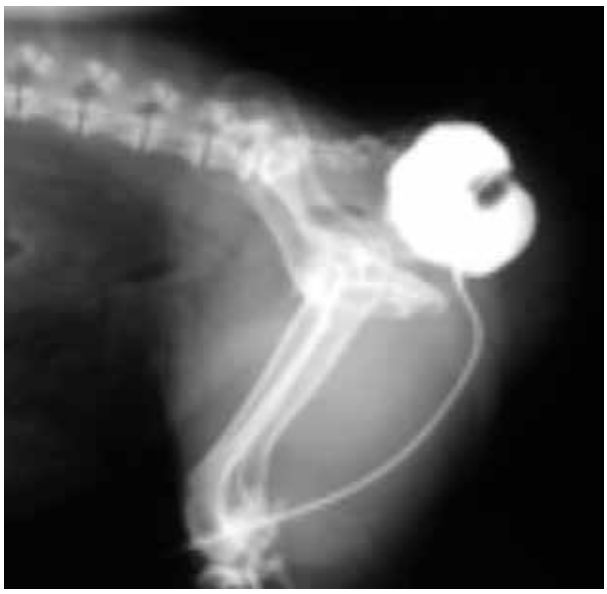
Left displacement of the rectum can be secondary to a right liver mass or masses in the right body wall.

Right displacement of the rectum can be due to mesenteric or small intestinal masses.

OTHER

Other abnormalities that may be seen include:

- Atresia recti
- Atresia ani
- Colitis
- Colonic stricture
- Neoplasia
- Foreign bodies and
- Perineal hernia



Cystography shows the bladder displaced with-in the perineal hernia.

The kidneys and ureters

In the puppies and cats the kidneys are visible in the dorsal retroperitoneal space. In the dog, the right kidney is usually at the level of 13th thoracic to 1st lumbar vertebrae while in the cat the right kidney can be located between the 1st and 4th lumbar vertebrae. The left kidney is usually located between the 2nd and 4th lumbar vertebrae in the dog, while in the cat at the level of the 2nd and 5th lumbar vertebrae. Kidneys are not always clearly visualised in adult dogs while they are visible in cats and puppies. Nephromegaly typically displaces small intestines ventrally, cranially and caudally, as well as to the opposite side of the abdomen to the affected kidney. Small kidneys can be very difficult to visualise on plain radiographs, and as normal kidneys are sometimes not visualised because of overlying abdominal organs, the lack of a visible kidney cannot be reliably used as a marker for reduced size. The ureters are not usually visualised without contrast and they are in the retroperitoneal space.

Adrenal glands

Usually not visible unless enlarged or calcified. In the cat calcification of the adrenals may be an incidental finding and it may involve one or both adrenals while in the dog it is usually associated with disease e.g. tumour. Both of the adrenals are usually at the craniomedial aspect of the respective kidneys.

Urinary bladder and urethra

The urinary bladder is usually in the caudoventral abdomen cranial to the pubis of the pelvis and ventral to the rectum and descending colon. The bladder may be large in size because of urethral calculi or compression by a mass or neoplasia affecting the trigone area at the beginning of the urethra or because the animal has not urinated for a while. It also may be secondary to neurogenic atony. A small bladder may be difficult to identify.

Causes of decreased bladder size include: empty bladder due to recent urination, frequent urination from cystitis, congenital anomaly like ectopic ureter or herniation to an abnormal location like the perineal area.

In the case of suspicion of ascites and non-visualisation of the bladder, bladder ruptures should also be suspected. Abnormal shape of the bladder may be due to external compression when it is not filled or due to infiltrative diseases that affect the bladder wall like in cases of cystitis, granulomatous cystitis and neoplasia. The bladder wall can be better evaluated after contrast studies like the one described earlier. In the lumen we may see various filling defects. A ruptured bladder can be usually identified on a contrast study when we see contrast outside the bladder lumen.

FREE LUMINAL FILLING DEFECTS AS SEEN IN DOUBLE CONTRAST CYSTOGRAPHY:

- Cystic calculi are in the centre and have a rounded shape with an indistinct margin.
- Blood clots are irregular in shape and margination and they can be anywhere in the bladder.
- Air bubbles are round and smooth with very distinct margins and they are at the periphery of the contrast puddle.

Female and male genital tracts

The female reproductive tract consists of two ovaries, the uterine horns, the uterine body, the cervix and the vagina. In the normal animal they are not usually visible on survey radiographs. In some very fat dogs and cats that are normal you may be able to see the uterine body between the rectum and the urinary bladder on a survey lateral radiograph. Foetal skeletons can be seen at approximately 41-45 days in the dog and 35-39 days in the cat. In early pregnancy a small dilated uterus may also been seen, while later we see foetal skeletons superimposed on each other on the lateral

view. It is better to count the skulls in order to have a more accurate foetal count. In general foetuses should be approximately the same size and have a similar ossification pattern.

The male reproductive system consists of the scrotum, the two testicles with respective epididymis and vans deferens, the prostate gland and the penis. The internal genitalia cannot be seen on survey radiographs. The os penis bone is located within the penile tissue and is in close association with the penile urethra.

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Neurology

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Working Experience

1992-1998 – Working experience in large and small animal medicine in university (Freie University Berlin) as well as in private practice in Berlin

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Since November 2002 – Department of Small Animal Medicine, University of Leipzig, Germany, Head of the section of neurology and neurosurgery

Veterinary and Academic Qualifications

1994 – Doctor medicinae veterinariae (summa cum laude)

2001 – Master of Veterinary Sciences (The Ohio State University, USA)

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2005 – Diplomate European College of Veterinary Neurology

2008 – European Specialist in Veterinary Neurology

2010 – Dr. med. vet. habilitatus (small animal surgery and small animal neurology)

2012 – Secretary of the European College of Veterinary Neurology

Since 2016 – President of the European College of Veterinary Neurology

Spinal radiographs for neurological diseases

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Advanced imaging such as computed tomography and magnetic resonance imaging have revolutionized spinal imaging and it has tremendously facilitated new developments in veterinary neurology. For many clinicians, that led to the impression that conventional spinal radiographs are outdated and therefore it is not an appropriate diagnostic tool for diagnosing spinal diseases anymore. Luckily enough, that is not the case. There is a lot to be seen on those images, if you know what to look for. Therefore, conventional spinal radiographs are one of the potential imaging option to diagnose spinal pathologies. However, clinicians have to be aware of capabilities and limitations of plain spinal radiographs. I general, those are able to detect any pathology affecting vertebra and altering their:

- shape
- structure
- alignment

If any of those changes are seen, conclusions can be drawn on how those pathologies may affect spinal cord structure and function without being able to visualize the spinal cord itself. Visualization of the spinal cord can be facilitated by adding a contrast agent into the subarachnoid space surrounding the spinal cord. However, true imaging of the spinal cord itself is the domain of magnetic resonance imaging.

I would recommend developing a standard operating procedure for reading spinal radiographs in order to make reading those images most effective. Here would be my suggestion. Go through all the following steps in reading any spinal radiograph rather than jumping to your most likely diagnosis right away:

1. **Quality and Positioning**
   - determine, if your image is of sufficient quality to be evaluated
   - determine which vertebrae you are seeing on your image
   - determine if the patient was positioned correctly
2. **Pathological changes**
   - check for abnormal shape of vertebrae
   - check if all vertebrae are correctly aligned
   - check for any structural changes of vertebrae
   - check the soft tissue adjacent to the spine for any pathological changes
3. **List all pathological changes**
4. **Create a weighted list of differentials or determine one diagnosis**

Quality and Positioning

Determining which vertebrae you have imaged (from – to) might not be crucial for interpretation, but it trains your ability to correctly identify vertebrae. In addition, it highlights the necessity that you have to have a section of the spine on your images that allows you to exactly determine where you are. That usually requires having at least one of the following areas on your image (C1, C7-Th1, Th13-L1, L7-S1). Usually our dogs and cats have 7 cervical, 13 thoracic, 7 lumbar and 3 fused sacral vertebrae (as well as a varying number of coccygeal vertebrae). For further invasive diagnostics and for surgical approaches it is important to detect individual variations of those numbers.

Exact positioning, however, is crucial in order to avoid misinterpretation. Nearly every vertebra has a different shape and no clinician does know the appearance of every vertebra in any possible projection. We cannot change the large variation of vertebral shapes, but at least we can image them in a standardized way. Usually a lateralolateral image is obtained. Ideally, it is combined with a ventrodorsal view. On a correctly positioned laterolateral view two paired structures from the left and right are superimposed over each other and therefore they can be visualized as one structure only (ribs, transverse processus, alar wings, iliac wings). That is often very difficult to achieve in an awake patient and therefore it may often some degree of sedation. If your image is obviously significantly rotated (transverse processus are projected into the vertebral canal, ribs are superimposed on dorsal spinal processus, dens can be seen), the image should be repeated. Correct positioning on dorsoventral views can be judged based on the position of the dorsal spinous processus which should be projected into the middle of the vertebral body.

Pathological changes

Shape

The shape of vertebrae can be altered due to congenital abnormalities, degenerative proliferations, abnormal growth

plate closure and fractures. In the thoracic spine adjacent vertebrae can be used for comparison. In the cervical area, there is quite some variation in the shape of vertebrae and therefore, comparison with a text book might be sometime necessary.

Congenital abnormalities may include: hemivertebrae, block vertebrae, butterfly vertebrae, spina bifida, caudal articular facet dysplasia and transitional vertebrae. Those abnormalities may result in kyphosis, lordosis or scoliosis. Vertebral malformations are very common in brachycephalic dogs, specifically in French Bulldogs, with about 80% of dogs being affected by at least one malformation. However, they cause neurological deficits in a small portion of dogs only. However, only 9% of neurological deficits localized to the spinal cord in French Bulldogs are caused by a compressive congenital vertebral malformation.[1] Hemivertebrae can cause significant kyphosis. The Cobb angle can be measured in order to quantify the severity of kyphosis. Cobb angles >35° are considered relevant and are very likely to cause neurological deficits.[2]

The most frequent degenerative change of vertebrae is spondylosis deformans (ventral bony proliferation starting adjacent to an intervertebral disc eventually bridging the gap) and spondylarthrosis (degeneration of the articular facets). Disseminated Idiopathic Skeletal Hyperostosis (DISH) may look very similar as spondylosis deformans by forming ventral bony proliferation. In DISH, however, that proliferation usually starts in the middle of the vertebral bodies (at tendon and ligamentous insertions) and then extending towards the intervertebral disc space. All those degenerative changes are rarely causing neurological deficits.

Generalized delayed growth plate dysplasia is very suggestive for mucopolysacharidosis (MPS; enzyme storage disease), which is known to cause neurological deficits in young dogs and cats. In addition, remodeling and change of the length of vertebrae as well as spondylosis deformans can be seen in those patients. The specific clinical symptoms depend on subtype MPS, of which currently eight are known.

Finally, the shape of vertebrae can be changed by fractures. Even the smallest dislodged bony fragment (especially in cats) may be indicative for a significant trauma event. Keep in mind, that vertebral body shortening may be the result of an impression fracture, where the fracture lines itself might be difficult to be appreciated. A fractured spine should be considered instable until proven otherwise (see presentation about spinal trauma). However, never base the prognosis of a vertebral fracture on spinal images alone. The degree of neurological deficits should be considered together with the results spinal imaging.

A small bony fragment at the dorsocranial edge dislodged from the vertebral endplate of S1 is usually not related to trauma but represents osteochondrosis dissecans, which is most commonly seen in young adult large breed dogs that undergo strenuous exercise for work.

Structural changes

There are only two frequently seen pathological changes that may change the structure of one or several vertebra: neoplasia and infection, with the first one being much more frequently. There are no specific features that allow differentiating between both entities. Single neoplastic lesions are usually caused by osteosarcoma (even though it might be causing multiple lesions in exceptional cases). Exclusion of metastatic pulmonary lesions may facilitate differentiating a single neoplastic lesion from osteomyelitis. Multiple lytic lesions in different vertebrae are usually neoplastic in nature: multiple myeloma, malignant histiocytosis (histiocytic sarcoma), lymphoma and metastasis. Differentiation between those potential differentials is based on cytology or histopathology of tissue specimen obtained from a lesion, which can be done by any clinician with an X-ray machine.

Sometimes radiographic changes in the soft tissue immediately adjacent to the spine may raise the suspicion of a neoplastic lesion affecting the spine and the spinal cord. Prostatic carcinoma may cause mineralization of the tumor itself as well as of the sublumbar lymph nodes, so that mineralization may extend well beyond the expected borders of a normal prostatic gland and therefore, it can be seen directly below the caudal lumbar spine. From there this process may extend into the spine causing neurological deficits in the rear limbs.

Infectious diseases causing lytic spinal lesions are much less common than neoplastic causes. However, there is one specific pathology that is seen on a regular basis: discospondylitis. It is an infection of an intervertebral disc as well as the two adjacent vertebral endplates. The discitis itself cannot be visualized on plain radiographs, but infection is clearly visible as lytic lesion affecting both endplates, which is sometimes extending into the vertebral bodies. In more chronic cases, collapse of the intervertebral disc space with sclerosis surrounding the lytic endplate lesions can be seen. Patients with discospondylitis, which is either bacterial or less commonly fungal in origin, are presented with fever and severe focal pain. There might be a time lag of up to three weeks between the onset of clinical symptoms and radiologically visible lesions. Therefore, radiographs may have to be repeated after two to three weeks in suspected cases. Discospondylitis may affect multiple intervertebral disc spaces in up to 25% of cases.

Generalized reduced vertebral density with cortical and trabecular thinning can be seen in nutritional (secondary) hyperparathyroidism. Those changes do not result in neurological deficits, as long as they do not cause a pathological fracture.

Alignment

Malalignment indicates spinal instability if it is seen following a trauma. Traumatic spinal instability without a concurrent spinal fracture (only due to soft tissue destruction) is more likely to require stabilization than some spinal fractures,

since long term internal stabilization as in fracture healing cannot be expected.

The following more specific syndromes of malalignment, that are not necessarily related to a trauma, can be seen:

- "Tipping" of a mid or lower cervical vertebra (the cranial tip points upward towards the spinal cord) is part of those pathologies that can be seen in the "Wobbler complex" (Caudal Cervical Spondylomyelopathy) especially in Doberman pinschers.
- Atlantoaxial instability can be detected in nearly any breed, but it is most commonly seen in toy breeds. It may be caused by a dens aplasia or hypoplasia as well as following traumatic rupture of those five ligaments connecting atlas and axis (or any combination of those). The dens can easily be visualized on images rotated along the long spinal axis (in return: being able to see the dens indicates that you did not perform an exact laterolateral imaging). Several measurements can be taken in order the diagnose atalantoaxial instability an laterolateral images. C1-C2 overlap ≤+1.55mm was the most sensitive (100%) and specific (94.5%) radiographic measurement in the diagnosis of atlantoaxial instability.[3] Care should be taken in obtaining flexed views in order to demonstrate atlantoaxial instability. If it is performed at all, it should be performed under fluoroscopic control only, so that flexion can be stopped if instability becomes obvious.
- Lumbosacral instability can cause ventral subluxation of the sacrum. Such subluxation should be evaluated by comparing the vertebral alignment on the floor of the vertebral canal rather than by comparing the position of the laminae of L7 and S1. It may not be seen in neutral view, but it may become obvious in extended views.

Based on all pathological changes seen on an image a weighted list of differentials should be provided. Sometimes, the findings might be pathognomonic for just one disease, so that a specific diagnosis can be made (i.e. discospondylitis).

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Spinal trauma

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Spinal trauma is a rather ill defined term since in addition to the trauma sensu strictu several different entities can be traumatic to the spinal cord (i.e. intervertebral disc disease, fibrocartilaginous embolism). In the context of this presentation, spinal trauma is defined as an insult to the spine caused by abnormal external force resulting in structural changes of the spine and/or resulting in spinal cord injury with or without neurological deficits. This definition does exclude disease as mentioned above.

Therefore, vertebral fractures and/or luxations caused by a traumatic event will be discussed here. Those are seen in up to 5% of cases with spinal lesions. Keep in mind that any patient who experienced a traumatic event being severe enough to cause a vertebral fracture or luxation is likely to have additional traumatic lesion throughout the entire body. Those might be acutely more life threatening than the spinal lesion itself and therefore, they may have to be addressed first. However, careful handling and minimizing spinal manipulation is crucial from the first moment on for minimizing further spinal cord damage. Patients should be placed on a stable surface and lifted using this plate rather than moving the patient itself.

Neurological Assessment

Routine neurological examination is supposed to determine the exact neurolocalisation of the lesion as well as to determine the severity of spinal cord damage, which is directly linked to the prognosis.

Neurolocalisation is done as in any other patient with acute spinal cord disease, but spinal manipulation should be reduced to the absolute necessary. There are two common finding that may be seen in spinal trauma that might be confusing. One is the Schiff-Sherrington-position, which is characterized by paraplegia (usually deep pain sensation negative) and rigidly extended front limbs. Those patients are usually presented in lateral recumbency, seemingly unable to walk with all four limbs. However, if supported, they will have normal voluntary motor movements in the front limbs, whereas the rear limbs remain paraplegic. The Schiff-Sherrington-position is caused by severe a Th3-L3 lesion (usually in cranial lumbar spine L1-5) affecting the so called border cells, since they located at the dorsolateral border of the ventral grey column. Border cells have an inhibitory influence on the front limbs that is lost in severe lesions affecting those cells deep inside the cranial lumbar spinal cord. The Schiff-Sherrington-position carries a guarded prognosis, however recovery can occur.

Another scenario seen in paraplegic patients following trauma is "spinal cord in shock". Those patients may loose all or some segmental spinal reflexes caudal to the lesion. Multisynaptic segmental spinal reflexes (i.e. flexor reflex) may be more commonly affected than monosynaptic reflexes (i.e. patellar tendon reflex). Loss of reflexes would indicate a lower motor neuron lesion even though the patient may have a more cranial Th3-L3 spinal cord lesion. Clinicians should be suspicious of spinal cord in shock in paraplegic patients if there is an obvious discrepancy between the neurolocalisation based on segmental spinal reflexes (L4-S3) and the cut-off of the panniculus reflex (T3-L3). In those cases, the panniculus does indicate the correct neurolocalisation. Spinal cord in shock might be responsible for the loss of deep pain sensation in those dogs rather than a true structural spinal cord lesion. It is subject to debate how long spinal cord in shock may last in in dogs and cats, which is important for the prognosis. Most likely, loss of deep pain sensation caused by spinal cord in shock does resolve within a few hours. In contrast, regaining normal segmental spinal reflexes may take several weeks.

Persistent loss of deep pain sensation beyond the time-frame of spinal cord in shock in dogs with spinal fracture and or luxation caries a grave prognosis.[1]

Imaging

Most spinal fractures and or/luxations can be diagnosed on plain spinal radiographs. However, computed tomography and magnetic resonance are needed to determine the full extend of the spinal pathology and the secondary changes in the spinal cord itself. Therefore, advanced imaging is very helpful for establishing a prognosis as well as for surgical planning. Be aware that in up to 10% of cases multiple fractures/luxation may exist in one patient.[1,2] If sedation or anesthesia has to be performed in order to obtain those images, extreme caution must be taken during moving the patient, since spinal stabilizing muscle tone is lost. Two projections (laterolateral and ventrodorsal) should be taken, with the latter preferably obtained in lateral recumbency. In cases with no obvious lesion, the spine can be tested for instability by taking carefully flexed and extended images.

In order to evaluate the spine for instability, the 3-compartment-theory can be used. The spinal bony and ligamental structures are divided into three compartments: dorsal compartment (lamina, dorsal spinous process and associated

ligaments; middle compartment (dorsal longitudinal ligament, dorsal annulus, dorsal cortex of vertebral bodies) and ventral compartment (ventral longitudinal ligament, ventral annulus, ventral cortex of vertebral bodies). Spinal instability is assumed if more than one compartment is affected.

Dorsoventral dislocation of fractured segments or between two adjacent vertebral bodies of more than 100% of the vertebral height is usually associated with a poor prognosis. However, prognosis is never based on results of imaging alone- the results of the neurological examination should be taken into consideration as well.

Treatment

The aim of any treatment is to provide circumstances that allow the spinal cord to regeneration and to recover neurological function. For that, stabilization either by internal surgical fixation or by external splinting has to be performed. In cases with proven instability surgical treatment is superior to conservative therapy. Thoracic fractures are often stable and therefore they do not require stabilization in many cases.

Complete rest without any stabilizing method is not recommended in cases with proven instability. Therefore, it is reserved for cases presumably without significant instability and for case with instability, were non-medical reasons do not allow any other treatment. It might be more effective in cats than in dogs.

Conservative treatment using an external cast can be most efficiently done in the cervical area. The cast has to be applied from the eyes to the midthoracic region preventing any movement in the entire cervical spine. It is less effective in thoracic and lumbar lesions. Follow-up radiographs are recommended every six weeks or in case of neurological deterioration. External stabilizing methods or strict cage rest should be applied for at least 3 months.

Surgical treatment can be demanding and therefore it belongs into the hands of an experienced surgeon who is familiar with orthopaedic surgery principles as well as with spinal surgeries. The aim is to reduce the fracture and to stabilize it. The exact stabilizing methods does probably depend more on the surgeon's personal experience and preferences than on clear surgical recommendations. It may include Steinmann pins or screws and polymethylmethacrylate (PMMA) as well as interlocking plates. Dorsal spinal stapling or the application of dorsally applied plastic plates (Lubra) is most commonly used in the thoracic and less commonly in the lumbar spine. Small dorsal spinal processus in the cervical spine prevent one from using that method there. For the thoracolumbar junction and lumbar spine vertebral plating or the use of pins /screws and PMMA seems to provide best stability. The latter might be easier to apply to all differently shaped vertebrae, whereas vertebral plating can be more challenging, especially in small dogs and cats.

Stabilization of fractures of the axis can be quite challenging as well. Historically a significant risk of intra-surgical mortality has been reported. In a very recent study in 66 dogs and 3 cats with C2 fractures a much better prognosis was described.[3] Ninety percent of all treated cases (92% of the conservatively and 88% of the surgically treated cases) did show ambulatory recovery with 77% becoming neurologically completely normal again.

There is an ongoing debate about the need to remove smaller bony fracture fragments from within the spinal canal. Smaller fragments can probably left in place, whereas fragments causing significant spinal cord compression (reducing the normal expected spinal diameter by more than one third) should be removed.

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Differentiating central from peripheral nervous system disease

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In the following, the term peripheral nervous system (PNS) is not only used in the strict sense of the meaning but in a broader sense including the alpha motor neuron of the spinal cord and the neuromuscular junction. That approach has been chosen for two reasons. Firstly, many underlying pathologies to not affect only the nerve itself, but involve the muscles primarily or secondarily as well. In addition, it can be sometimes quite challenging to different between pure neuropathies and such pathologies affecting nerve and muscle at the same time since both form a functional unit. Therefore, the term PNS is used as described above.

Why is differentiating central nervous system (CNS) lesions and PNS lesions on our initial examination so important? Let's use an example: a patient being completely paralyzed is presented. For most of us, a spinal cord disease would be the most likely explanation and consequently, spinal radiographs might be taken. In cases, where the paralysis is caused by PNS pathology, taking spinal radiographs would be inappropriate, since none of the potential underlying pathologies could potentially be diagnosed on those radiographs. Completely different diagnostic test are necessary in those patients. Therefore, we have to differentiate between CNS and PNS disease during the first visit. And here is one more argument for those clinicians without direct access to advanced imaging such as CT or MRI. Patients with CNS pathology may have to be referred for CT or MRI to an imaging center or to a referral hospital. Patients with suspected PNS, however, can diagnosed further in your own facility (to a certain degree). Therefore, the section about diagnostics (further down) will focus on the diagnostic workup of PNS lesions.

Patients presented for PNS lesion exhibit normal mentation and behavior since the CNS is not affected. It might be difficult to evaluate behavior in a patient being completely paralyzed due to PNS disease. However, taking some time may clearly demonstrate normal behavior in those patients. Sometimes, dogs with severe PNS disease are still able to wag their tail if they are happy even though they are completely recumbent.

Cranial nerve examination may reveal deficits in several patients with generalized PNS lesions. That is not the case since the brain stem is affected, were most cranial nerves originate from, but because cranial nerves are peripheral nerves as well. The optic nerve is an exception to that rule. This nerve is rather an extension of the brain carrying more characteristics of the central nervous system than of a peripheral nerve. Therefore, cranial nerve II is usually not affected by generalized PNS diseases, whereas involvement of other cranial nerves may lead to dysphonia, laryngeal paralysis, difficulties prehending and swallowing food as well as facial nerve deficits (droopy lip, hanging ear, excessive "salivation" which is more an inability to prehend saliva. Often those deficits are the first recognized by the owner, since they are more obvious than mild gait abnormalities. However, cranial nerve deficits can be seen with central nervous system (CNS) lesions as well. Therefore, cranial nerve deficits alone are not suitable to differentiate between CNS and PNS lesions

Patients with generalized PNS lesions may show a combination of sensory and motor deficits: ataxia, conscious proprioceptive deficits and paresis/plegia. Diseases purely affecting the sensory nerves causing ataxia and conscious proprioceptive deficits without paresis or disease purely affecting the motor nerves causing paresis/plegia can be seen but those are much less common. Motor deficits in generalized peripheral neuropathy can be pronounced, often being much more severe than in spinal cord disease. Paresis/plegia is usually flaccid. Significant neurogenic muscle atrophy can commonly be appreciated within one week.

I have described many symptoms that should raise the clinician's suspicion of a PNS disease. However, there are two very specific, even though completely different, clinical presentations that can easily be identified and that should lead the clinician directly to the suspicion of a PNS lesion:

1. Neurological deficits are seen in one limb only
2. Tetraparesis/plegia and reduced segmental spinal reflexes in all four limbs

In the first case, the lesion is located within the peripheral nerves of the affected limb and commonly include trauma to peripheral nerves in acute cases, whereas the majority of cases with chronic-progressive signs might be affected by a neoplasia (i.e. peripheral malign nerve sheath tumor, lymphoma).

The second scenario is caused by a more generalized PNS disease. Reduced segmental spinal reflexes in all four limbs in a tetraparetic/tetraplegic patient clearly indicate a generalized peripheral nervous system lesion. However, not all segmental spinal reflexes in all four limbs have to be reduced to the same extent. Often, flexor reflexes (withdrawl reflexes) are affected most, whereas muscle tendon reflexes (patellar tendon reflex, biceps reflex, triceps reflex) or muscle reflexes (extensor carpi reflex, cranial tibial reflex) might still be preserved. In addition to the deficits described so far, innervation of the esophagus may be affected leading to megaesophagus in some dogs. Therefore, in any dogs with suspected generalized PNS lesion taking chest radiographs is indicated. In cats, generalized peripheral nervous system disease does much less commonly cause megaesophagus. That difference between both species is largely

explained by fact that in dogs the esophagus is entirely composed of striated muscle, while in the cat only the cranial third consist of striated muscle whereas most of the esophagus is composed of smooth muscle.

Symptoms that can be seen either in CNS or PNS disease:

- paresis or plegia (para or tetra)
- cranial nerve deficits
- ataxia
- vestibular syndrome
- reduced conscious proprioception (paw positioning reaction)
- Horner's syndrome

Symptoms that can be seen in CNS disease only:

- hemiparesis/plegia
- altered mentation and behavior
- seizures
- central blindness
- intention tremor
- hypermetria

Symptoms that can be seen in PNS disease only:

- monoparesis/plegia as single symptome
- tetraparesis/plegia with reduced segmental spinal reflexes in all four limbs
- megaesophagus
- neurogenic (fast) muscle atrophy

Diagnostic workup in dogs with peripheral nervous system lesions

Diagnostics may include:

- chest radiographs to check for magaesophagus, thymoma and aspiration pneumonia
- acetylcholine receptor antibody titer
- tensilon test (alternatively: neostigmine)
- muscle enzymes (CK, LDH, ASAT) in serum
- lactate, pyruvate concentration in serum
- urinary amino acid profile
- carnitine concentration in muscle, plasma and urine
- 2M-antibody titer
- serology or PCR for infectious agents
- testing for endocrinopathies
- DNA testing for known genetic diseases
- toxicological screening
- botulinum tests (toxin-Ab titer in serum, clostridium botulinum test in feces)
- electrodiagnostics
- nerve/muscle biopsies

Electrodiagnostic tests are based on electrical measurements obtained from nerves and muscles with or without prior electrical stimulation. Those tests are performed in order to: 1. confirm or rule out peripheral nerves system disease; 2. differentiate neuropathy from myopathy; 3. differentiate between motor, sensory and mixed neuropathy; 4. differentiate between demyelinating neuropathy and neuropathy with predominately axonal loss or mixed; 5. differentiate between proximal and distal nerve disease; 6. define suitable nerves and muscle for biopsy.

The following electrodiagnostic tests are available:

- electromyogram (EMG)
- motor and sensory nerve conduction velocity (NCV)
- F-waves
- H-reflexes
- repetitive nerve stimulation (RNS)
- cord dorsum potentials

EMG in dogs and cats are performed under heavy sedation or general anesthesia. Under those circumstances, healthy muscle membranes are electrically silent. After inserting the needle electrode into a muscle no electrical activity should be observed following the initial insertional activity, except in those cases were the needle is inserted close to a neuromuscular endplate which may cause physiological endplate potentials. In contrast, in cases with primary muscle pathology or muscle denervation of at least 5-7 days duration, spontaneous electrical activity can be recorded from muscles. There are different types of spontaneous activity that can be associated more frequently with certain

diseases (fibrillation potentials, positive sharp waves, myotonic discharges, pseudomyotonic discharges). However, none of those is pathognomonic for specific diseases. Spontaneous activity in primary myopathy is often more pronounced in proximal limbs muscles, whereas activity might be more obvious in distal limb muscles in primary neuropathy with secondary muscle denervation.

Abnormal EMG confirms diseases in the peripheral nervous system. Differentiation between myopathy and neuropathy, however, requires additional measurements such as NCV. For motor NCV, peripheral nerves are stimulated electrically in the proximal nerve region and measurements are taken from distal muscles, where the so called M-wave represents the corresponding muscle contraction. Time delay between stimulation and appearance of the M-wave allows calculation of the NCV, the speed a nerve is transmitting an impulse. NVC is a measure for nerve myelination and therefore prolonged NCV is indicative of demyelinating neuropathy. In contrast nerve pathology not affecting the myelin sheath but reducing the number of transmitting axon, called axonopathy, may not affect NCV but it may reduce the amplitude of the M-wave. Axonopathies usually cause more severe EMG changes than demyelinating neuropathy.

The NCV test mentioned so far fail to evaluate the most proximal part of a peripheral nerve. F-waves (pure motor event) and H-waves (sensory and motor events) can be used to test the more proximal area of a nerve, nerve roots as well as relay areas within the spinal cord. F-waves are recorded from a motor nerve similar as M-waves. Those waves, however, appear much later than M-waves. After stimulating a peripheral motor nerve, the electrical impulse travels within the nerve distally causing the already described M-wave (prodromic). At the same time the electrical impulse is traveling in the opposite direction towards the spinal cord as well (antidromic). The spinal cord ventral horn motor neurons respond to that stimulus and send a second impulse distally arriving in the muscle later as the original M-wave. The second wave is called F-wave. Similarly, the H-wave can be recorded after stimulating a sensory nerve and recording from muscles innervated by a corresponding motor nerve, thereby evaluating the entire reflex arc (sensory nerve, spinal cord dorsal horn and ventral horn, motor nerve).

In addition, the transmission of an electrical impulse from a motor nerve via the neuromuscular endplate onto the muscle can be evaluated by repetitive nerve stimulation (RNS). In myasthenia gravis, the most common canine neuromuscular endplate disorder, RNS results in decreased M-wave amplitudes (decrement).

Nerve and muscle biopsy

Once generalized peripheral neuropathy has been confirmed by electrodiagnostic testing, taking biopsies of one or several nerves can be indicated. Those biopsies should be combined with biopsies of a muscle supplied by the same nerve. Biopsies are either taken from most severely affected areas or alternatively from routine biopsy sites (i.e. common peroneal nerve and cranial tibial muscle). Make sure that you don't take a biopsy from a muscle that may be artificially altered by needle insertion during your prior electrodiagnostic tests. Don't store nerve or muscle biopsies in formalin. In most cases, samples are shipped without any fixative overnight to a laboratory being experienced in evaluating those samples. In cases, where electrodiagnostics cannot be performed, taking a muscle biopsy of a standard muscle (see above) can still be done, whereas I would discourage performing a nerve biopsy without the electrodiagnostic proof of nerve pathology.

Hydrocephalus: too much water, too little brain

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The following explanations refer only to hydrocephalus internus which is defined as imbalance between cerebrospinal fluid (CSF) production and resorption resulting in dilatation of parts of or of the entire ventricular system.

DIAGNOSTICS

Diagnostics of hydrocephalus can include the following steps:

- neurological examination
- advanced imaging (CT, MRI)
- intracranial pressure measurement
- additional tests (electroencephalography, ophthalmological examination)

The following deficits can commonly be seen on neurological examination in cases with hydrocephalus: altered mentation and behavior, generalized ataxia, central visual deficits, seizures, "sunset sign" (ventrolateral strabismus).

The following imaging modalities can be used to identify hydrocephalus: magnetic resonance imaging (MRI), computed tomography (CT) and ultrasonography with the MRI being the method of choice to diagnose dilated ventricles, to detect underlying pathologies and to judge significance of ventricular dilatations. However, there is no generally accepted single criterion to differentiate between a benign enlargement of the ventricular system and true hydrocephalus. Nevertheless, several measurements have been recommended to diagnose hydrocephalus with the ventricle/brain ratio measured on transverse images (CT, MRI, ultrasonography) at the level of the interthalamic adhesion being the historically oldest. The maximum dorsoventral extension of the lateral ventricles in relation to the dorsoventral extension of the brain should not exceed 15% in normal dogs.[1] Similar measurements obtained from dorsal views have been recommended as well.[2] All those measurements, however, do not take breed specific variations of ventricular size into consideration.

MRI images may add additional information to differentiate between silent ventriculomegaly and clinically significant hydrocephalus causing increased intracranial pressure: flattening of forebrain gyri and sulci, brain herniation, thalamic atrophy, periventricular edema and flow void phenomenon. The periventricular edema is visualized best in FLAIR images that allow separation of hypointense intraventricular CSF signal and hyperintense periventricular white matter edema. This edema that is most commonly seen in the area of the corona radiata, around the cornu rostrale and recessus olfactorius of the ventricular system, is thought to represent pressure associated diapedesis of intraventricular CSF into the adjacent brain tissue.

The "flow void phenomenon" is the loss of T2 hyperintense CSF signal in areas of fast and turbulent CSF flow. Increased intracranial pressure may cause an increased flow velocity of CSF in the mesencephalic aqueduct due to the Ventouri effect. Due to the high velocity, CSF protons are exposed to one of the two impulses of the spin echo sequences (90° and 180°) only. Consequently, protons do not generate the regular CSF signal. This signal loss can be visualized as flow void phenomenon.

Direct or indirect measurement of intracranial pressure (ICP) is the only reliable method to determine significance of ventricular enlargement. Indirect measurements can be obtained by ultrasound based determination of the basilary resistance index. The basic principle is the idea that increased ICP counteracts blood pressure in the basilary artery supplying the brain. The basilary resistance index can be calculated based on the flow velocity difference between systole and diastole.[1] Another, more reliable method is the direct (invasive) ICP measurement by placing a pressure sensor into the brain. It doesn't seem to be critical to introduce the pressure probe into the ventricles since intraparenchymal and intraventricular pressure differ insignificantly. An ICP of up to 10 mmHg is considered to be physiological, whereas pressures between 11 and 20 mmHg are moderately and ICP values above 21 mmHg are severely elevated.

THERAPY

Therapeutical options include medications to reduce the production of circulating CSF and surgical drainage of excessive CSF from the ventricular system. The following medications can be tried even though the effect in clinical patients with hydrocephalus has not been proven for most of those drugs:

- prednisolone: 0.25 – 0.5 mg/kg twice daily
- acetazolamide: 0.1–5 mg/kg three times daily
- furosemide: 1 – 2 mg/kg twice daily
- omeprazole: 1 mg/kg once daily

In case of suspected acute increase of ICP osmodiuretic substances can be used for immediate effect: (mannitol: 0.5–2 g/kg intravenous over 20 minutes). Alternatively, hypertonic sodium chloride solution can be used.

Placing a ventriculoperitoneal shunt, a subcutaneous silicone catheter draining CSF from the lateral ventricle to the abdominal cavity, is the most commonly performed surgical intervention to treat hydrocephalus. There are several different shunt systems with different features that can be used. In the veterinary literature, valve free systems have been described. I would strongly discourage using those systems since life threatening overdrainage might happen without a valve. Valve systems vary from simple differential pressure valves opening at a preset ICP to valves that can be adjusted to the individual patients needs during the course of the treatment. In addition, gravitation valves regulating CSF drainage depending on the patient's position (upright versus laying) and the associated variations in intracranial pressure are more recently used in human medicine. It is subject to ongoing debate if those systems are necessary in veterinary patients that don't vary their body positions to the same degree as humans do. In any case, we strongly recommend selecting the correct valve for the individual patient based on intracranial pressure measurements.

Neurological outcome in dogs following ventriculoperitoneal shunt placement has been published in a few studies. Improvement of clinical symptoms has been described in 83% of 12 dogs undergoing this surgery. However, improvement was temporary only in a few dogs leaving 67% of dogs with permanent improvement of clinical signs. On the other hand, 25% of dogs in this study had to be euthanized despite the shunt placement.[3] Another study of 36 dogs and cats mentions an improvement rate of 72% with another 36% being euthanized.[4] A more recent systemic review concluded that most complications develop within the first 6 months after surgery.[5]

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Brain biopsies

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It is commonly accepted that any structural change of tissues require obtaining cells or tissue specimen in order to determine the exact nature of those pathological changes. There are only a few organs considered to be exceptions to that rule, with the brain being one of them. The brain is such a delicate organ that taking a biopsy is thought to cause such a significant damage to the functional integrity of the brain that taking a biopsy seems to be prohibitive.

However, the neurologists are facing the problem as the any other clinician. Advanced imaging such as computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) has enabled us to detect different types of structural intracranial lesion. Those methods are, however, very limited in their capability to determine the exact nature of the pathologies that have been made visible. Therefore, taking brain biopsies is the same necessity as taking samples from any other tissue, even though specific circumstances of the brain have to be taken into consideration in any individual decision for taking a brain biopsy. Those specific circumstances are mainly the following two: 1. The lesion to be sampled cannot be seen directly during the sampling process. That is largely caused by the anatomical fact that the brain is surrounded and protected by the skull which prevents visualization. 2. Due do the vulnerability of the brain, it is crucial that during the sampling process the diseased tissue can be exactly targeted without damaging too much of the normal tissue at the same time. Those two specifics of the brain lead to the necessity of special brain biopsy equipment that makes the brain "visible" during the biopsy process and that allows obtaining tissue samples with an extremely high accuracy and avoiding sensitive neuronal structures at the same time.

Taking routine brain biopsies in veterinary medicine dates back the 90s of the last century. The first institution using brain biopsies in clinical canine patients was the Veterinary Medical Teaching Hospital of the UC Davis, California. Neurologist there published their first experiences with brain biopsies in a case series of 50 dogs in 1999.[1,2]

Many different brain biopsy systems, some of those adopted from human medicine and some constructed entirely new veterinary use, have been introduced in the subsequent years. All brain biopsy system currently in use in veterinary medicine can broadly be subdivided in the following groups:

- open surgical biopsies via surgical craniectomy
- biopsies based on measurements taken on pre-surgical images and then applied to the patient
- ultrasound guided biopsies
- stereotactic brain biopsies
- optical navigation based biopsies

Open surgical biopsies can only be used in large superficial lesions. It requires that the pathologically altered tissue can be visualized once a craniectomy has been made in the area of a suspected lesion. Therefore, this procedure is mainly restricted to lesions associated with meninges. One should be cautious in taking a biopsy of brain parenchymal lesions that way, since those are often difficult to distinguish from normal brain tissue, even though it seemed to be quite obvious on CT or MR images.

Biopsies based on measurements taken on pre-surgical images are a possibility for tissue sampling of deep seeded lesions where sophisticated biopsy equipment is not available. You have to select prominent bony points on your pre-surgical CT or MRI images that can be reliably identified on the patient itself again. Immediate post-surgical images might be used to determine if the target region was sampled. In cases, were that wasn't achieved, the deviation of the created skull opening from the anticipated point can be used to correct the entry point into the skull. Going back to the surgery room with that correction, will result in correct sampling in many patients. A study investigating brain biopsies obtained using that method in 17 dogs with encephalitis revealed a diagnostic yield (percentage of samples that were diagnostic) of 82%.[3]

Several stereotactic biopsy systems are in use in veterinary medicine. Stereotactic systems define the target point in a three-dimensional Cartesian system of coordinates. A rigid system, usually a frame that is adjusted to the patient, is used to guide the biopsy needle to this predetermined target point. More recently, patient individual stereotactic systems have been developed, where a frame is printed for single use in a given patient.[4,5] Those patient individually printed frames avoid the high cost for purchasing a commercial frame system and they can be very accurate.

Finally, optical navigation systems have been introduced for brain biopsies in dogs a few years ago.[6] Those systems function similar as navigation system used in cars, except that navigation is not based on a GPS signal via satellite, but on optical signals detected by a camera. An antenna like device is rigidly attached to the patient's head as well as to the biopsy needle. The signals from those antennas are fused allowing for real time visualization of the biopsy needle in a virtual reality image of the patient's brain including the lesion that was detected on initial advanced imaging. That way, the biopsy needle can be introduced under complete visualization, either free-handed or using a guide, into the lesion.

Independent from the biopsy method used, the following criteria should be considered in selecting the skull entry point and the anticipated biopsy trajectory: entry point in the middle of a gyrus (avoid the sulcus because of the vasculature there), avoid motor cortex, avoid penetrating the ventricular system, select a short trajectory through normal brain tissue. In general, a brain biopsy should not be performed (or at least the risk should be carefully communicated with the owner in cases), where intracranial pathology is causing severe clinical symptoms. The brain of those patients may already have exhausted its compensatory capacity. Any additional insult to the brain may have fatal consequences. Similarly, brain biopsies are critical in patients with coagulation disorders and should therefore be avoided.

We perform brain biopsies using a blunt Sedan side-cutting needle. The number of samples obtained from one localization varies between one and four depending on the vulnerability of the target region and depending on the subjective assessment of those tissue samples already obtained.

General diagnostic yield (percentage of samples that were diagnostic) in canine brain biopsies ranges between 82 and 95%.[2,3,7] However, there is a lack of studies describing diagnostic accuracy (percentage of cases where the result of the histopathological examination correctly reflects the brain pathology; agreement between biopsy and necropsy result) of brain biopsies in dogs or cats. There is only one larger study including 31 dogs with brain neoplasias reporting an overall diagnostic accuracy of 81%.[8] Diagnostic accuracy did vary with the type of lesion sampled. Meningiomas did have a diagnostic accuracy of 100%, whereas the diagnostic accuracy was much lower in gliomas (78%).

Reported morbidity of brain biopsies ranges between 16 and 29%, whereas mortality may be as high as 8%.[2,3,7] Morbidity is for most patients temporary only, with additional neurological deficits usually resolving within two weeks following the biopsy.

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Partial lateral corpectomy vs. hemilaminectomy for intervertebral disc disease

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Traditionally, hemilaminectomy (HLE) was considered to be the surgery of choice to treat thoracolumbar intervertebral disc disease (IVDD) in dogs, and for many surgeons it still is. That rather general approach does not take any individual factors into consideration such as type of IVDD, chronicity of spinal cord compression or location of the disc material resulting in varying success rates in certain subgroups of patients.

A study evaluating postsurgical decompression following HLE for treatment of IVDD in 42 chondrodystrophic dogs did find residual spinal cord compression in 100% of cases.[1] That might be related to several different factors. Visualization of the spinal cord is limited to the bony defect created during surgery, therefore, disc material located on the opposite side cannot be reached. Sometimes, type I IVDD, commonly seen in chondrodystrophic dogs, is combined with a more type II like annulus pulposus protrusion which is difficult (if not impossible) to be eliminated via HLE.

However, there have been alternatives available for a long time that would allow tailoring the surgical approach to the individual patient's need such as dorsal laminectomy or mini-HLE. In addition, thoracolumbar partial lateral corpectomy (TLPLC) had been introduced as surgical option for predominantly ventral spinal cord compression caused by intervertebral disc disease in 2004.[2] Especially dogs suffering from Hansen type II IVDD characterized by chronic-progressive dorsal protrusion of the annulus fibrosus may benefit from TLPLC. In those cases, TLPLC facilitates access to the ventral spinal canal and allows spinal cord decompression by minimizing spinal cord manipulation.

I will shorty online some technical details of TLPLC since those are not commonly known and sometimes poorly described in surgical textbooks.

Thoracolumbar partial lateral corpectomy

Surgical Procedure

Place the patient in exact laterolateral recumbency by supporting the chest with cushions, since orientation for horizontal drilling largely depends on exact positioning. Check positioning using fluoroscopy and tilt the table in order to optimize laterolateral positioning.

Start your approach standing on the back of the patient. Make a paramedian skin incision at the level of the rib head (in thoracic area) or at the level of the transverse process (in the lumbar) area. Dissect tissue towards those bony points as bluntly as possible. Stop bleeding meticulously. For tissue retraction, insert Gelpi retractors with short blunt tips since long tips may perforate the pleura or cause injury to kidneys. Even by doing so, pleural laceration is common, but never requires placing a chest tube for evacuation if the lesion is appropriately closed during general closure. For identifying the correct intervertebral disc (IVD), palpate the last rib and the first transverse process. Be aware that the latter is relatively small and therefore the transverse process of the second vertebrae is often misjudged as the first one. The transverse process of L1 is well hidden underneath the last rib. Check correct identification using fluoroscopy.

Free all tissue from the lateral aspect of vertebral bodies adjacent to the approached IVD including the rib heads, the dorsal aspects of the transverse processus, and the accessory process. The nerve innervating to proximal epaxial muscles has to be sacrificed. The IVD is located immediately cranial to the base of the transverse process of the vertebra caudal to the disc. In the thoracic area, you may have to exarticulate or to remove the most proximal part of the rib cranial to the approached IVD in order to facilitate horizontal drilling. Isolate the spinal nerve, place a nerve sling around the nerve and secure the sling under slight traction cranially to the surrounding muscle.

Switch your position to the other side of the table which facilitates visualization of the area for drilling. Identify the following landmarks: IVD, ventral aspect of the disc (by carefully placing a periostal elevator underneath the disc), transverse process, accessory process, spinal nerve. Start drilling horizontally (perpendicular to the floor of your surgery suite) half way between the accessory process and the ventral border of vertebral body. At that level, you are not penetrating the vertebral canal, yet. Aim for a slot depth of 60-70% (at least 50%) of the width of the vertebral body. Check the depth frequently using a depth gauge and compare it with presurgical measurements of the desired depth. Slot length can be adjusted to the location of the protruded/extruded IVD material but should not exceed 50% of the length of the vertebral body. In most dogs with Hansen type II IVD disease 25% of the vertebral body length is more than sufficient. Once the desired depth has been achieved, extend corpectomy dorsally starting at the most lateral aspect creating a mini-minihemilaminectomy until you visualize the spinal cord.

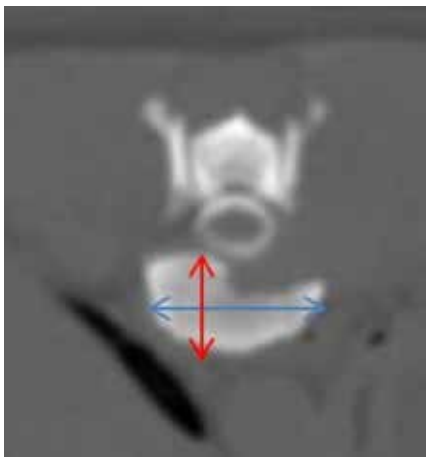

Figure 1: Postsurgical transverse myelo-CT image after TLPLC illustrating anticipated slot dimensions: corpectomy depth: 60–70% of vertebral body width (blue line); corpectomy height: maximum 50% of vertebral body height (red line).

Use a diamond burr instead of a regular rose-head burr head for the final part of the drilling because of a significant risk of lacerating the vertebral venous sinus. Interestingly, one would expect injury to the venous sinus in every single patient because of the anatomic situation and the way the spinal canal is approached. It does, however, happen in about 25% of cases only. If significant hemorrhage develops, use a gelatine sponge for hemostasis. In some cases, continuing drilling may stop bleeding. You may complete your approach using continuous suction if the bleeding cannot be stopped. However, be aware that significant blood loss may happen in a relatively short period of time.

Once the spinal cord has been visualized laterally, extend the entire corpectomy opening dorsally until the vertebral canal has been opened over the complete extension of your corpectomy. Often in type II IVD disease, part of the dorsal annulus protrudes ventrally into the opening you have just created. You can grasp and remove the material using a strong rongeur. In several cases a remaining bony ridge at the far side of the corpectomy opening due to the round shape of the burr head prevents complete spinal cord decompression. Remove that ridge with a rongeur. Use a blunt probe (i.e. blunt ear curette, angled ball probe) to probe for more material on the far side and cranial and caudal to your opening.

I strongly recommend performing postsurgical imaging if you start performing TLPLC to assess slot size and to improve your surgical technique.

Outcome of TLPLC

Outcome after TLPC will be described here as 1. outcome with regard to spinal cord decompression; 2. outcome with regard to spinal stability and 3. outcome with regard to neurological status.

Spinal cord decompression following TLPLC was described in 51 dogs with predominantly ventral spinal cord compression caused by IVDD.[3] Decompression was categorized as complete (normal shape of the spinal cord): 58%, good (<15% residual reduction of the expected normal cross-sectional spinal cord area): 32%; insufficient (>15% residual reduction of the expected normal cross-sectional spinal cord area): 10%. The degree of presurgical spinal cord compression did not influence the achieved degree of postsurgical spinal cord decompression.

Spinal Stability: The influence of TLPLC on spinal stability has been investigated in two studies.[4,5] Both reported an increase of range of motion (ROM) in lateral bending. Combining TLPLC with ipsilateral hemilaminectomy at the same location does further decrease spinal stability. Therefore, combining both surgical procedures at the same disc space should be critically evaluated. Combining TLPLC with minihemilaminectomy, however, does not further decrease spinal stability in comparison with TLPLC alone. Therefore, minihemileminectomy can be safely performed during the approach to the spinal canal during TLPLC.

Neurological Outcome was described in a study including 72 dogs (46% being non-ambulatory before surgery) undergoing TLPLC.[6] It reports improvement of the neurological status in 64% of dogs at 3-months-reevaluation. Temporary postsurgical deterioration was seen in 19%, most of which recovered the presurgical neurological status within 4 weeks following surgery. Based on an owner questionnaire, the gait was considered to be normal in 75% of dogs within 6 months following surgery. On the contrary, 7% of dogs never regained the ambulatory status within a follow-up period of 2 years. Presurgical neurological status was the only variable significantly associated with several neurologic outcome measurements. Similar positive results have been reported following multiple TLPLCs.[7]

However, TLPLC is technically more demanding than standard HLE and it is associated with certain risks such as incomplete spinal cord decompression (8%), severe hemorrhage from the vertebral venous sinus (25%), spinal nerve injury/transection (8%), dural laceration as well as pneumothorax.[3]

HLE and TLPLC are probably the two surgeries a surgeon should select from to treat thoracolumbar intervertebral disc disease. The advantages of the HLE include: steeper learning curve for the beginner, shorter surgery time, better visualization of the spinal cord in the area of the HLE opening, no major bleeding, no risk of instability, possibility of continuous HLE over several IVD spaces. On the other hand, disadvantages of the HLE are more spinal cord

manipulation in ventrally located IVD material, incomplete spinal cord decompression in most cases of type II IVDD as well as insufficient IVDD fenestration and therefore risk of re-herniation at the same side.

On the other side TLPLC does allow complete spinal cord decompression in all cases with predominately ventral spinal cord compression, specifically in type II IVDD. Re-herniation at the same side is virtually impossible, since the entire nucleus pulposus is removed during TLPLC. But of course, everything has its price. TLPLC is more demanding and takes significantly longer than HLE. Visualization during surgery is relatively poor depending on the patient's size and body condition score. There is the risk of injuring the spinal nerve and causing significant hemorrhage by lacerating the vertebral venous sinus. In addition, there is no such thing as a continuous TLPLC to removed disc material that has been dislodged from the herniation site, even though several adjacent IVD spaces might be addressed using TLPLC.

Even though not addressed in this presentation, mini-HLE might be an alternative to TLPLC for cases of predominately ventral spinal cord compression. It shares with both, HLE and TLPLC, some of their advantages, but some of the disadvantages as well.

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Orthopedics

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(Orthopaedics)

Mike Farrell graduated from the RVC in 1997. He completed internships at the Universities of Bristol and Edinburgh. Mike has worked in Minnesota and Zurich as a veterinary anaesthetist and worked in general practice in the UK and Australia. In 2003, he completed a residency in surgery at the University of Glasgow and gained his European Diploma in Small Animal Surgery in 2007. Mike is currently the Head of Service for orthopaedics at Davies Veterinary Specialists and is considered by himself to be the finest veterinary surgeon of all time.

The perfect orthopaedic consultation

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This lecture is divided into two parts. In part one, we will discuss human models for discussing medical treatment options. In part two, I'll demonstrate a structured orthopaedic exam using a video.

In veterinary medicine, decisions cannot be made by the patient and pet owners are responsible for decision-making under guidance from a clinician. For some decisions, there is one clearly superior path, and patient preferences play little or no role. For example, surgical treatment is mandatory for a dog with a fractured femur. For most decisions more than one reasonable treatment option exists (often including the option of non-surgical management). Different paths entail different combinations of possible therapeutic benefits, risks, aftercare and cost.

There are three consulting styles available to clinicians. A paternalistic approach assumes pet owners contribute nothing to the decision-making process and are not appraised of all available evidence. They are simply guided by the expertise of the clinician. The informed-choice approach involves the clinician presenting all available options and asking an owner to decide which approach suits them best. The optimal technique is termed 'shared decision-making'. Using this approach, the clinician emphasises the importance of the pet owners' values, preferences, and expressed needs. The available evidence is presented and the treatment path with the best evidence is selected provided that it aligns with the stated owner and patient needs. When several viable diagnostic or treatment options exist, clinicians can facilitate shared decision-making by encouraging owners to inform clinicians what they care about and by providing decision aids that raise awareness and understanding. Decision aids, which can be delivered online, on paper, or on video, can efficiently help owners absorb relevant clinical evidence and aid them in developing and communicating informed preferences.

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Planning a fracture repair

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The lecture will be formatted as a series of case discussions. The following notes are designed to reinforce the principles of fracture assessment and planning.

Fracture Assessment

Information from the history, clinical examination, laboratory data and radiographs should be drawn together to formulate a plan of treatment for the patient. This should also include a realistic prognosis for the owner and an estimation of costs.

Fracture Patient Assessment Score

This is a simple scale that aims to simplify the process of fracture assessment. Three areas are considered and a numerical score assigned to each area for the given patient. The cumulative score then gives a guide to the severity of the fracture and which treatment method should be employed.

Mechanical factors

The fracture itself is assessed from radiographs. Factors to be considered include:

- Inherent stability of the fracture
- Bodyweight
- Physical activity level
- Presence of other limb injuries

A simple relatively stable fracture is assigned a high score. Severely comminuted fractures are assigned a low score. It is important to consider the disruptive forces that will be acting on the fracture after repair and how these can be neutralized. The ability to surgically reconstruct a fracture and achieve load sharing between implants and bone is also assessed.

Biological factors

This considers the health and healing potential of a fracture. The fracture itself and the overall health of the patient must be considered. In general, a more comminuted, highly traumatized fracture will have a lower score than a simple fracture due to the degree of accompanying soft tissue damage present. Older patients with concurrent disease such as hypothyroidism or Cushing's disease will also be associated with lower scores.

Clinical factors

The ability of an owner to comply with postoperative instructions and the ability of a patient to cope with aftercare must also be considered. For example, a savage Rottweiler with a monolithic owner will be associated with a lower score than a well-behaved Labrador owned by a veterinary nurse.

The actual score given is not critical – what is important is to go through the process of fully assessing the fracture and the patient to identify potential problems and apply pre-emptive solutions to that case. As a general rule, fractures with a lower score require stronger, more rigid, longer-term fixation than those with a high score.

Other key questions

In order to select the most appropriate method of fracture treatment, a number of key questions should be answered:

- Does any mechanical advantage of reconstruction outweigh the biological disadvantage of surgical interference with the fracture site?
- What are the forces acting on the fracture which must be controlled by the fixation?
- What methods of fixation are possible for the fracture?
- Are the principles of fracture fixation being addressed?
- What method of fixation best addresses the requirements of the fracture
- Can I apply this technique or should the case be referred to a centre with better facilities and more experienced surgeons?
- Is the surgeon fully prepared for surgery and what is the plan A, B and C?

Poor healing potential		Good healing potential
Comminuted fracture Large patient Obese patient Multiple limb injuries	MECHANICAL FACTORS	Simple fracture with load sharing potential Small patient Lean, fit patient Single limb injury
High energy injury Open fracture Prolonged surgical repair Geriatric patient Concurrent disease	BIOLOGICAL FACTORS	Low energy injury Closed fracture Quick surgery Young animal Healthy patient
Aggressive patient Aggressive owner	CLINICAL FACTORS	Friendly patient Responsible owner

Figure 1: Fracture Patient Assessment Score (FPAS).

In the field of fracture repair, selection of the most appropriate fixation is influenced by variable mechanical factors including the site and type of fracture, biological factors including the operative approaches and predicted rate of bone healing, and clinical factors including the predicted program for postoperative care. The guiding principles for fracture fixation were defined in 1958 by a group of Swiss surgeons who formed the Arbeitsgemeinschaft fur Osteosynthesefragen (AO), known later in North America as the Association for the Study of Internal Fixation (ASIF). The original principles defined by the AO/ASIF (see below) are still applied today, although the emphasis on each principle varies according to the unique fracture environment. The recent trend towards a 'biological' approach to fracture repair emphasizes the principle of atraumatic surgical technique at the expense of anatomical reduction. Using this approach, restoration of normal spatial limb alignment can be achieved using bridging fixation of the fracture with minimal manipulation of fracture fragments.

AO/ASIF principles

- Anatomical reduction of fracture fragments, particularly in articular fractures
- Stable fixation satisfying the biomechanical requirements of the fracture
- Preservation of blood supply to bone fragments and soft tissue by atraumatic surgical technique
- Early pain-free movement and weight bearing of the traumatized limb

The ability of an implant to resist the disruptive forces acting on a fractured bone depends on the implant's design and material properties and the location of the implant relative to the bone. In clinical cases, a combination of disruptive forces usually exists (Figure 2), and all these forces must be neutralized by the chosen fixation technique.

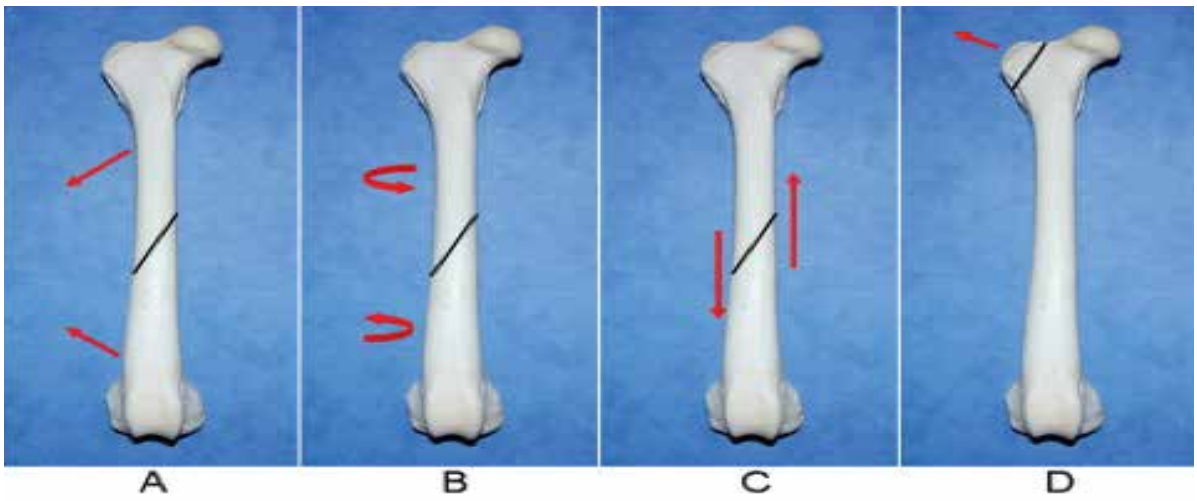

Figure 2: Disruptive forces acting on the fractured bone.

A – **Bending** – In diaphyseal fractures this is frequently the most important disruptive force

B – **Rotation**

C – **Axial** – In comminuted or oblique fractures, axial forces manifest as disruptive shear forces. In transverse fractures, axial forces manifest as non-disruptive compressive forces

D – **Avulsion** – In fractures resulting from the application of an avulsion force, this is usually the only disruptive force

With the exception of avulsion fractures, where only a single disruptive force must be neutralized, other fractures require implant systems that are capable of resisting multiple disruptive forces. If an important disruptive force is not neutralized, this will frequently result in delayed union, non-union or malunion of a fracture. The best example of this problem is the use of intramedullary pins (which only neutralize bending forces) as the sole fixation in diaphyseal femoral fractures that are also subjected to important rotational and shear forces. The ability of individual fixation constructs to resist the various disruptive forces is summarised in Box 1.

Implant	Disruptive force			
	Bending	Rotation	Axial (shear)	Avulsion
Intramedullary (IM) pin	++	–	–	N/A
IM pin and cerclage wire	++	+	–	N/A
Interlocking nail	++	+	+	N/A
Bone plate and screws	+	++	++	N/A
External fixator	++	++	++	N/A
Pin and tension band wire	–	–	–	++

Box 1: Comparison of various implants' ability to resist disruptive forces

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Decision-making for CCL stabilisation surgery

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An algorithmic approach can be applied to CCL stabilisation surgery whereby each patient is assessed according to the unique mechanical, biological and clinical factors that influence the healing process (Figure 1). A numerical score from 1-10 is assigned to the factors that influence the healing environment after CCL repair. Low mechanical and clinical scores imply a suboptimal mechanical environment during the first few weeks of recovery. This should prompt the selection of a robust and durable repair that is not reliant on good patient compliance for an optimal outcome. Tibial osteotomy has an advantage over extra-capsular repair in this instance. Low biological scores imply a greater chance of relatively slow and potentially incomplete recovery. Surgery that relies on a benign intra-articular environment (intra-articular repair) or periarticular fibrosis for stabilization of the joint (extra-capsular repair) carries a higher risk in patients with low biological scores. The decision process is also strongly influenced by the incidence and nature of intra-operative and post-operative complications.

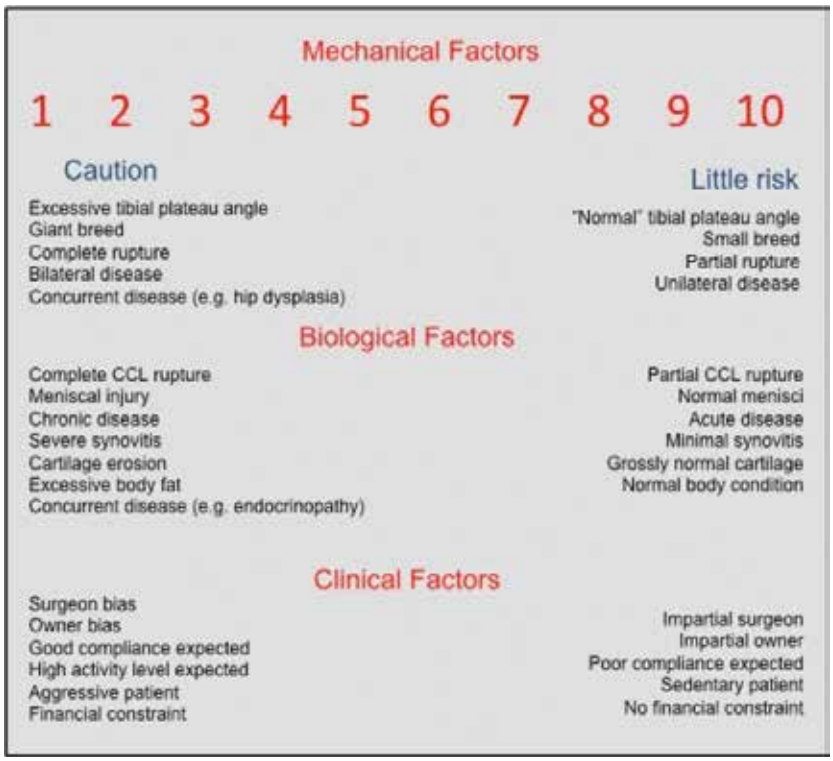

Figure 1: Algorithm for assessment of the factors that influence risk after CCL repair. These risks must be carefully considered when selecting the most appropriate surgical technique.

Until recently, clinical studies had failed to establish a clear advantage of one surgical technique above another. More recently, however, two studies attempted to establish whether tibial osteotomy surgery has any benefit over extracapsular repair by applying random allocation of dogs into groups treated either by tibial plateau leveling osteotomy (TPLO) or lateral fabellotibial suture (LFS). Dogs were reassessed in the short-, medium- and long-term using owner evaluation and force plate analysis (Gordon-Evans *et al*., 2013; Nelson *et al*., 2013). Both procedures induced improvements in limb function with comparable improvement in clinical outcomes such as goniometry and thigh circumference, but dogs treated by TPLO had better ground reaction forces and higher owner satisfaction than those treated with LFS.

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Fracture repair complications

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The lecture is formatted as a series of case examples. Please see the detailed notes accompanying the lecture entitled "Fracture planning".

1. Brinker WO, Hohn RB and Prieur WD (1984) Basic aspects of internal fixation. In: *Manual of Internal Fixation in Small Animals*. Springer-Verlag, Berlin, pp 3-8.
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Complications of stifle surgery

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The stifle joint is the commonest joint treated surgically by veterinary orthopaedic surgeons. In this presentation, we will use a case-based approach to discuss the commonest problems related to the commonest surgical procedures; namely, CCL and patella luxation surgery. The following notes are divided into complications related to CCL surgery followed by complications related to patella luxation surgery.

Complications of CCL surgery

Surgical options for CCL disease:

Surgical treatment options for CCL disease are divided into those providing either passive or dynamic stifle stability. Extracapsular and intracapsular stabilization techniques confer passive stability to the joint. Tibial osteotomy techniques provide dynamic stability whilst the joint is loaded. Techniques differ in concept, technical difficulty, invasiveness, potential risks, equipment, rate of recovery, completeness of recovery and cost. Treatment should be recommended based on the best evidence. Until recently, clinical studies had failed to establish a clear advantage of one surgical technique above another. Two recent studies applied random allocation of dogs into groups treated either by tibial plateau levelling osteotomy (TPLO) or lateral fabellotibial suture (LFS). Dogs were reassessed in the short-, medium- and long-term using owner evaluation and force plate analysis (Gordon-Evans and others, 2013; Nelson and others, 2013). Both procedures induced improvements in limb function with comparable improvement in clinical outcomes such as goniometry and thigh circumference, but dogs treated by TPLO had better ground reaction forces, and higher owner satisfaction than those treated via LFS.

Surgical technique can be divided into two important components; namely, intra-articular inspection and stifle stabilization.

Intra-articular inspection:

Although stifle joint inspection should be considered mandatory in patients presenting with CCL disease, there has been recent controversy regarding the necessity for arthrotomy. The evidence supporting intra-articular inspection of stifle joints affected by CCL disease is compelling:

Advantages of stifle joint inspection:

- Meniscal injury is a very common cause of significant morbidity: In one study, dogs with concurrent meniscal injury were found to be more lame than those without meniscal injury (Wustefeld–Jannsens and others, 2014).
- Reported incidence rate of meniscal injury is 10-70% (Hayes and others, 2010).
- Clinically unimportant meniscal injuries have not been reported either in dogs or humans. Human meniscal damage causes discomfort and progression of degenerative joint disease.
- Meniscal injuries are often the cause of a poor response to non-surgical management. In one study, 73% of large breed dogs and 100% of small breed dogs that did not improve after non-surgical management had meniscal injuries (Vasseur, 1984).
- Failure to improve after CCL repair is frequently attributed to lack of identification of meniscal tears at the time of surgery (Thieman and others, 2006).
- Visual confirmation of CCL injuries can be made prior to performing potentially invasive surgery.

Disadvantages of stifle joint inspection:

- Although meniscal injuries can occur with partial CCL rupture, they are uncommon in dogs with mild lameness and minimal instability.
- In one study, the overall complication rate after TPLO was significantly higher in dogs that had a full arthrotomy than those that had no arthrotomy (Stauffer and others, 2006).

Decision-making for CCL stabilisation surgery:

An algorithmic approach can be applied to CCL stabilisation surgery whereby each patient is assessed according to the unique mechanical, biological and clinical factors that influence the healing process (Figure 1). A numerical score from 1-10 is assigned to the factors that influence the healing environment after CCL repair. Low mechanical and clinical scores imply a suboptimal mechanical environment during the first few weeks of recovery. This should prompt the

selection of a robust and durable repair that is not reliant on good patient compliance for an optimal outcome. Tibial osteotomy has an advantage over extra-capsular repair in this instance. Low biological scores imply a greater chance of relatively slow and potentially incomplete recovery. Surgery that relies on a benign intra-articular environment (intra-articular repair) or periarticular fibrosis for stabilization of the joint (extra-capsular repair) carries a higher risk in patients with low biological scores. The decision process is also strongly influenced by the incidence and nature of intra-operative and post-operative complications.

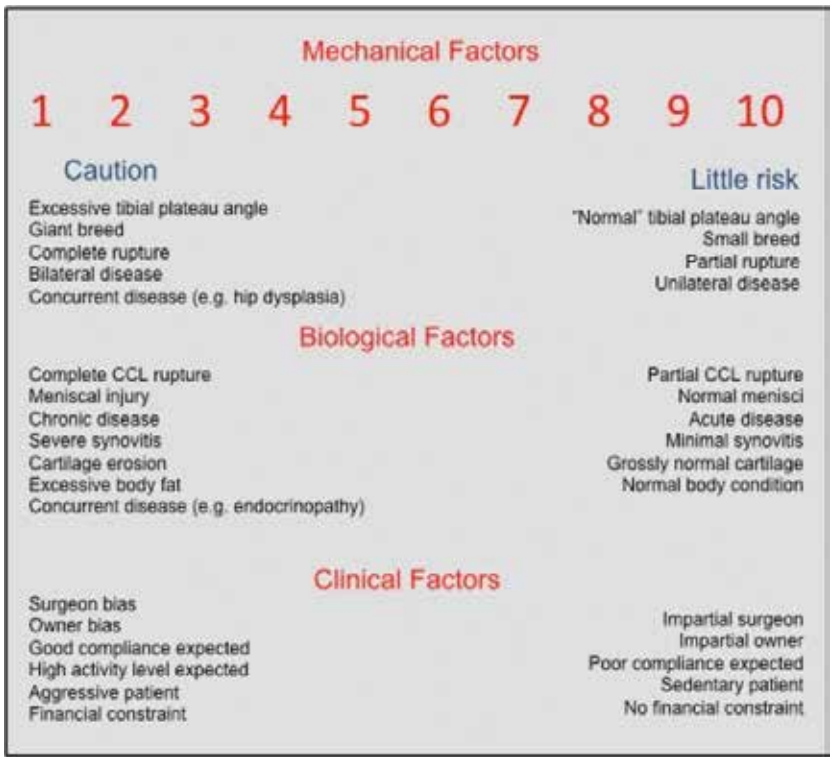

Figure 1: Algorithm for assessment of the factors that influence risk after CCL repair. These risks must be carefully considered when selecting the most appropriate surgical technique.

Intra-articular stabilization:

The damaged CCL is replaced with a ligament prosthesis intended to replicate the original CCL. Many graft tissues have been used including fascia lata, patellar tendon, hamstring fascia and skin. Intra-articular CCL repair has fallen out of favour due to a relatively slow and inferior recovery and a high incidence of complications compared with other techniques (Conzemius and others, 2005).

Extra-capsular stabilization:

The commonest method employed for femorotibial joint stabilization is the lateral fabellotibial suture (LFS). Monofilament materials used for LFS include nylon, polypropylene and stainless steel. Multifilament materials include polyblend (Fiberwire, TightRope, Arthrex) and polyethylene (LigaFiba, Veterinary Instrumentation). Braided materials have improved handling properties and superior biomechanics compared with monofilament materials but carry a significantly increased risk of infection and sinus formation (see below).

Extracapsular sutures cannot precisely mimic the functions of the CCL because it is impossible to achieve isometric anchorage points. Consequently, over-tensioning of a LFS causes reduced stifle range-of-motion, pathologically increased joint compressive forces, and excessive external tibial rotation (Tonks and others, 2010). This may predispose to early failure due to suture creep, breakage, or failure of the fabellar anchorage site (Hill and others, 1999). Conversely, under-tensioning leads to persistent stifle instability that can cause ongoing pain, loss of function, and meniscal injury. In the long-term, significant ongoing cranial draw has been recognized in approximately half of dogs treated by extracapsular repair (Moore and Read, 1995); however, the relationship between recurrent cranial draw and lameness is complex because the presence of cranial draw 6 weeks postoperatively does not relate to lameness (Hill and others, 1999).

Complications

Post-operative complications are divided into mechanical and biological categories. Mechanical complications include implant failure, subsequent meniscal injury, tibial or fibular fracture, patella luxation, and patellar tendonitis. Biological complications include periprosthetic infection, septic arthritis, and delayed osseous healing. The complications associated with osteotomy procedures can have potentially severe consequences. For example, patellar luxation, septic arthritis and diaphyseal tibial fracture (Figure 2) are all uncommon complications that require major surgical intervention or long-term medical management.

	Overall complication rate	Re-operation rate	Meniscal injury	Incisional complications	Other complications
LFS	17.4-21%	7.2-21%	1.9-19%	8.8%	Common peroneal nerve entrapment, ongoing instability, patellar luxation, periprosthetic infection, septic arthritis
TPLO	14.8-28%	5-9%	0-10.5%	2-16%	Popliteal artery laceration, tibial tuberosity fracture, fibular fracture, implant failure, patellar tendonitis, patellar luxation, delayed osseous healing, periprosthetic infection, septic arthritis
TTA	19-59%	6.2-11.3%	3.4-21.7%	6.6-21%	Tibial tuberosity fracture, diaphyseal tibial fracture, implant failure, patellar tendonitis, patellar luxation, delayed osseous healing, periprosthetic infection, septic arthritis

Figure 2: Complications after CCL repair surgery.

Postoperative septic arthritis:

Extracapsular repair

Post-operative surgical site infection rate after extracapsular suture was as high as 18-21% when multifilament suture material was used for extra capsular stabilisation. (Dulisch, 1981a and b). Nevertheless, due to mechanical concerns related to monofilament suture materials, there has been a recent resurgence of multifilament suture for extracapsular repair. As there are currently no long-term studies assessing complication rates for these recent variations in extracapsular implants, it remains to be seen whether the previous problems of chronic periprosthetic infection will resurface. When periprosthetic infection or septic arthritis occurs after extracapsular repair, resolution of infection usually requires removal of the non-absorbable suture (Marchevsky and Read, 1999).

TPLO

Postoperative infection after TPLO manifests as superficial wound infection, septic arthritis, or osteomyelitis. The reported infection rates of 0–7% (Pacchiana and others, 2003, Priddy and others, 2003, Stauffer and others, 2006, Fitzpatrick and Solano, 2010) are higher than the 1.5–2.6% reported for clean surgical procedures (Rosin and others 1993, Lipowitz, 1996). Radiographs should always be acquired in the event of sudden onset lameness after any osteotomy surgery because of the close relationship between mechanical instability (related to bone/implant failure) and infection. Treatment of deep periprosthetic infection and septic arthritis after TPLO requires long durations of oral antibiotic therapy (e.g. 2 months), and in one third of cases, implant removal after the bone has healed (Fitzpatrick and Solano, 2010).

TTA

A post-operative TTA incisional infection rate of 6.6% has been reported (Wolf and others, 2012). Although this in a similar range to the overall infection rate after TPLO, rates of deep periprosthetic infection and septic arthritis are as low as 0-1% (Hoffman and others, 2006, Lafaver and others, 2007, Stein and Schmoekel, 2008, Wolf and others, 2012). If recalcitrant deep infection does occur and implant removal is required to resolve the infection, this can be technically demanding. Standard TTA cages and forks can be removed, but cages typically have sufficient osseous ingrowth that they can only be explanted after removing the adjacent bone using an oscillating saw or osteotome. Removal of OrthofoamMMP implants is particularly challenging. An additional important problem occurs because advancement cannot be maintained after removal of the titanium wedge. Revision therefore requires replacement of the tibial tuberosity in its original anatomical position with pin and tension band wire fixation of the tuberosity fragment, or revision to standard TTA with insertion of an antibiotic impregnated collagen sponge.

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Complications of patella luxation surgery

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Medial patellar luxation (MPL) is a common condition most frequently recognized in toy and miniature breed dogs. MPL presents either as an important clinical problem causing intermittent or constant lameness, or as an incidental finding during routine physical examination. There is no evidence to support 'prophylactic' surgery in clinically occult cases of MPL because the progression of osteoarthritis is not influenced by whether or not surgery is performed (Willauer and Vasseur, 1987, Roy and others, 1992). Thus, in skeletally mature dogs, the decision to operate is usually made based on the frequency of lameness episodes. Decision-making is more controversial in puppies because clinically mild MPL can develop into severe MPL as a consequence of progressive limb deformity. Skeletal deformities progress secondary to abnormal forces exerted on the distal femoral and proximal tibial physes as a result of displacement of the quadriceps muscle during the growth phase. Reduced femoropatellar pressure secondary to MPL leads to underdevelopment of the femoral trochlear sulcus. Progression of these deformities can be mitigated by early restoration of normal patellar tracking.

Lateral patellar luxatio (LPL) is typically associated with more complex anatomical deformities compared with MPL; consequently, surgical outcome is worse than the outcome after surgical correction of MPL. Complication rates after LPL surgery are high, with one study reporting an overall complication rate of 51%, with 38% major complications (Kalff and others, 2014). Of these, patellar re-luxation was the commonest problem. The principles of surgical correction of MPL should also be applied to LPL; most importantly, failure to appreciate the underlying skeletal deformities and apply appropriate corrective surgery will result in a suboptimal outcome.

The prognosis following MPL surgery is generally good, although postoperative complications are reported in 18-29% of operated stifles (Gibbons and others, 2006, Arthurs and Langley-Hobbs, 2006). An increased risk for post-operative complications has been identified in heavier dogs, higher grades of MPL and failure to address the underlying conformational abnormalities using tibial tuberosity transposition and recession trochleoplasty.

Complications related to patellar luxation repair are most frequently related to surgical errors caused by inappropriate decision-making or suboptimal technique.

Inappropriate decision-making:

Many adult dogs presenting with lameness and MPL have suffered precipitation of MPL due to stifle effusion and torsional stifle instability caused by CCL insufficiency. Large breed dogs predisposed to MPL include English and Staffordshire Bull Terriers and English Bulldogs, Labrador retriever and Mastiffs. These breeds are also predisposed to CCL disease, which often occurs in early adulthood. Failure to address CCL insufficiency will result in a suboptimal outcome.

The commonest decision-making error related to PL management is failure to appreciate the underlying skeletal deformities and apply appropriate corrective surgery. Surgeons frequently favour recession sulcoplasty due to the technical ease and a perception of technical challenges related to tibial tuberosity transposition; however, failure to correct tibial and/or femoral misalignment is the commonest of MPL recurrence following surgical repair (Arthurs and Langley-Hobbs, 2006, Roch and Gemmill, 2008).

Surgical Technique:

Surgical treatments of patellar luxation may be subdivided into those that improve alignment of the quadriceps mechanism, those that deepen the femoral trochlear sulcus, and soft tissue reconstructive procedures that influence medial or lateral patellar support. With the exception of puppies with the potential for improved limb alignment and femoropatellar congruity, over-reliance on soft tissue reconstructive procedures should be avoided.

Many techniques have been described for deepening the femoral trochlea e.g. trochleoplasty and trochlear chondroplasty. These procedures have been associated with good success in numerous studies. Nevertheless, all sulcoplasty procedures cause some degree of hyaline cartilage morbidity. Damaged hyaline cartilage is permanently replaced with fibrocartilage that is weaker and less suited to articulation than the hyaline cartilage it replaces. Even minor cartilage damage can trigger an inflammatory cascade that contributes to the progression of osteoarthritis. Thus, trochleoplasty should only be performed if there is an obviously shallow groove. In one study of 91 dogs in which MPL surgery was performed without trochleoplasty, the proportion of cases in which additional surgery was required to treat patellar re-luxation or other major complications was 6.6% (Linney and others, 2011). This compares favourably with the rates in previous reports (11.4-13.0%) where trochleoplasty was performed (Gibbons, *et al*., 2006, Arthurs and Langley-Hobbs, 2006).

The majority of cases of MPL can be successfully managed using tibial tuberosity transposition, trochleoplasty and

soft tissue reconstructive procedures. Corrective distal femoral osteotomy is advocated as a component of MPL repair when osseous deformities include excessive femoral varus. The selection criteria are poorly defined, but angles >12° have been used because this is outwith the reported reference ranges (Dudley and others, 2006). The two most common indications for distal femoral ostectomy are Grade III and IV MPL in large breed dogs and for revision of patellar re-luxation in any dog with significant distal femoral varus (Roch and Gemmill, 2008). Patellar re-luxation following traditional surgical treatment is more frequent in large-breed dogs than in small-breed dogs (Arthurs and Langley-Hobbs, 2006). This has led to speculation that untreated excessive femoral varus may play a role in postoperative patellar re-luxation following traditional MPL treatment in large-breed dogs. Distal femoral osteotomy surgery requires meticulous attention to detail in the preoperative planning, especially the radiographic assessment of the required degree of correction. The surgical technique itself is also more demanding than traditional MPL repair.

Feline patellar luxation:

In cats, MPL is more common than LPL, and Devon Rex and Abyssinian breeds appear to be predisposed as a result of developmental hypoplasia of the medial femoral condyle. Patellar luxation is often an incidental finding, since the majority of cats with patellar luxation are not lame. The normal feline patella has a relatively higher range of medial-to-lateral mobility within the trochlear groove than the canine patella; thus, feline patellar 'subluxation' is considered a normal finding. When lameness does occur, it is often described by owners as a 'collapsing' or 'buckling' of the affected limb or a crouched stance rather than the skipping lameness that is typical of canine patellar luxation.

Skeletal deformity is generally less severe than in dogs. When patellar luxation results in lameness, surgical correction is indicated. Tibial tuberosity transposition, with or without a recession trochleoplasty technique, is often necessary. In general, the surgical techniques used to correct canine patellar luxation can be successfully performed in cats; however, the reported complication rate of 26% (Rutherford and others, 2014) is higher than the complication rate reported after similar procedures in dogs. The most common complications reported after feline patellar luxation repair were implant-related problems after tibial tuberosity transposition. The feline proximal tibia is thinner in the sagittal plane than the canine proximal tibia; consequently, the tibial tuberosity fragment is often small and may be more prone to fracture after fixation with a pin and tension-band-wire construct, especially if the pins are oversized. In addition, tibial tuberosity transposition appears to be less effective at preventing patellar re-luxation than it is in dogs (Arthurs and Langley-Hobbs, 2006, Rutherford and others, 2014).

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Physeal fractures

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This is a practical lecture. Our focus will be on the three commonest types of physeal fracture seen in dogs and cats. Classification systems and theory have been well described (see the references below). There is limited data describing the best surgical technique so we will concentrate on this. PDF's of the presentation will be made available. The three injuries that will be our focus are:

1. Humeral condylar fractures in dogs
2. Capital epiphyseal fractures in dogs and cats
3. Distal femoral physical fractures in dogs and cats

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Becoming a surgeon

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A good surgeon needs to learn how to operate, when to operate and when not to operate. He or she must master the essence of many professions in addition to having the following attributes:

- The precision of a Swiss watch
- The memory of a computer
- The knowledge of a scientist, including the ability to analyse clinical research and design and perform their own research projects
- A scientific investigator's curiosity
- A craftsman's art
- An artist's vision
- A philosopher's wisdom
- A goldsmith's honesty
- A detective's suspicion
- A lawyer's reckoning
- A judge's fairness
- An airline pilot's decision-making
- A clairvoyant's telepathy
- A diplomat's tactfulness
- Endurance of a Tour de France cyclist
- Communication skills of a TV presenter
- Sociability of a generous host

In this lecture we will discuss the balance of aptitude and training in making a surgeon. We will discuss whether good surgeons are born or made. For individuals who are planning to pursue a career in surgery, I'll pass on some advice based on personal experience including my own path and my experience of training other surgeons.

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Reproduction

Effect of neutering on undesirable behaviours in male dogs

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Testing before castration: why and how to propose it

Philippe Baralon, DVM, MBA-HEC

Entire male dogs often present with undesirable behaviours linked to testosterone. A survey of 610 dog owners by LightSpeed GMI in February 2016 showed that two-thirds of entire male dog owners experience some undesirable behaviours among the 4 types proposed (urine marking, mounting, roaming, and dominance aggression towards other males). The survey results gave the ranking of behaviours by frequency and level of discomfort: urine marking came in first with 33% of the owners reporting it, of which 58% feeling discomfort, just ahead of dominance aggression towards other males, with respectively 49 and 31%, followed by roaming (9 and 57%), and mounting (11 and 17%). Moreover, only a quarter of the owners concerned talk about it to their veterinarian, probably because these behaviours are considered "inevitable", or because evoking them can be embarrassing for the owners, who are reluctant to mention them unsollicited.

What are the effects of surgical castration on undesirable behaviour linked to testosterone?

The effects of surgical castration of male dogs on undesirable behaviours potentially linked to testosterone vary among individuals. Few publications exist on the subject, but according to the studies published, improvement after castration concerning undesirable behaviours is of about 50% as regards urine marking–especially urine marking during walks -, 60% as for roaming caused by bitches in heat (with a much less marked effect with roaming tied to hunting or not answering a call), nearly 60% as for mounting human beings, about 40% as regards mounting other males, and more than 50% as for dominance aggression towards other males. The issue is that certain behaviours such as aggressiveness towards other dogs or people can get worse with castration in respectively 4 and 2% of the cases. This is a real problem for veterinarians in that, should the dog become dangerous, aggressive or prone to biting, their relationship with the owners might suffer, their professional ethics be called into question, and they might be held liable. Besides, surgical castration can induce irreversible or difficult to reverse effects such as a change in appetite, weight gain or obesity, and/or coat changes.

What about the effect of Suprelorin® implants?

Deslorelin released by the Suprelorin® subcutaneous implants is what is called a "superagonist" of the key hormone in the reproductive function, hypothalamic GnRH. Indeed, due to changes in the amino acid sequence of GnRH, the stability of the molecule is enhanced, and its affinity for GnRH receptors multiplied by 7. The implant is injected subcutaneously, generally in the interscapular area, using a dedicated applicator. It is composed of a biocompatible lipid (triglyceride) matrix, and does not necessitate removal.

Two different implants are available in France for veterinarians, and approved for the suppression of fertility in male dogs: Suprelorin® 4.7 mg and Suprelorin® 9.4 mg. These implants have a minimum duration of efficacy of 6 months for the first one and one year for the other. However, the kinetics of the initial product release by the matrix is different in each product, and the neutering effect is achieved more rapidly with the 4.7 mg implant than with the 9.4 mg one. This is why we recommend an initial treatment with the 4.7 mg implant, followed 6 months later by the administration of either a 4.7 mg or a 9.4 mg implant. The dog could then be reimplanted every year, for example, and hence "chemically castrated" for life, or simply surgically castrated a few months after implantation, if the desired effects on behaviour are achieved.

Indeed, several studies conducted in The Netherlands and France have shown that the effects of the Suprelorin® implants on behaviour are highly predictive of those achieved with surgical castration. In other words, Suprelorin® can be used as a test before possibly opting for surgical castration at a later date.

What approach for this service offer?

It is thus possible to propose a science-based approach to detect and manage in an optimal way undesirable behaviour linked to testosterone in entire male dogs.

If we consider the preventive medicine schedule until the age of two years, it can be easily understood that the appropriate period starts at puberty. In veterinary clinics that have made a puberty consultation for puppies systematic, that consultation gives a chance to make owners of entire male dogs aware of the existence of these behaviours and

how to control them, notably through education. Besides that, all the clinics offer two annual checkups that take place, according to the vaccination schedule recently proposed by the WSAVA, at 52 weeks of age at the latest for the first one, a year later for the second one. These two appointments offer the best opportunity to actively screen undesirable behaviours linked to testosterone in entire male dogs. In concrete terms, 4 questions concerning behaviour need to be included in the medical history: is there urine marking? mounting? roaming? aggressiveness towards other males? The value of active diagnosis arises from the low rate of unsollicited reporting of such behaviours by the owners to their veterinarians (one in four, see above).

As soon as one of these undesirable behaviours is reported (in two out of three cases, see above), the veterinarian explains what this is about, the possible link with testosterone, and the value of castration, that brings improvement in about 60% of the cases (see above). This rate is sufficiently high to deserve consideration, not high enough to justify immediate resorting to surgical castration, by definition irreversible. This is why it is worthwhile to propose a test prior to surgical castration, by using a Suprelorin 4,7 mg® implant, which will produce a real chemical, reversible castration, lasting at least 6 months, and whose effects will be highly predictive of those of a surgical castration.

Owners must be made aware of an important clarification in order to obtain their informed consent. In the few days after implantation, and before achieving hypophyseal inhibition and the neutering effect, desloreline temporarily activates the secretion of LH and FSH by the pituitary gland (flare-up effect). For several days, a transitory increase in plasma testosterone levels occurs, which may result in a slight increase in activity and/or urine marking from the dog. That is why it is recommended that the owner systematically call the clinic about two weeks after implantation, to check how the first phase went, and if need be reassure the owner.

When the owner, duly informed of the procedure and the budget, consents to implantation, the veterinarian can evaluate the effects during a consultation at about 6 months after implantation. It is then that the owner and their veterinarian can decide on the course of action. If the undesirable behaviour has not receded, or even gotten worse (which rarely happens), the recommendation will obviously be to discontinue the protocol, but in such a situation, the veterinarian can draw satisfaction from not having immediately advised surgical castration for the animal. If, on the other hand, the desired effects are obtained, the owner can decide to opt for a permanent solution, i.e. surgical castration, or for the administration of a new Suprelorin® 4.7 mg or 9.4 mg implant, the latter being effective for at least a year.

All things considered, this service offer can significantly improve the management of undesirable behaviours that owners of entire male dogs were rather resigned to, even though such behaviours could be very bothersome. This represents a significant improvement for the owners. For their part, veterinarians have at their disposal a solution that is both ethical and respectful of animal welfare, which allows transforming a result probable enough to merit consideration (60% success rate), yet too uncertain to risk recommending surgical castration as first line treatment , into a protocol that is both reassuring and loyalty-building for the owners. Moreover, this procedure is simple to implement and can be included as part of an existing schedule of visits, that is, the first two annual checkups, which makes these more substantial.

In Germany, this protocol has been routinely used by veterinary practitioners for nearly ten years. The sterilisation rate in male dogs reaches 30% there as opposed to 25% in France, while the use of Suprelorin® is nine times higher. Implantation does not replace surgical castration but is essentially used to test its effects. The owner can later choose between two options: keep implanting regularly, or opt for surgery.

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Respiratory Medicine

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How to approach to the coughing dog

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Coughing is a protective mechanism which allows clearance of debris from the airway. Airway irritation and inflammation, excessive secretions and airway collapse will all trigger coughing. Productive or moist coughs are usually seen in infectious or inflammatory airway conditions, however harsh or dry coughs can be seen in the earlier stages of disease.

As with any medical problem, evaluation starts by taking a detailed history, this is followed by a full clinical examination and careful thoracic auscultation of both the heart and the lung fields. In young dogs acute onset coughing is likely to represent infectious causes such as infectious tracheobronchitis (ITB, 'Kennel cough') or parasites such as *Angiostrongylus vasorum* or *Olserus osleri*. However airway foreign bodies, pneumonia (for example secondary to inhalation) and cardiac disease should also be considered possible causes, especially if signs are not self-limiting.

Canine infectious tracheobronchitis (ITB, 'Kennel cough') is highly contagious and common in any large transient population of dogs and is an acute. Dogs typical present with an acute onset paroxysmal coughing (which may be productive) and sometimes oculo-nasal discharge. Many different agents contribute to the clinical syndrome of ITB, and multiple infections are likely to be common. The most frequently isolated agents are *Bordetella bronchiseptica* and canine parainfluenza virus. Other agents including adenovirus, herpes virus and reoviruses are isolated on occasions. The use of antibiotics in ITB cases generally has limited efficacy and is rarely indicated unless there are signs of bronchopneumonia or systemic infection. Antimicrobial resistance is widely reported in Bordetella species, so when required doxycycline or trimethoprim/sulphonamide are usually used. In uncomplicated cases if the coughing is severe, anti-tussives (butorphanol or codeine), anti-inflammatories (NSAID or low dose prednisolone) and bronchodilators (theophylline, terbutaline) may be helpful.

Respiratory parasites such as *Olserus osleri* or *Crenosoma vulpis* are uncommon. However, In the last couple of decades disease due to infection with *Angiostrongylus vasorum* has been increasing documented across most of the UK and Europe, linked to the increased prevalence of infection in foxes and there increasing urbanization. Most dogs develop coughing due to larval migrating however a significant proportiondevelop signs secondary to coagulopathy. A rapid patient side blood test with good sensitivity and specificity has recently become available, greatly improving the ease of diagnosis. Imadaclopid / moxidectin, mibemycin and fenbendazole are all effective treatment options, with imadacloprid / moxidection and mibemycin also being an effective prophylactic treatment.

With acute onset coughing in the clinical well dog, faecal parasitology or trial treatment will allow exclusion of respiratory parasites and symptomatic therapy may be appropriate at this stage. Thoracic radiographs are usually the first imaging step in further evaluating the cause of a more chronic or severe cough. Further investigations such as echocardiography, endoscopy and collection of airway wash samples may then be indicated.

In older dogs acute onset coughing is most likely infectious such as secondary to infectious tracheobronchitis (ITB, 'Kennel cough') or parasites such as Angiostrongylus vasorum or Olserus osleri. However, chronic coughing, usually defined as a cough that has been present for more than 8 weeks, is more prevalent with age and chronic bronchitis, tracheal collapse, laryngeal paralysis, neoplasia, pulmonary fibrosis and congestive heart failure all need to be considered as possible causes. Diagnosis may not be straight forward as in older patients several aetiologies may be present, worsening the signs seen. For example there is usually much debate as to the cause of coughing in small breed dogs with congestive heart failure. The presence of pulmonary oedema alone does not usually lead to coughing however the presence of brochomalacia leading to bronchial collapse, will and this may be exacerbated by dilation of the left atrial leading to airway compression.

As with any medical problem, evaluation starts by taking a detailed history, this is followed by a full clinical examination and careful thoracic auscultation of both the heart and the lung fields. In acute onset coughing in the clinical well dog, faecal parasitology or trial treatment will allow exclusion of respiratory parasites and symptomatic therapy may be considered appropriate at this stage.

For more chronic cases blood work is usually a good starting point, to exclude concurrent illness, although is rarely specific for the aetiology of the cough. Measurement of NT-proBNP, which is produced my cardiac muscle in response to volume overload, is helpful to ascertain if animals may be coughing due to cardiac or respiratory disease, allowing further diagnostic tests to be better focused. Thoracic radiographs are usually the first imaging step, either conscious if there are concerns about cardiac function or where possible, inflated views under general anaesthesia, noting that if tracheal collapse is considered both inspiratory and expiratory phases will be required to make a diagnosis. Where cardiac disease is suspected echocardiography will be helpful to assess cardiac structure and contractility. The information gained by cardiac ultrasound will vary depending on the degree of experience of the operator, however

simple objective measurements such as left atrium to aortic root ratio (LA:Ao) and left ventricular fractional shortening will be helpful in determining if cardiac disease is present. When airway disease is suspected endoscopic evaluation and collection of airway wash samples is helpful in understanding the underlying aetiology and making treatment decisions.

Treatment will depend on the underlying aetiology and focus on addressing the cause of excessive coughing, such as limiting airway inflammation in chronic bronchitis or controlling congestive change in heart dogs with heart failure. Antitussives should be used judicious, but will help limit airway sensitivity and as a result improve quality of life.

How I perform bronchoscopy

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Bronchoscopy, or more correctly tracheobronchoscopy, allows evaluation of the larynx, trachea and bronchial tree. With good quality endoscopes becoming more readily available, it is becoming increasingly possible to perform bronchoscopy in small animal patients in general practice. The level to which can be examined depends on the diameter and length of the endoscope used, however evaluation to the level of the tertiary bronchi is possible in most cases.

As with all forms of endoscopy, although gross evaluation may reveal a definitive diagnosis (e.g. the presence of an airway foreign body), it is most commonly performed at the end of a diagnostic pathway. As always this should start with a full history and thorough clinical examination, and may include haematology, biochemistry, faecal parasitology and thoracic radiographs. If imaging is performed it is often combined under the same anaesthetic as bronchoscopy, with inflated views being taken prior to the endoscopic procedure. Bronchoscopy is useful in many patients (Table 1) but is most commonly used in the assessment of chronic coughing, respiratory distress and haemoptysis. Samples can also be collected and submitted for cytology and culture.

As part of the investigation of :
Coughing
Haemoptysis
Airway collapse (especially dynamic changes)
Pulmonary parenchymal disease
Evaluation of unexplained radiographic lesions
Halitosis
Removal of airway foreign bodies
Placement and evaluation of tracheal stents

Table 1: Indications for Bronchoscopy.

Equipment

Flexible fibreoptic or video bronchoscopes are preferred for bronchoscopy as they allow a thorough evaluation of the respiratory tract (Figure 1). Paediatric bronchoscopes with a diameter of 3-4mm are used cats and small dogs, however there working length is usually short (50-60cm) which can be prohibitive in larger patients. In this case adult bronchoscopes (diameter 5-6mm) or fine paediatric gastroscopes may be used as they have a longer working length (100-120cm). Bronchoscopes usually only have 2 way deflection (up and down), however rotation can be achieved by twisting the hand piece and therefore the insertion tube gently along its long axis (Figure 2).

Rigid fibreoptic endoscopes can also be used and are useful for evaluation of the larynx and trachea, however evaluation of the lower airways is difficult. Cytological samples cannot be directed with a rigid endoscope. Hollow rigid endoscopes can be useful to allow removal of tracheal foreign bodies.

Figure 1: A 3.8mm human paediatric bronchoscope, suitable for bronchoscopy in small to medium dogs.

Figure 2: The bronchoscope hand piece, with suction, 2 way deflection and open wash channel.

Patient Preparation

Bronchoscopy is always performed under general anaesthesia to control reflex coughing and gagging on passage of the endoscope. Premedication with an opioid and low dose acepromazine is used in most cases. Terbutaline, a bronchodilator, is useful to reduce bronchospasm and improve oxygenation. This is especially useful in cats and is usually given intra muscularly at the time of induction. General anaesthesia is most easily maintained by total intravenous anaesthesia (TIVA), with propofol being the agent of choice in most cases. This allows endoscopy with out the risk of leakage of anaesthetic gases.

In large dogs the endotracheal tube may have a large enough diameter to allow passage of the endoscope, without complete occlusion of the tube (at least 25% of the diameter of the tube should remain with the endoscope in place). If this is the case a T-adapter may be used to allow oxygen delivery (anaesthesia is usually still maintained via TIVA as there is still a risk to personnel of anaesthetic gases escaping (Figure 3).

Figure 3: A T-adapter, which will allow passage of the endoscope (though the yellow port) into the endotracheal tube

Unfortunately most cats and small dogs have airways too narrow to allow passage of the endoscope through the endotracheal tube. In these cases the endoscope is advanced directly into the airway to allow evaluation. To allow this the patient is anesthetised and an endotracheal tube placed initially to allow stabilisation of the patient and, if needed, inflated thoracic radiographs to be taken. Once ready, the endotracheal tube is removed and the endoscope is passed to allow evaluation. Local anaesthetic can help reduce laryngospasm during passage of the endoscope. Once the bronchoscopy is finished the endotracheal tube is replaced to allow the patient to recover.

Endoscopy without an endotracheal tube does not allow assisted ventilation so careful consideration should be given to oxygen supplementation. This can be provided via the endoscope wash channel, via a urinary catheter placed in the airway alongside the endoscope or via flow by oxygen. Oxygen flow rates of 1-3 litre / minute can be used safely in most cases. Care should be taken not to over inflate the small airways and the patient should be carefully monitored to ensure adequate oxygenation; a pulse oximeter is very useful in this respect. If the patients oxygenation becomes a concern the procedure should be paused and the endoscope removed to allow better ventilation of the patient.

Tracheobronchoscopy is best performed in sternal recumbency, with the head elevated on a sand bag or foam pad to allow easy passage of the endoscope. A gag should be placed to protect the endoscope.

Tracheobronchoscopy

A laryngoscope is helpful to guide the passage of the endoscope through the larynx into the cervical trachea, which should be near circular in normal patients. The Tracheal cartilages are seen as C shaped rings under the mucosal surface and are connected by the dorsal membrane (Figure 4). This thin strip of muscle helps orient the picture and should not deviate into the airway.

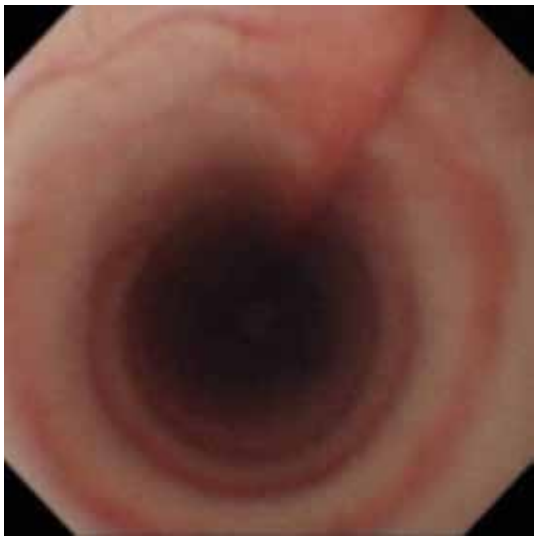

Figure 4: Normal Canine Trachea.

The tracheal mucosa should appear smooth, with a light pink appearance. Sub mucosal vessels are normally visible, but become more prominent in inflammatory disease (Figure 5). Inflammatory disease can also lead to airway having a hyperaemic, oedematous appearance. Bleeding is possible on the passage of the endoscope and polypoid lesions are occasionally seen in chronic inflammatory conditions. *Oslerus osleri* infection leads to parasitic nodule formation in the distal trachea and larger bronchi. A small amount of airway secretion is normal in cats and dogs. Excessive mucus secretion is usually associated with chronic inflammatory processes such as chronic bronchitis and eosinophilic bronchopneumopathy. Airway haemorrhage can also been seen in association with trauma, foreign bodies and *Angiostrongylus vasorum* infection (Figure 6).

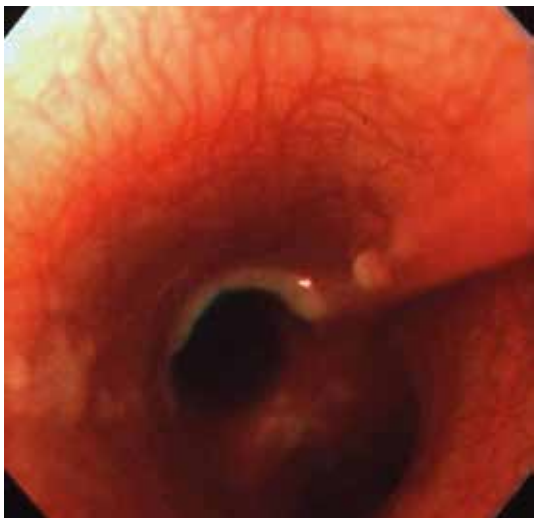

Figure 5: Hyperaemic trachea with prominent submucosal vessels and mucus accumulation in a dog with infectious tracheobronchitis.

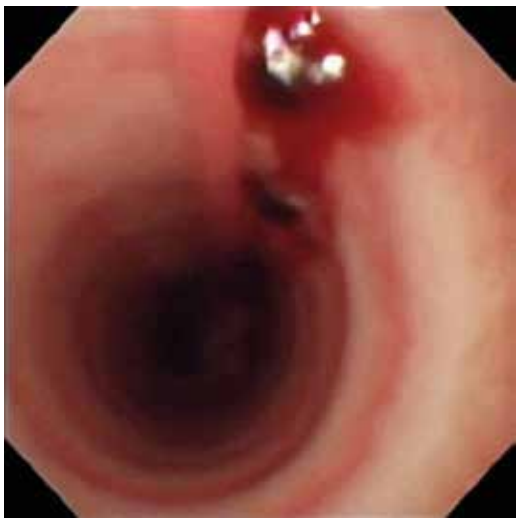

Figure 6: Airway haemorrhage in a dog with *Angiostrongylus vasorum* infection.

In small breeds of dog tracheal collapse is relatively common and changed in airway diameter should be assessed during each phase of respiration as collapse is often a dynamic process (Figure 7 & 8). If medial management fails to control signs of tracheal collapse endotracheal stent placement can be considered. Tracheoscopy is used to help stent deployment and to assess placement (Figure 9).

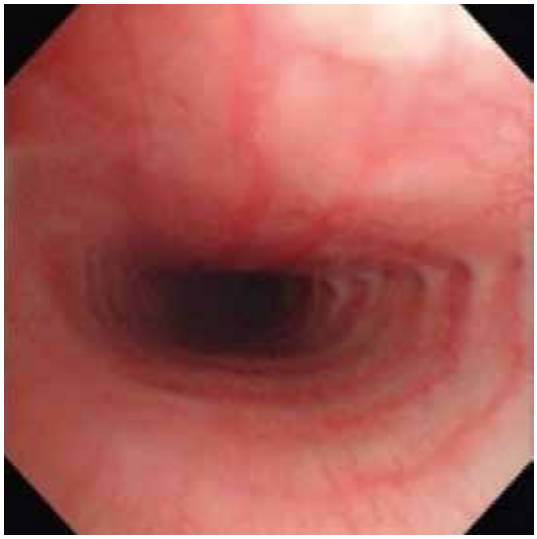

Figure 7: Mild (Grade II/IV) tracheal collapse in a Yorkshire terrier.

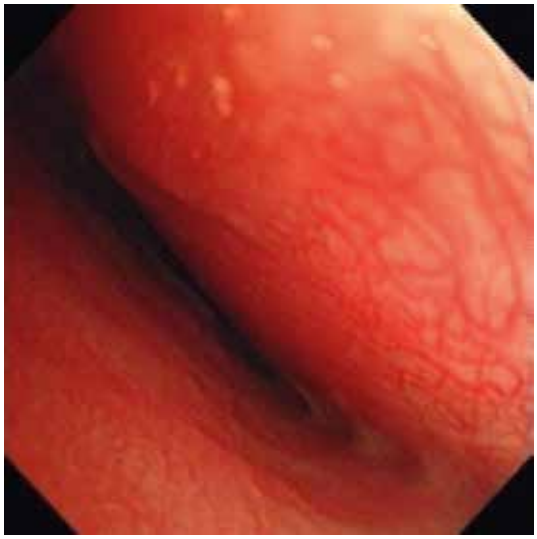

Figure 8: Severe (Grade IV/IV) tracheal collapse.

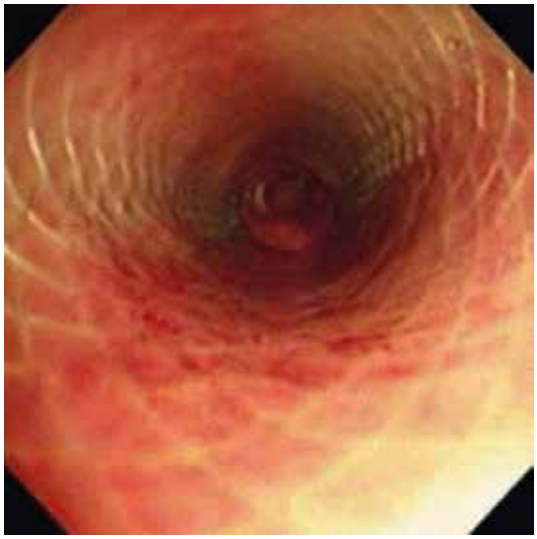

Figure 9: A tracheal stent in place.

Once the cervical tracheal has been examined the endoscope is gradually advanced, through the intra thoracic trachea to the tracheal bifurcation or carina. The endoscope should be centred in the middle of the airway to avoid trauma to the mucosal surface. The tracheal bifurcation is seen as a sharp division between the left and right mainstem bronchi (Figure 10). The right mainstem bronchus is usually straight ahead of the endoscope, with the left mainstem bronchi requiring some deflection to the right to allow entry. For this reason airway foreign bodies are more commonly seen in the right mainstem bronchi (Figure 11). Segmental collapse can occur in the mainstem bronchi (alone or in association with tracheal collapse) and the left atrial enlargement can cause left mainstem bronchial compression (Figure 12).

The bronchial tree should be systematically and fully evaluated, allowing visualization of each lobar bronchus and as many segmental divisions as possible. Each lung has a cranial and caudal lobe, with the right side having both a middle and accessory lobe (Figure 13 and 14). Each segmental airway should be evaluated and changes in shape, size and mucosal appearance. The normal lower airways should have crisp divisions between the airways and have a pale pink mucosal appearance (Figure 15).

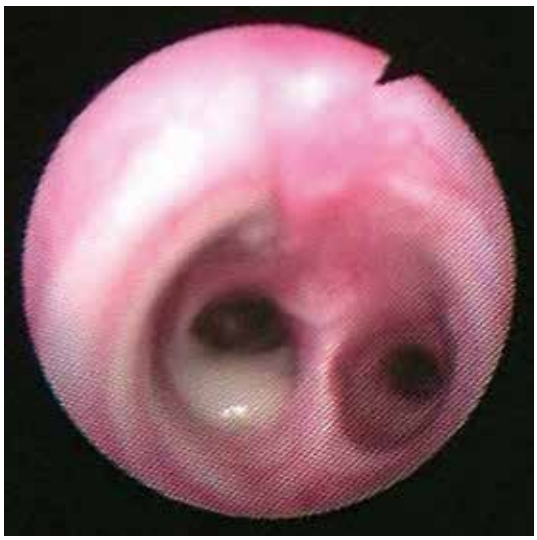

Figure 10: View of the carina in a dog with chronic bronchitis. There is a large plug of mucus in the right main stem bronchus.

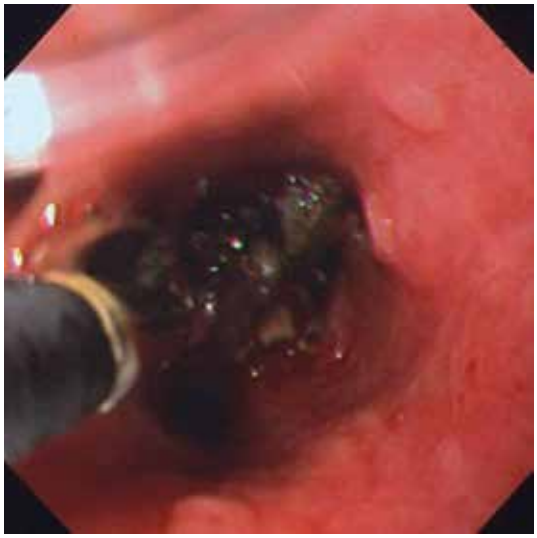

Figure 11: A bronchial foreign body (head of corn) lodged in a right caudal bronchi. (Photograph courtesy of Jon Wray)

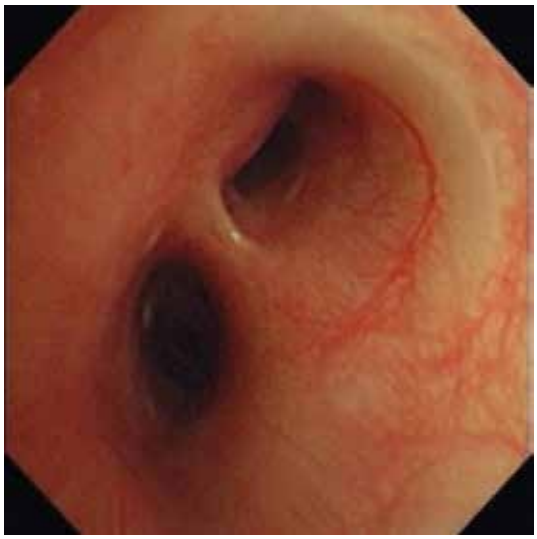

Figure 12: Left main stem bronchus compression as result of left atrial enlargement.

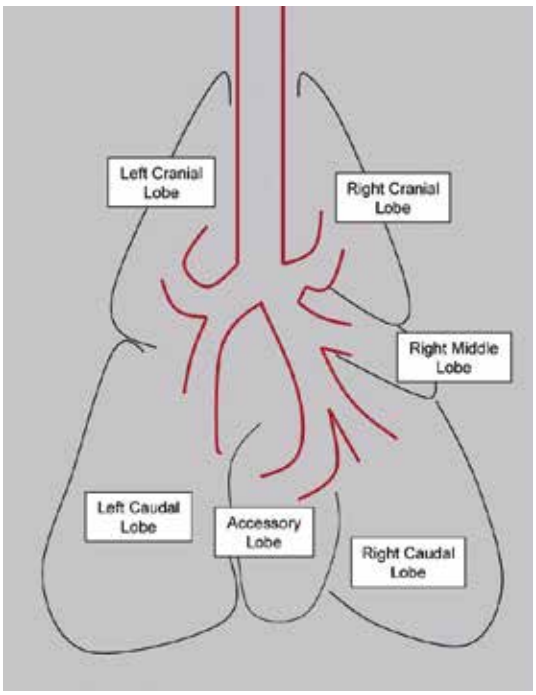

Figure 13: Schematic representation of the canine bronchial tree.

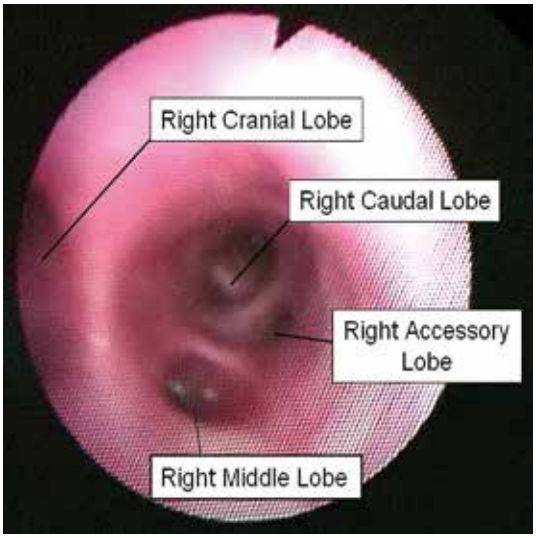

Figure 14: Normal anatomy of the right mainstem bronchus.

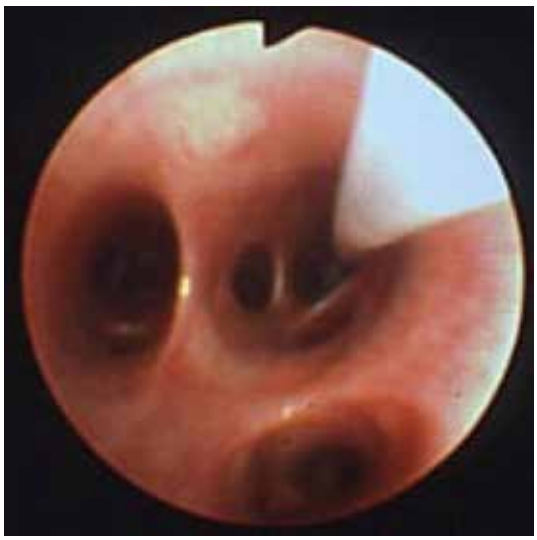

Figure 15: Normal canine distal segmental airways, a BAL catheter is in place.

Once the airways have been fully examined samples should be obtained for cytology and microbiology, as gross changes are not usually pathognomonic for specific disease. Sampling is best achieved via bronchoalveolar lavage (BAL) allowing material to be collected from the lower airways, which avoids potential contamination from the upper respiratory tract. Samples are obtained by wedging the endoscope into a terminal bronchus and instilling saline. This best done via a wash tube inserted through the working channel of the endoscope (Figure 16), but can be done using a wash trap directly through the wash channel (Figure 17).

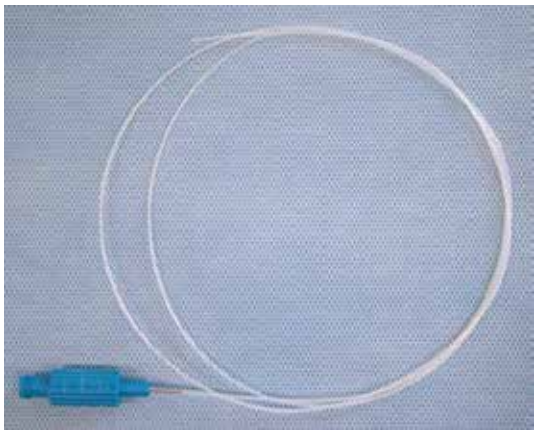

Figure 16: A wash tube used for collecting BAL samples.

Figure 17: BAL collected through the endoscope working channel using a wash trap.

Aliquots of sterile saline (0.9% sodium chloride) are instilled to allow collection of representative samples. Typically 1ml/kg saline is used, with aliquots of 3-5ml used in dogs and 5-10ml in larger dogs. Saline is absorbed readily from the lower airways so although care should be taken, patients cope very well with the volume of fluid instilled. Typically only 25-75% of wash fluid is retrieved and should be stored into EDTA tubes for cytology and plain tubes for culture. If the wash channel was used for sample collection, culture results should be interpreted with caution and culture of saline flushed through the wash channel prior to BAL collection may help exclude contamination. Culture results must always be interpreted in the light of cytology results obtained.

Once positioned in a terminal bronchus saline is instilled and an assistant applies coupage to the dog's chest. The fluid is left for a few second and then suctioned via the wash tube or endoscope channel, moving the endoscope gently backwards and forwards by a few millimetres during suction may air sample collection (Figure 18). Flushing is repeated until good samples are obtained, these should have a frothy appearance as a result of surfactant being present (Figure 19). BAL samples should be obtained from at least 2 sites (usually the left and right sides) as well as any focally abnormal areas. Brush cytology and aspirates taken via endoscopic injection needles can be helpful in the investigation of focal abnormalities and airway masses. Biopsies can also be taken with forceps inserted through the working channel. These are helpful in both the investigation of masses and the collection of samples for electron microscopy to evaluate ciliary function.

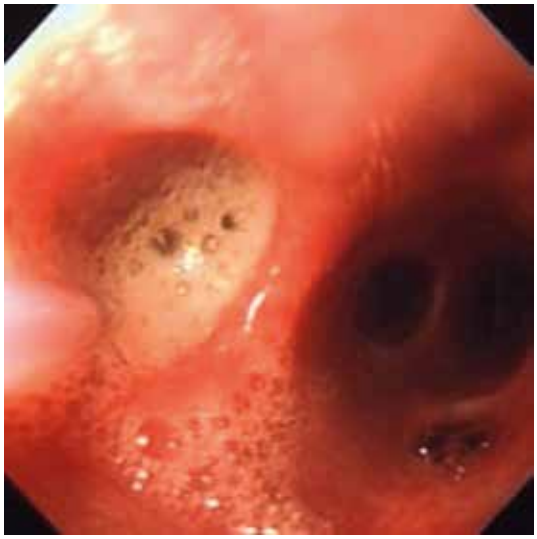

Figure 18: Frothy liquid appearing from a terminal bronchus during BAL collection using a wash tube.

Figure 19: Frothy BAL fluid, confirming fluid has been obtained from the alveoli as it contains surfactant.

Postoperative management

Post bronchoscopy the patient is usually intubated and maintained on 100% oxygen until stable, and then recovered from anaesthesia. Patients need to be monitored closely on recovery and supplemental oxygen provided as needed. Patients are generally hospitalized for 12-24 hours after the procedure and monitored closely for complications.

Bronchoscopy is generally a safe procedure however a number of complications are possible (Table 2). Perhaps the most common complication is bronchospasm seen post bronchoscopy or BAL in cats, which can lead to severe respiratory distress immediately after the procedure or on recovery. Pre-treatment with terbutaline may reduce its incidence. Oxygen supplementation and intravenous or inhaled steroid may be needed to control airway constriction post procedure.

Excessive reflex stimulation • Coughing, Laryngospasm, Bronchospasm
Barotrauma • Air trapping during oxygen therapy in small patients, Pneumothorax
Haemorrhage • Due to mucosal friability, post biopsy
Anaesthetic complications • Hypotension, hypothermia, arrhythmias
Hypoxia
Infection

Table 2: Possible complications of bronchoscopy.

Diagnosis and management of pyothorax

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Pyothorax is the accumulation of exudate within the pleural space caused by the presence of an infectious agent and has been documented after thoracic trauma, migrating foreign bodies, extension of pulmonary abscesses and haematogenous spread from a distant focus, however it is unusual to document the underlying cause. When no obvious underlying aetiology can be found, the migration of inhaled grass awns is often suspected.

Animals with pyothorax will present with signs associated with the presence of fluid in the pleural space, most commonly this is bilateral, but may be unilateral or asymmetric in distribution. The presence of the fluid leads to a restrictive or choppy breathing pattern, and leads to an absence of breath sounds ventral on auscultation and dullness on thoracic percussion. The presence of a large volume infection within the pleural space may also be associated with signs of sepsis and associated hypotension and pyrexia. Diagnosis is usually made of the basis of documenting the presence of fluid with in the pleural space either on ultrasound or radiograph and then collecting a sample via thoracocentesis.

The ideal position for therapeutic thoracocentesis in which to place the animal can vary. Conscious, dyspnoeic patients often prefer sitting, sternal recumbency or standing during the procedure. Lateral recumbency can be used providing it does not cause distress or further respiratory embarrassment. Mid-way up the thoracic wall at the seventh or eighth intercostal space (caudal to the sixth rib to avoid the heart) is usually suitable for drainage of pneumothorax. The site is clipped and aseptically prepared. Sterile gloves should be worn. A butterfly needle or over-the-needle cannula is inserted perpendicular to the chest wall, along the cranial aspect of the rib at the chosen intercostal space to avoid iatrogenic damage to the neurovascular bundle. Pleural membrane puncture can be painful but is usually well tolerated by dyspnoeic patients treated with relatively small diameter needles or cannulae. Local anaesthesia may help to easy this and small volumes of lidocaine usually work well (this can be buffered 1 part 8.4% sodium bicarbonate to 9 parts lidocaine to neutralise its acidity and reduce the 'stinging' effect of injection'). Effective thoracocentesis in an animal experiencing significant hypoventilation will usually result in almost immediate improvement in respiratory character and oxygen saturation. When draining fluid a 2-way centesis valve may be helpful to avoid the frustrations of having to move a three-way-tap.

The mediastinum is often incomplete in small animals with the result that it is sometimes possible to drain both sides of the chest via unilateral thoracocentesis. Thoracic auscultation,or a very brief ultrasound scan, following unilateral thoracocentesis is useful to evaluate whether bilateral thoracocentesis is necessary. It is not uncommon for a small volume of fluid or air to remain following successful thoracocentesis. Post-drainage radiographs are important both to assess efficacy of drainage and to act as a reference point against which future images can be compared to determine the rate or presence of ongoing leakage; they may also elicit any underlying pathology.

If fluid is obtained samples should be submitted for cytology (EDTA and smear), biochemistry (plain tube) and culture (plain tube) to determine the cause of its presence (see Table). Analysis of this fluid in the face of pyothorax will confirm the presence of an exudate with a high number of degenerate neutrophils and bacteria.

The treatment options for the management of pyothorax include a wide range of medical and surgical techniques and there is much debate as to which treatment option is best. In general, the placement of a chest drain to remove the accumulated exudate is needed, followed by lavage and long-term antibiotics. Where underlying thoracic pathology is present (e.g. a pulmonary abscess), early explorative surgery is indicated to remove the underlying focus of infection.

To place a drain the lateral thorax should be clipped and aseptically prepared for surgery. A small skin incision is made at the junction of the middle and dorsal two thirds of the thorax over the 9th, 10th or 11th intercostal space, and the chest drain introduced through this stab incision. The chest drain should be 'primed' by holding the wings of the connector against the middle and forefinger of the dominant hand and pushing the head of the trochar with the ball of the thumb: this stretches the drain slightly and minimises the chance of the drain being damaged during placement. The chest drain is tunnelled under the cutaneous trunci and latissimus dorsi in a cranioventral direction towards the seventh intercostal space. The subcutaneous tunnel helps to prevent air tracking into the pleural space. The chest drain is elevated perpendicular to the seventh or eighth intercostal space and introduced through the intercostal muscles into the pleural space. The non-dominant hand is positioned around the tube 2-3 cm from the skin and will act as a 'stop' preventing inadvertent damage to intrathoracic organs when the tube is pushed through the intercostal muscles. Once the intercostal muscles have been penetrated, tilt the tube caudally again and withdraw the sharp tip of the trochar into the tube. Advance the tube in a cranioventral direction for a few centimetres. The tube is then pushed off the trochar to a pre-determined point generally the second or third sternebra. Placing the tip of the thoracic drain further cranially can lead to the folds of the mediastinal tissues occluding the drainage holes in the drain.

	Transudate	Modified Transudate	Exudate	Chyle
Gross appearance	Clear	slightly cloudy	often cloudy-turbid, maybe serosangiunous	cloudy white/cream, maybe sanguinous
Specific gravity	<1.017	1.017-1.025	>1.025	>1.025
Protein content (g/l)	<25	25-50	>30	>25
Nucleated cells (mm^3)	<2500	<7000	>7000	1500-10,000
Cytology	few cells	Mainly macrophages & meosthelial cells	Reactive mesothelial cells septic:degenerate neutrophils, macrophages and intracellular bacteria non-septic: lymphocytes; macrophages carcinomatosis: malignant cells	predominately lymphocytes
Other features				Trig content>plasma Chol content <plasma

The tube is cross-clamped before the trochar is removed fully to prevent pneumothorax. After removing the trochar fully, the tube is connected to an appropriate adapter system. A purse-string suture may be placed around the drain exit site. The drain is secured to the thoracic wall using a diagonal overlapping suture pattern or Chinese finger lock suture. The position of the tube within the chest should be confirmed radiographically and two orthogonal views are required. The tube is bandaged against the chest using a flexible net dressing such as Surgifix before the animal recovers. All animals with a chest drain in place MUST wear a Buster collar.

The position of the tube within the chest should be confirmed radiographically and two orthogonal views are required. The tube is bandaged against the chest before the animal recovers.

Once the chest drain is in place, it allows continued drainage of exudate and lavage of the pleural space by the instillation of sterile saline. The benefits of thoracic lavage are controversial, logically, there would seem to be some benefits of lavage to aid the remove purulent material from the pleural space however a published study suggested that the one-off drainage using a chest drain, of pyothorax via a chest tube, followed by its removal and long term antibiotics, resulted in a good clinical outcome in all cases treated.

When the drain is no longer needed it is removed by placing firm pressure over the subcutaneous tunnel and pulling the drain out briskly. Pressure is maintained for 2-3 minutes and the skin incision left to heal by secondary intension. It should be remembered that the presence of a chest drain will lead to a small amount of irritation within the thorax and a small volume of pleural fluid (0.5-1ml/kg/day) will be produced as a result.

Systemic antibiotics should be continued for 6-8 weeks or two weeks after the resolution of clinical and radiographic signs. Many types of bacteria have been implicated in pyothorax and a mixed culture is most commonly found, with *E. coli*, Actinomyces and Nocardia being amongst the most commonly cultured organisms.

Cultures are a useful guide to antibiotic choice, however as anaerobic bacteria are hard to culture and negative cultures are possible due to prior antibiotic use. Broad-spectrum antibiotic combinations to cover both anaerobic and aerobic bacteria are indicated, such as co-amoxiclav and metronidazole or a fluoroquinolone with either metronidazole or clindamycin.

With appropriate treatment the long-term prognosis of uncomplicated pyothorax is good. Survival past 48 hours is a significant prognostic indicator, with most patients making a recovery from this point.

Tracheal collapse; medicine or surgery?

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Canine tracheal collapse is a progressive disease seen in mainly middle aged, small and toy breed dogs. Degeneration of the tracheal cartilage rings as a result of reduced glycosaminoglycan and cellularity, leads to dorsoventral flattening of the trachea and laxity of the dorsal tracheal membrane. Changes can be focal or generalised and are often associated with collapse of the main stem bronchi and lower bronchioles (bronchomalacia). Clinical signs depend on the severity of the collapse, from mild airway irritation and a classic paroxysmal 'goose-honking' coughing, through to respiration distress and dyspnoea as a result of dynamic airway collapse. Many dogs improve with medical management (weight control, use of harnesses, cough suppressants, anti-inflammatory steroids and bronchodilators), however in severe cases, where airway collapse and respiratory distress is documented, structural support of the trachea may need to be considered, in the form of surgery to place extraluminal protheses or placement of an intraluminal stent.

Pathophysiology of tracheal collapse

The aetiology of tracheal collapse is complex and as yet, poorly understood. It is likely multifactorial, with the development of clinical disease resulting from weakening of the tracheal rings but also secondary factors that lead to the initiation of clinical signs. Dogs with tracheal collapse have reduced glycosaminoglycan, glycoprotein and chondroitin sulphate content of the hyaline cartilage that forms the tracheal rings. These structural changes within the cartilage matrix alongside its reduced water content lead to reduced functional rigidity. This structural change to the cartilage gives an anatomic tendency to the development of tracheal collapse and around a quarter of dogs will become symptomatic by six months of age supporting a congenital origin. Many dogs remain asymptomatic until later in life with degenerative change of the tracheal cartilage and secondary factors triggering the clinical syndrome of tracheal collapse. Secondary factors linked with the development of clinical signs include airway irritants, chronic bronchitis, laryngeal paralysis, respiratory tract infection, obesity and tracheal intubation, as well as postulated alterations of the elastic fibres in the dorsal tracheal membrane and annular ligament.

Once symptomatic, dynamic collapse of the airway perpetuates a cycle of chronic inflammatory change within the tracheal mucosa, which is worsened by the coughing this causes. Ongoing tracheal mucosal inflammation has been associated epithelial squamous metaplasia leading to loss of normal ciliary clearance. This mucosal change and hyperplasia of the subepithelial glands, which secrete increasingly viscid mucus, leads to coughing becoming the major tracheobronchial clearing mechanism.

Tracheal collapse is commonly seen in small breed dogs with Yorkshire terriers representing between a third and two thirds of reported cases. Other breeds commonly affected include the Miniature poodle, Pugs, Maltese, Chihuahua and Pomeranian. No sex predisposition has been reported. Clinical signs can develop at any age. Most dogspresent in middle age, although many will have had signs for significant periods previously. Cats and large breed dogs are rarely affected by tracheal collapse. Concurrent bronchomalacia is reported in 45-83% of dogs with tracheal collapse and most commonly affects the right middle and left cranial bronchi. Bronchomalacia can occur without tracheal collapse in large breed dogs, suggesting the pathophysiology of collapse may not be the same in the trachea and the bronchus. Comparing a population of coughing dogs those with dynamic airway collapse were significantly older, of lower body weight and in higher body condition compared to those without airway collapse.

Presentation and diagnosis

Most dogs with tracheal collapse are presented for evaluation of a paroxysmal dry harsh cough, which is usually described as 'goose-honking' in nature. The cough is often triggered by excitement, exercise or eating and may be associated with upper airway stridor. Usually the history is chronic with signs developing over weeks to months. Some dogs will present acutely with respiratory distress due to airway obstruction, which is often precipitated by heat, excitement, stress or concurrent respiratory disease, such as pneumonia.

Clinical examination of dogs often reveals them to be in excessive body condition but may otherwise be normal depending on the severity of the collapse. The respiratory pattern present will also depend on the location of the collapse. Extrathoracic trachea collapse is usually associated with increased inspiratory effort, whereas collapse of the intrathoracic trachea and bronchomalacia is associated with increased expiratory effort. The trachea should be palpated careful as it is often sensitive and examination may elicit paroxysmal bouts of coughing. Occasionally it is possible to palpate abnormalities in tracheal structure, with flattened cartilage rings. Auscultation of the laryngeal area may elicit stridorous inspiratory upper airway noise due to the narrowing of the extrathoracic trachea but concurrent laryngeal

paralysis should be considered and has been documented in up to 60% of cases. Careful thoracic auscultation should be performed to document any evidence of concurrent respiratory pathology and for the presence of a cardiac murmur. A study of coughing dogs documented 17% of dogs with airway collapse also had a murmur associated with mitral valve disease compared to 2% of dogs without airway collapse, suggesting concurrent mitral valve disease is common in breeds affected by airway collapse. The role of left atrial enlargement in the aetiology of coughing in dogswith airway collapse has been associated with much controversy. A recent study documented similar severity and location of airway collapse in dogs with and without left atrial enlargement suggesting other factors such as airway inflammation, rather than external compression by the left atrial, as the cause of the cough. Mild hepatomegaly is commonly associated with tracheal collapse and elevations in bile acids have been reported, suggesting hypoxic liver changes.

History and clinical examination findings may be very strongly suggestive of tracheal collapse, however the diagnosis needs to be confirmed by documented evidence of the collapse, as well as its location and severity. As tracheal collapse is a dynamic process care must be taken to interpret radiographs in light of the respiratory phase. Inspiratory films can often appear normal, even in dogs with severe collapse, and contrary to normal radiographic technique expiratory films should also be taken (Figure 1). Even so, radiographs frequently underestimate the severity of tracheal collapse and may fail to document collapse at the carina. As a result, films taken under negative pressure ventilation may be useful. Radiographs are essential to evaluate the lung fields for concurrent respiratory disease. Radiographs have been shown to underestimate tracheal diameter compared to computed tomography, which may be significant when selecting tracheal stent sizes.

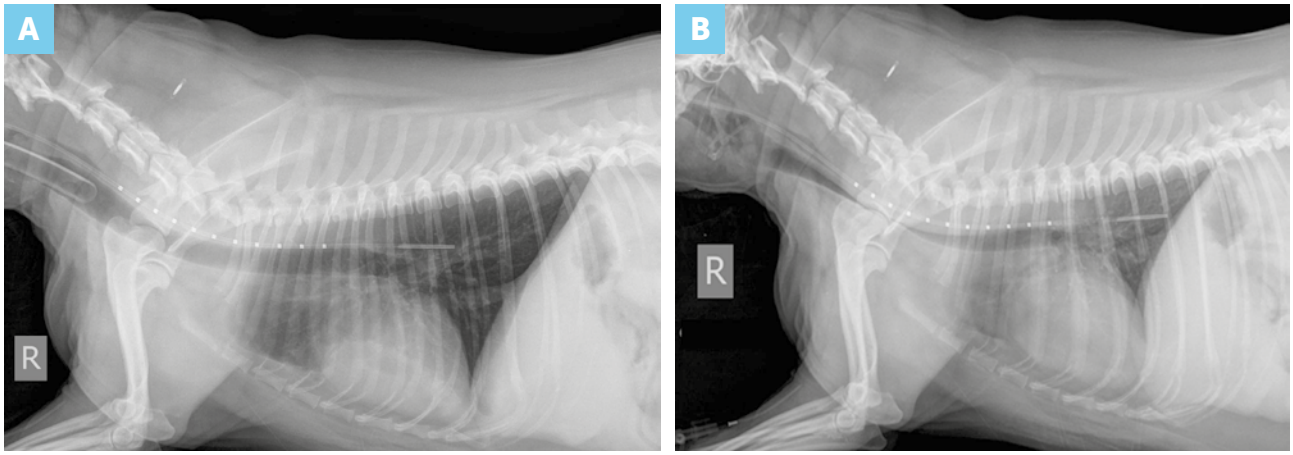

Figure 1: Right lateral radiograph of a Yorkshire terrier at peak inflation to positive 20cm of water (A); this reveals no evidence of tracheal collapse. (B) At peak expiration; this reveals marked tracheal collapse across the thoracic inlet. Note: a marker catheter is positioned within the oesophagus.

Where available, fluoroscopy offers much better evaluation of airway collapse allowing dynamic real time evaluation of the trachea during all phases of respiration, as well as during episodes of coughing (Figure 2). Fluoroscopy has been shown to be more accurate in documenting the location of tracheal collapse compared to radiographs and one study documented tracheal collapse in 8% of dogs in which it could not be documented on radiographs (Figure 3). Ultrasound has been used successfully to document real time dynamic tracheal collapse through changes to the tracheal air shadow during the respiratory cycle.

Bronchoscopy allows direct dynamic visualisation of the tracheal and lower airway structures to document the degree and location of collapse. The degree of collapse present is graded from I to IV and allows more detailed evaluation of bronchial changes compared to fluoroscopy. Bronchoscopy requires general anaesthesia, meaning that tracheal diameter cannot be assessed during normal respiration, however the application of negative pressure will allow the location and degree of collapse to be documented; induction gives an opportunity to evaluate laryngeal function. Common findings include evidence of airway inflammation such as hyperaemia and mucus accumulation. Bronchoalveolar lavage should be performed to evaluate possible concurrent lower airway disease. Mild neutrophilic and lymphocytic infiltrates are commonly documented in dogs with tracheal collapse, however it is unclear if the inflammation precedes or follows on from airway collapse.

Treatment

Priorities at presentation depend on the degree of tracheal collapse and the severity of the dogs clinical signs. If the animal is in severe respiratory distress, then stabilisation is essential before diagnostic evaluation and a firm diagnosis is reached. Oxygen supplementation with inspired concentrations >40%, minimising stress and a cool environment should help the patient to settle. When needed sedation with acepromazine (0.01-0.03mg/kg i/v or i/m) or butorphanol (0.05-0.1mg/kg i/v or i/m) either alone or in combination can be very effective. In severe cases the patient may require intubation, in which case diagnostics should be performed at this point and procedures such as surgery or stent placement may be more appropriate than medical management.

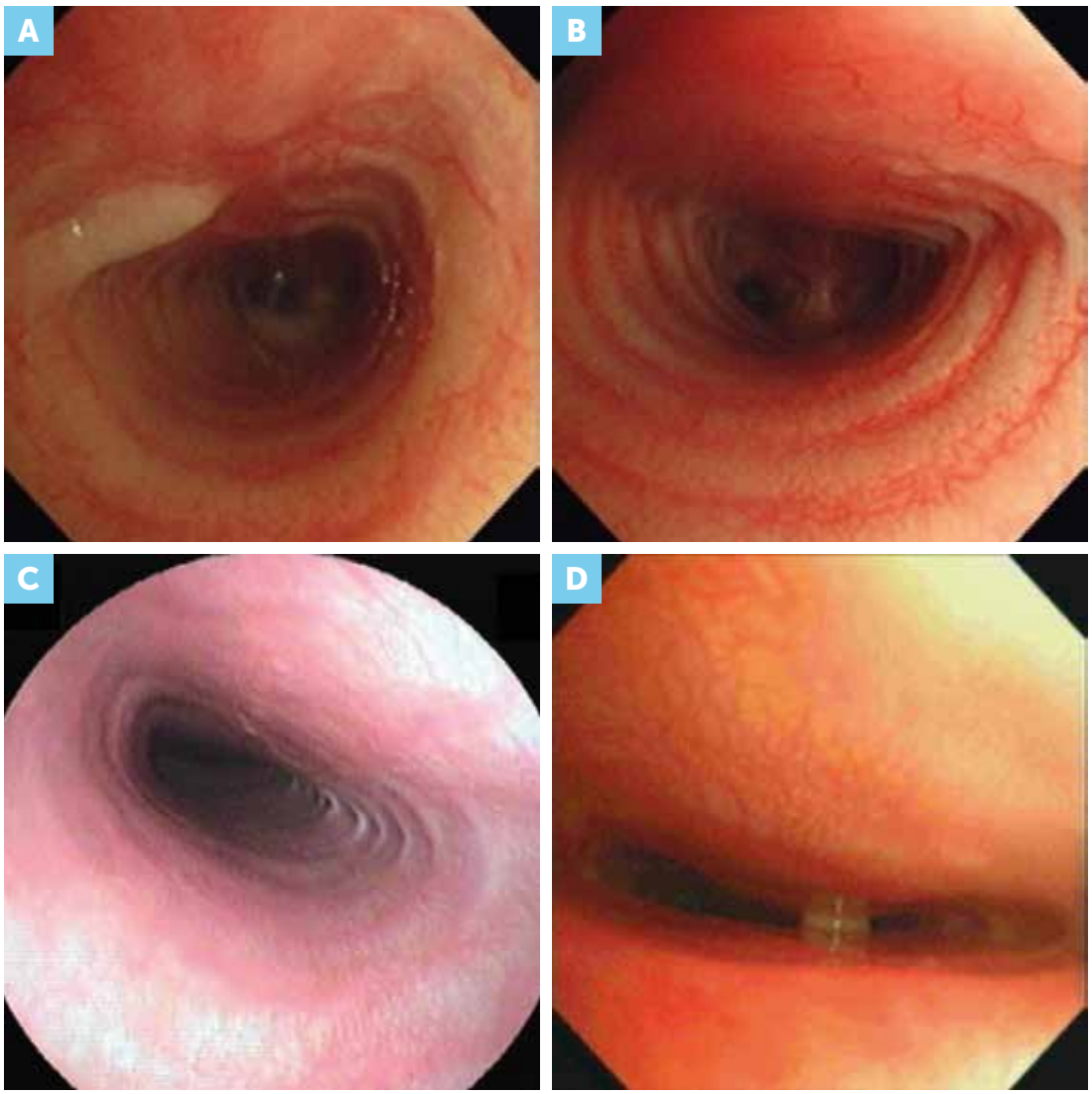

Figure 2: Bronchoscopic images of tracheal collapse. (A) Grade I collapse (resulting in loss of 25% of the tracheal lumen) (B) Grade II collapse (resulting in loss of 50% of the tracheal lumen), (C) Grade III collapse (resulting in loss of 75% of the tracheal lumen) and (D) Grade IV collapse with complete loss of the tracheal lumen.

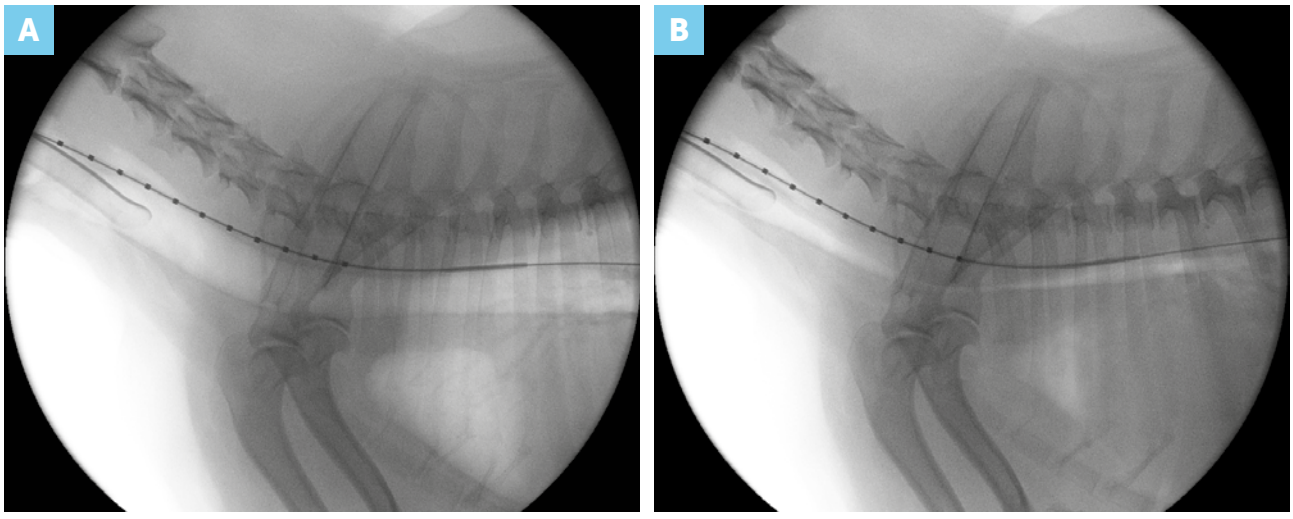

Figure 3: Fluroscopic images taken in right lateral recumbancy at peak inflation to positive 20cm of water (A). This film should be used to identify the measurement landmarks of the tracheal bifurcation and this carina, to measure tracheal length, as well as assess tracheal width. (B) Images taken under negative pressure (to negative 20cm of water) allow documentation of the area of collapse, here the whole length of the trachea is affected. Note: a marker catheter is positioned within the oesophagus.

Medical management

Many dogs will respond well to medical therapy, with surgical interventions reserved for dogs refractory to treatment or with severe clinical signs, such as cyanosis, exercise intolerance or dyspnoea. The aim of medical management is to break the cycle of inflammation triggering coughing, and that coughing worsening inflammation. Studies have documented that between 71% and 93% of dogs responded well to medical management for a period of more than 12 months, with over half of dogs being able to have their medication gradually withdrawn.

A good proportion of dogs with tracheal collapse are overweight and the accumulation of intra-thoracic adipose tissue may reduce respiratory function by limiting thoracic movement and reducing chest wall compliance. Strict weight loss regimes, with dietary management and controlled exercise programs, will lead to improved clinical signs in many of dogs. Avoidance and removal of environmental inhaled irritants (namely tobacco smoke) will help in many dogs, although compliance may be difficult to achieve. A harness rather than a collar should be used to reduce tracheal compression and associated irritation. Diligent management of comorbidities such as congestive heart failure and respiratory tract infection will also improve clinical signs. Additionally, any upper airway narrowing, for example secondary to brachycephalic upper airway syndrome or laryngeal paralysis, will increase intra-thoracic pressure and worsen tracheal collapse; careful consideration to surgical management of the upper airway should be given in these dogs.

Antitussive therapy

In the United Kingdom the use of co-phenotrope (Lomotil which contains diphenoxylate hydrochloride and atropine) has been the main stay of medical management for dogs with tracheal collapse. Diphenoxylate acts as a narcotic anti-tussive with the atropine purportedly acting to reduce the volume of mucus secreted into the lower respiratory tract and acts as a muscarinic bronchodilator. The atropine is present in the formulation as a bittering agent to prevent abuse of the narcotic agent diphenoxylate; as to whether the level of atropine present is at a dose to have clinical effects is unknown. Although no clinical studies are available to support its use, anecdotally there has been widespread acceptance of its benefit in affected dogs. Doses of 0.2-0.5mg/kg q12 hours have been suggested with constipation an occasional side effect seen (these effects are usually managed easily with dietary manipulation or the addition of faecal softeners). Due to supply and manufacturing issues co-phenotrope is currently inconsistently available to the veterinary market.

In the United States hydrocodone is used commonly (0.22mg/kg q6-12 hours), with codeine (0.5mg-2mg/kg q12 hours) and butorphanol (0.5-1mg/kg q6-12 hours) being more commonly used as anti-tussives in Europe. Anecdotally some agents may be more effective in individual dogs and drugs may need to be changed over time to find the most beneficial agents. Dosing can also be an issue as there are no licensed veterinary products in the United Kingdom and the human tablets are often very large for the small breed dogs affected. Re-compounding pharmacies may be able to help with drug formation into liquids or smaller tablets for smaller sized dogs.

Steroid therapy

The use of carefully judged steroid therapy is likely to be beneficial to many dogs with tracheal collapse through reduction of airway inflammation. They should be used strategically, for short courses and at the lowest doses possible to control clinical signs, as adverse effects may worsen clinical signs in the longer term. In particular their use may increase the risk of bacterial infection, increase respiratory rate and may make weight loss very difficult to achieve. Initial doses of prednisolone (0.5mg/kg q12 hours) have been suggested, with the dose being tapered quickly to the lowest level that controls signs. Inhaled steroids such as fluticasone (125-250µg used through a spacer q12 hours) may be of benefit to some dogs that are dependent on oral steroid to reduce airway irritation, where the side effects of these are adversely affecting their quality of life.

Recently, an experimental study evaluating the administration of stanozolol, an anabolic androgenic steroid, documented potential beneficial effects in the management of dogs with tracheal collapse. It is postulated that stanozolol may enhance protein synthesis, increase collagen synthesis and chondroitin sulphate content.

Bronchodilators

Bronchodilators are suggested in the management of tracheal collapse to induce bronchial dilation, which at least in theory, should reduce intra-thoracic pressure during expiration and reduce expiratory tracheal collapse. Methylxanthine based bronchodilators (such as theophylline 15-20mg/kg q12-24 hours) may be potentially beneficial by improving mucociliary clearance and reducing diaphragm fatigue, as well as increasing airway diameter. A_2-adrenergic bronchodilators such as terbutaline, have also been suggested, with injectable or inhaled administration being most useful in the emergency setting. The benefit of bronchodilators in dogs with tracheal collapse has not yet been fully evaluated, so their introduction should be regarded as a therapeutic trial, andwithdrawn if no improvement is seen. Some dogs, especially older dogs, appear very susceptible to the effects of methylxanthines. Restlessness and anxiety are commonly seen side effects and if these affect the patient's quality of life, medication should be swiftly withdrawn.

Antimicrobials

Antimicrobial administration is not usually indicated unless there is evidence of concurrent secondary infection which can act as an inciting cause to airway irritation. When antimicrobials are indicated, agents with efficacy against *Mycoplasma* infection, such as doxycycline, should be considered pending culture results from bronchoalveolar lavage.

Surgical interventions

If options for medical therapy have been fully explored and not controlled clinical signs then surgical management should be considered. The aim of surgical intervention is to improve the tracheal anatomy to allow increased airflow, without disrupting the mucociliary system. No surgical procedure will cure tracheal collapse and continued medication is often needed, to control coughing or manage concurrent lower airway collapse, however the quality of life of many dogs can be improved significantly when medication alone is inadequate. Patient selection is key to obtaining good outcomes and only dogs with severe collapse (Grade II and higher) should be considered surgical candidates . Age at intervention also appears to be associated with long-term outcome, with dogs less than six years of age being reported as having better outcomes compared to dogs older than six, despite having less severe tracheal collapse. Various different surgical procedures have been reported for the management of tracheal collapse and include surgeries such as tracheal ring chondrotomy and plication of the dorsal tracheal membrane (which have largely fallen out of favour due to reported tracheal narrowing), the placement of extraluminal ring prostheses and more recently intraluminal stent placement.

Extraluminal ring prostheses

Extraluminal support of the trachea with the placement of synthetic prostheses allows restoration of the tracheal diameter during respiration and coughing, and does not interfere with mucociliary function. C-shaped prostheses are placed via a ventral, median approach separating the sternohyoideus muscles to expose the cervical tracheal. The thyroid arteries and recurrent laryngeal nerves are identified and gentle dissected from the trachea to allow prosthesis placement. Prostheses are placed at regular intervals, usually every 2-3 tracheal ring spaces, from the cranial portion to the thoracic inlet and sutured to the tracheal cartilages and trachealis muscle. Prostheses have been formed from polypropylene syringe casings, polyvinyl chloride drip chambers of giving sets and commercially available ring prosthesis. Spiral rings have also been used as they are flexible and provide circumferential support to a collapsing trachea compared to c-shaped rings, however the dissection required for placement has been shown to disrupt the lateral pedicles containing the tracheal vasculature and as a result individual C-shaped rings are preferred.

Good outcome has been reported in 75–89% of dogs after the placement of extraluminal C-shaped prostheses. Weight, sex, breed, severity of collapse and duration of clinical signs do not seem to be associated with outcome. In one case series 72% of dogs were reported as no longer needing medication and having normal exercise tolerance with no coughing documented at follow up 6-36 months after surgery. A recent study reported median survival times of 4.6 years after the placement of extraluminal tracheal rings.

Complications associated with the placement of extraluminal tracheal rings are frequent, with 5% perioperative mortality and 19% of dogsrequiring a tracheostomy in one series of 90 dogs. In this series coughing dyspnoea and laryngeal paralysis where reported in 31% of dogs after a month and 56% of dogs at some point after the surgery; 23% of dogs treated died of respiratory complications with a median survival time of 25 months. In early studies vascular damage to the trachea resulting in necrosis was reported in a small number of dogs, however this has not been reported in more recent studies. Tracheal ring migration has also been reported in one dog.

Postoperative laryngeal paralysis, due to iatrogenic nerve damage, is a well-documented complication of extraluminal ring placement and is reported in 11 to 21% of dogs in the immediate postoperative period. Immediate post-operative paralysis (approximately half of cases) is attributed to inadvertent damage or transection of the recurrent laryngeal nerves intraoperatively, with a smaller proportion developing paralysis as a late complication, potentially due to long-term rubbing, granulation tissue formation or contact with a prosthesis. Concurrent left arytenoid lateralisation has been reported in conjunction with extraluminal ring placement, and lower rates of postoperative complications of 4% were reported with 75% of dogs having a good long-term outcome. Laryngeal lateralisation has been performed when needed rather than routinely in other series due to the potential complications of fixing the larynx in an open position.

Due to the high morbidity documented in association with placement of extraluminal prosthesis around the intrathoracic trachea the technique is usually limited to the support of the extrathoracic portion of the trachea. Extraluminal support of the cervical trachea has generally been discouraged in dogs with concurrent collapse of the intrathoracic trachea however a recent study documented that the presence of intrathoracic collapse did not significantly affect survival and outcome in dogs treated with extraluminal rings along the cervical trachea.

Intraluminal stent placement

The placement of intraluminal tracheal stents is a minimally invasive procedure compared to placement of extraluminal ring prostheses with rapid improvement seen in most dogs post placement. A number of different stent types have been evaluated for the treatment of canine tracheal collapse. These include balloon-expandable (Palmaz) stents, self-expanding stents made from stainless steel, woven and laser cut nitinol.

Stents are placed in lateral recumbency and under fluoroscopic guidance (Figure 4). Prior to placement measurements of the tracheal width and length are taken from lateral radiographs or, where possible, under fluoroscopy. Stent sizing is critical to the successful outcome of stent placement; if too small the stent will migrate or shorten, and too large, pressure necrosis of the wall can occur. Stent shortening initially was documented in a high proportion of dogs, however recent advances in the understanding of appropriate stent sizing have reduced the reported rate of stent shortening from 30% to 11%. Current advice is that the stent diameter chosen is oversized by approximately 10-20% to minimise the risk of stent shortening and migration. This also counters the effect that the trachea is oval in cross section, usually having a slightly larger diameter across its width, compared to its height.

To enable accurate measurement an endotracheal tube is placed just caudal to the larynx and measurements of maximal tracheal diameter are taken during positive pressure ventilation (to +20cm of water). This is then compared to a measurement catheter which is placed within the oesophagus limiting any effect of magnification. Evaluation of the collapsing portion is done under negative pressure (to -20cm of water) and it is possible to only stent the extra thoracic or intra thoracic portion of the trachea. Most clinicians stent the whole length of the trachea, as disease progression will usually mean a second stent is needed if only a portion of the trachea is stented. Placement should be at least 5mm caudal to the larynx and the cricoid cartilage is usually used as this landmark; stenting within the larynx may lead to laryngospasm, cough and laryngeal dysfunction. The caudal edge of the stent should be placed at least 5mm cranial to the tracheal bifurcation and placement too caudally can lead to the caging of a main stem bronchus leading to mucus entrapment and complications such as infection. To avoid these potential problems, the suggested guidelines for stent measurement is that the stent is placed 10mm caudal to the cricoid cartilage to 10mm cranial to the tracheal bifurcation.

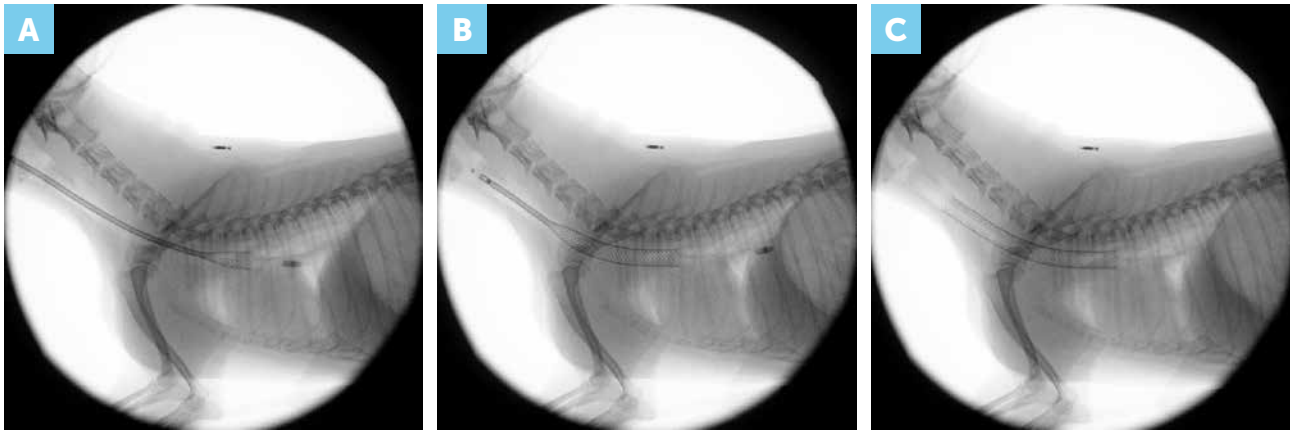

Figure 4: Stent deployment under fluoroscopic guidance. (A) The caudal edge of the stent is positioned 5-10mm cranial to the tracheal bifurcation. (B) The stent is slowly deployed with in the trachea, if positioning is sub optimal the stent can be reconstrained and its position adjusted. (C) Once deployed the delivery system is removed and positioning assessed. The caudal edge should be no closer than 5mm, but ideally 10mm form the carina.

Studies have documented improvement in 75-90% of dogs treated with intraluminal stainless steel self-expanding stents and long-term improvement in 10 out of 12 dogs treated with nitinol self-expanding metallic stents, with 9 dogs alive after 1 year and 7 dogs alive after 2 years. An owner based survey of the owners of 18 dogs with nitinol self-expanding metallic stents reported good to fair improvement in all dogs after stent placement. Stent placement is not a curative procedure and owners should be carefully counselled that continued long-term medical management and careful monitor is essential to achieve a good long-term outcome.

Tracheal stents are made from durable materials; however excessive compression or movement, such as that caused by coughing, can lead to metal fatigue and subsequent fracture. Case series reported relatively high rates of stent fracture, with fractures reported in 5 of 12 dogs and 4 of 18 dogs which had had self-expanding nitinol stents placed. Recent advancement in stent design has led to the development of more flexible stents, with more elastic materials expected to reduce the risk of fracture through metal fatigue. Care not to oversize the stent by more than 20% and control of coughing may limit this risk. The introduction of tapered stents has helped to reduce the need to over size stents in the trachea, where there is a marked difference in the proximal and distal tracheal diameter. If stent fracture occurs, stability is usually obtained by the placement of a second stent within the lumen of the fractured stent. This can be more technically challenging and the placement of a guidewire through the fractured stent lumen is suggested to confirm that stent placement will be intraluminal before deployment. Alternatively it may be possible to remove the stent and apply extraluminal prostheses.

A common consequence of stent placement is the formation of excessive inflammatory tissue within the trachea and is reported in 28%–33% of cases. This is most commonly seen at the ends of the stent and is likely to be associated with excessive movement of the stent, most often as a result of coughing. The development of woven stents with rounded edges and a high quality finish to the nitinol, anecdotally seem to have reduced the formation of inflammatory tissue compared with open mesh steel stents. This has not been rigorously proven and it may be that other factors such as better stent sizing and more aggressive cough suppression have reduced the apparent frequency of this complication. Rigorous attention to the control of coughing and inflammation after stent placement are key to limiting the potential formation of inflammatory tissue, this requires owners to understand continued medication after placement is required and to be compliant with its longer term administration.

Inflammatory tissue within the trachea reduces tracheal diameter and leads to reduced airflow, with signs of exercise intolerance and respiratory distress. Radiographs may document the presence of inflammatory tissue, but this is best observed endoscopically. Most excessive inflammatory tissue will respond rapidly to medical therapy with steroids and a 6-8 week course (starting dose prednisolone 2mg/kg/day) tapering to the lowest dose that controls clinical signs is

suggested. Oral colchicine use has also been reported and may be useful in the management of refractory cases. In some instances excess granulation tissue can be removed endoscopically with loop electrocautery or laser resection.

Bronchial collapse

Dogs with tracheal collapse often have concurrent bronchial collapse, due to progressing cartilage weakness. At present stent placement within the bronchus is not routinely recommended as the stent will cage off lower bronchi and preventing mucus drainage. In addition, disease progression will usually lead to lower airway collapse limiting the efficacy of the stent placed. In dogs with both tracheal and bronchial collapse, tracheal stent placement may help to improve airflow, especially if the dog's main sign is inspiratory dysponea. Short bronchial stent placement may also be useful in dogs that have not improved after tracheal stenting due to focal mainstem bronchial collapse A recent case report documented a successful outcome after bronchial stent placement in a dog with focal left mainstem bronchial collapse and left atrial enlargement. Although the case report documents severe respiratory distress after stent placement quality of life was improved in the longer term.

Conclusion

Tracheal collapse is a relatively common condition seen in middle aged, small breed dogs. Most dogs will respond well to medical management, however those that do not, or that have respiratory compromise, may benefit from surgical intervention. Making the decision as to when, and which, surgical intervention may be beneficial, is complex and multifactorial, depending on personnel experience, owner preference and available finance.

In recent years, procedures to provide extraluminal support to the trachea have fallen out of favour due to the development of intraluminal stenting, due to the less invasive nature of the procedure and perceived lower perioperative morbidity. Experience with the long-term management of dogs post stent placement is growing however information about their long-term outcome is limited. Ongoing medical management is required in most dogs post stent placement to prevent coughing and inflammation, this is compared to the majority of dogs with successful extraluminal support being able to stop medication completely.

Recent work has suggested that the placement of extraluminal tracheal rings is still a valid option for the treatment of tracheal collapse, especially if cervical collapse alone is present. The finding that dogs with intrathoracic collapse appear to have a good outcome with extraluminal support of the cervical trachea has led to questioning of the previous held view that extraluminal support is not appropriate for the management of dogs with intrathoracic tracheal collapse.

As a result, the best approach as to providing intraluminal or extraluminal support in dogs with tracheal collapse remains unresolved, with decisions needing to be made on a patient by patient basis.

Soft Tissue Surgery

Laurent Findji (UK)

DMV MS MRCVS DiplECVS (Soft tissue surgery)

Laurent graduated from Paris' vet school, the Ecole Nationale Vétérinaire d'Alfort, in France in 1995 and was assistant instructor in the anatomy department the following year. He then qualified for a 2-year surgical internship in the same school and later completed a Master of Science in Biology and Physiology of Circulation and Respiration, as well as a university degree in Experimental Surgery and Microsurgery.

After having worked for 3 years in a large private practice outside Paris, he spent 4 years at the Centre Hospitalier Vétérinaire Frégis, near Paris, where he completed an ECVS residency. He became a diplomate of the European College of Veterinary Surgeons in 2008 and was recognized as a specialist in small animal surgery by the Royal College of Veterinary Surgeons in 2012. Laurent worked at VRCC Veterinary Referrals in Essex, United Kingdom, where he was one of the full-time soft-tissue surgeons and directors from 2006 to 2014. He moved to the Oncology and Soft Tissue Surgery department of Fitzpatrick Referrals in October 2014. Laurent is a member of several professional boards and committees, regularly contributes to international publications and book chapters, and gives lectures and presentation in many countries. His fields of interest include surgical oncology, reconstructive surgery and general soft tissue surgery.

Approach to lumps and bumps

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Fitzpatrick Referrals, United Kingdom

The following are proposed flowcharts of the approach of lumps and bumps in dogs and cats. They are by no means exhaustive or perfect. Their indications obviously need to be adapted to particular cases or situations, as well as to take in consideration the constraints and expectations of owners.

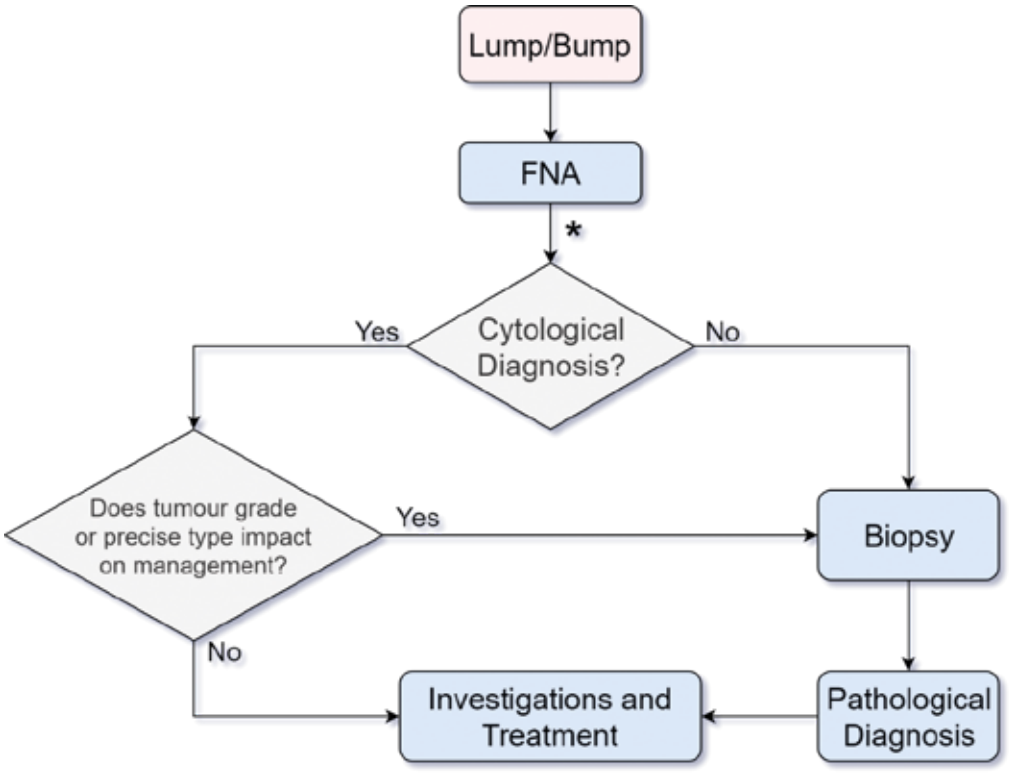

Figure 1: Initial approach to a externally palpable mass in dogs and cats.
* (The flow between the performance of fine-needle aspirates and obtaining a working diagnosis detailed in Figure 2)

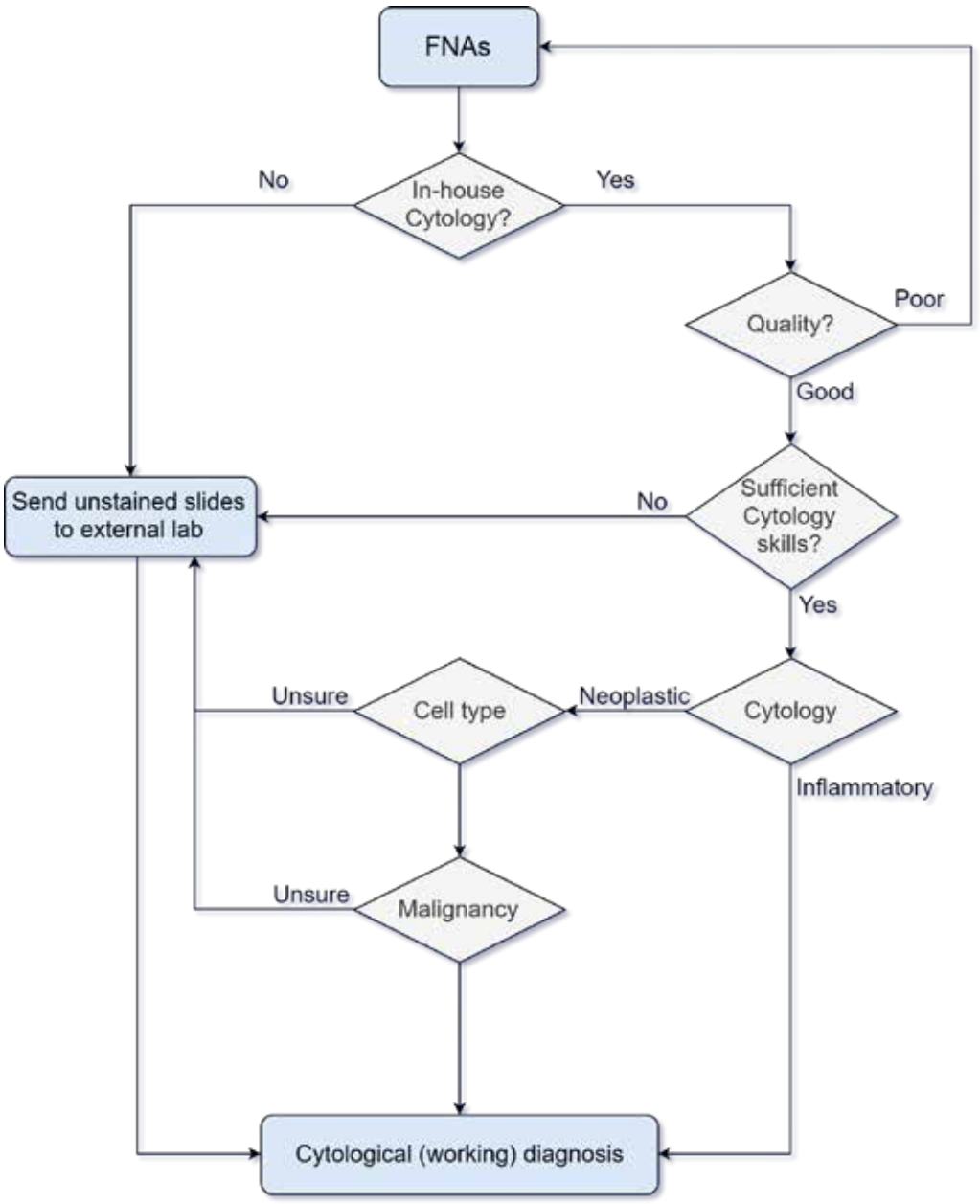

Figure 2: Approach to obtaining a cytological diagnosis from fine-needle aspirates.

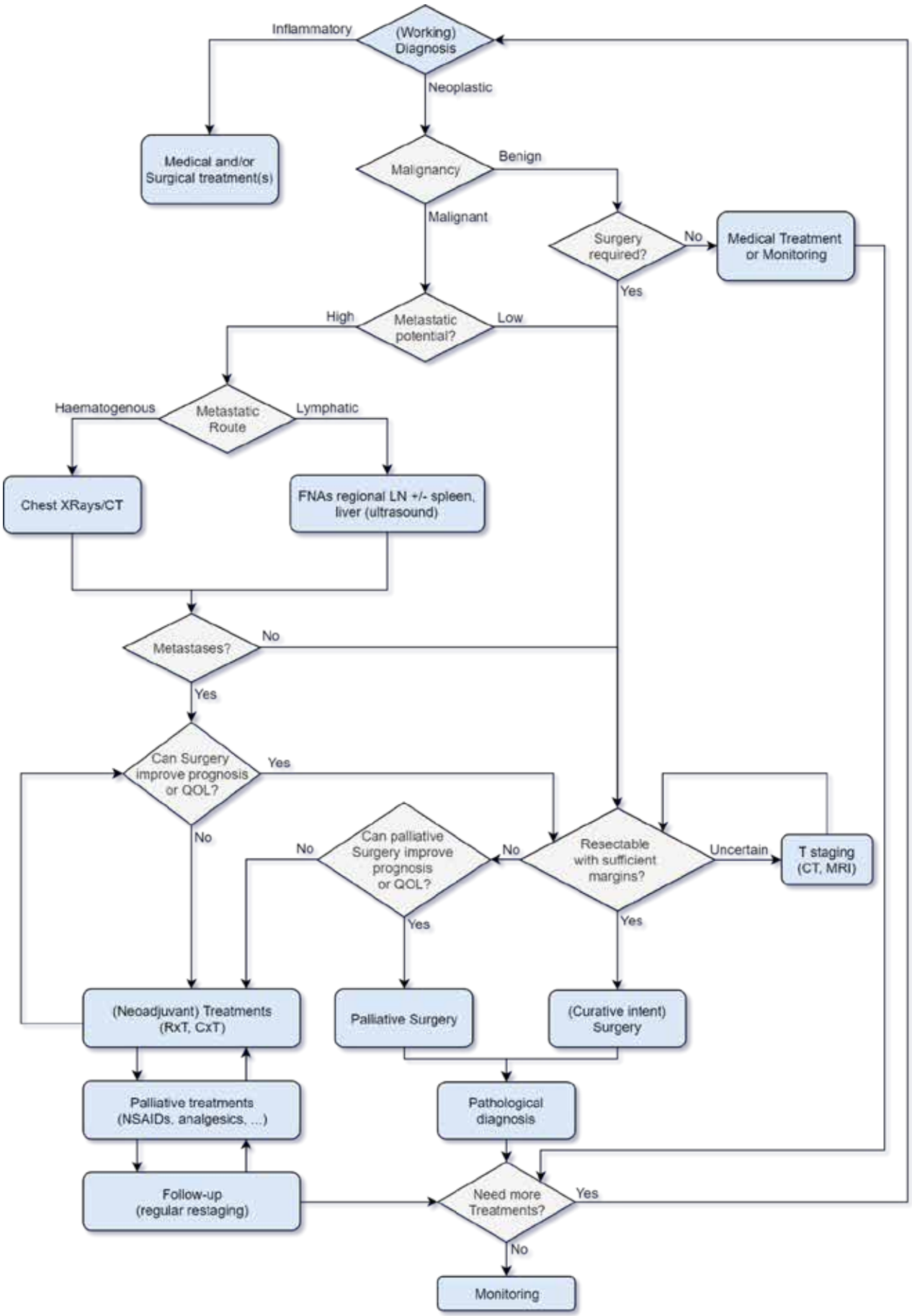

Figure 3: Management of cutaneous and subcutaneous masses from their working diagnosis.

Diaphragmatic hernias

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Diaphragmatic hernias (DHs) consist of the protrusion of one or several organs into the pleural or the pericardial cavity through a defect in the diaphragm. They can be congenital or acquired. Congenital DHs include pleuroperitoneal and peritoneopericardial hernias. Acquired DHs are more common (approximately 85% of cases) and result from blunt trauma applied to the abdomen while the glottis is open. Acquired DHs can be acute or chronic.

The diaphragmatic defect can have different shapes, and variable combinations of abdominal organs herniate into the thorax, depending partially on the location of the defect. It is a surgical condition and the treatment involves replacing the abdominal organs in place and repairing the diaphragm.

Technically, repair of diaphragmatic hernias is seldom demanding. The difficulty in managing such cases lies in the pre and postoperative management. The key to success should be sought in these phases more than in the surgical procedure itself.

The clinical signs associated with DHs are most commonly respiratory. Occasionally, the main presenting signs can be gastrointestinal, resulting from the entrapment or incarceration of portions of the digestive tract. Patients presented for acute DH can suffer from concomitant orthopaedic or neurologic lesions.

Preoperatively, management of animals with diaphragmatic hernia relies on gentle manipulation avoiding any supplemental stress, providing oxygen supplementation and optimising the patient with regards to any concurrent hypovolaemia, blood loss and acidosis. Hypotensive optimisation is indicated rather than aggressive fluid therapy, as these animals will be prone to pulmonary oedema in the postoperative period.

Diaphragmatic hernias will cause a restrictive dyspnoea. Either muffled or increased cardiac and pulmonary sounds can variably be heard on thoracic auscultation. Borborygmi can also be heard if portions of the gastrointestinal tract are herniated.

The diagnosis is most commonly made from thoracic radiographs. Caution must be exerted with patients in respiratory distress or unstable. A conscious, dorsoventral view can be obtained in compromised animals. Abdominothoracic ultrasound is another reliable modality to confirm the presence of a DH, by detecting the presence of abdominal organs into the chest or the abnormal position of t abdominal organs. Lastly, if available, conscious CT scans can also be used to confirm the presence of a DH. These latter modalities have largely superseded the used of contrast studies (e.g. barium ingestion study, pneumoperitoneography, peritoneography, pleurography, angiography).

Early studies report increased mortality in animals operated on an emergency basis, i.e. within 24 hours. This has led to the widespread idea that these animals should not be operated early after presentation, unless the stomach is herniated. When reviewing the evidence supporting this idea, it seems that other factors may have been responsible for this apparent increase in mortality. More recently, this dogma has therefore been challenged and it should no longer be strictly obeyed. Instead, animals with diaphragmatic hernia should be optimised and surgically addressed, as soon as shock is treated and the animal is stable from a cardiovascular viewpoint. Presence of the stomach in the thorax changes little to this plan. When necessary, the stomach may be deflated by thoracocentesis or by placing a nasogastric tube to allow more time for preoperative stabilisation. One situation in which emergency surgery may be required is intractable bleeding from the herniated organs, such as the liver. This is however rare.

Animals are preoxygenated by mask or flow-by. Induction of anaesthesia must be quick so that patients do not fight and tracheal intubation is not delayed. The entire abdomen and chest are clipped and prepped. Compromised animals can be prepped in an inclined position, head up, so that the herniated organs cause less compression on the chest.

The abdomen is approached through a xyphopubic median coeliotomy. The falciform ligament is resected to improve exposure of the cranial portion of the abdomen. The entire abdominal cavity is inspected. The diaphragm is examined in its entirety, even if a hernia is readily visible, as multiple hernias are not exceptional. Hernias can be radial, circumferential or combined (Figure 1).

Herniated organs are gently replaced in the abdominal cavity. If they cannot be replaced without considerable traction, the hernial ring may need to be enlarged to facilitate reduction of the hernia. This is most frequently necessary for chronic DHs, in which the hernial ring can be fibrous and retracted. Reduction of herniated organs can also be made difficult in chronic DHs if adhesions have formed between herniated and thoracic organs. If considerable traction seems required to reduce the hernia, it is preferable to extend the coeliotomy incision cranially by caudal median sternotomy, to get direct visual control of the adhesions and debride them. Herniated organs are then inspected for any lesions, which can be repaired or resected as appropriate. A small-bore thoracic drain is placed in the chest under direct visual control while the hernial ring is still open. The hernia is then repaired, typically using an absorbable

monofilament suture in a continuous pattern. In chronic DHs, the edges of the diaphragm may need to be trimmed before herniorraphy. Complex hernias (e.g. involving the oesophageal, aortic or caval hiatuses) may need to be closed by pre-placing interrupted sutures. In circumferential and combined hernias, the avulsed edges of the diaphragm are sutured to the last ribs and/or xyphoid process. Large congenital or chronic hernias may not be amenable to simple closure and may require resorting to muscle flaps or meshes to be closed.

Throughout the procedure, the lungs must not be overinflated. The minimal positive pressure allowing good ventilation and oxygenation should be used, not exceeding 15-20 cm H_2O. The longer the lungs have been collapsed, the more important this is. Similarly, once the diaphragm is sealed, the pneumothorax should only be drained sufficiently to obtain good ventilation parameters. Portions of the lungs still remaining atelectatic should be left unaddressed and the pleural space should be drained just enough for the breathing to be effective in maintaining normal oxygen saturation. A residual pneumothorax is therefore considered normal, if not even preferable. It should slowly be drained over 12-24 hours after surgery. Previous recommendations that the lung should be re-inflated as much as possible during the surgical procedure and the thorax be thoroughly drained at the end of the intervention should therefore be abandoned!

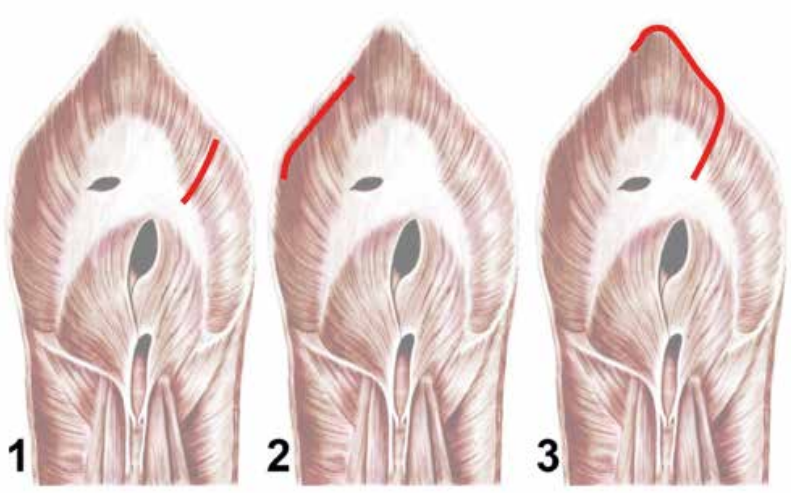

Figure 1: Types of diaphragmatic hernias (1. radial; 2. circumferential; 3. combined).

The second critical period is postoperative recovery. Pulmonary oedema is a severe potential complication from lung re-expansion and ischaemia-reperfusion injuries, which are more likely when lungs have been collapsed for a long time. The patient is then closely monitored for pulmonary oedema. Oxygen supplementation and cautious fluid therapy are maintained as deemed appropriate according to perfusion and oxygen assessment parameters. The thoracostomy tube is removed when it is unproductive (usually within 24 hours).

The prognosis for DHs undergoing surgical repair is fair, with survival rates between 81% and 92%.

Why is this wound not healing?

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Non-healing wounds are abnormal, as the body has a natural drive to heal. Failure to do so can result from systemic (i.e. related to the patient) or local (i.e. related to the wound) causes.

Patient factors

Species: Wound healing is clinically different in dogs and cats. Cats heal more slowly than dogs and are more reliant on the presence of subcutis for their skin to heal. "Pseudo-healing", a phenomenon in which a wound appears to have healed but has not and therefore easily reopens if sutures are removed, is more common in cats than in dogs.

Hypoproteinaemia: Animals whose total plasma protein levels are lower than 2 g/dl have a slower and a poorer quality of wound healing, resulting in a scar with low mechanical resistance, because of inhibition of the fibroblastic phase.

Anaemia: Anaemia does not impede wound healing, but some physiologic changes impairing the microcirculation, that can be associated with anaemia, like hypovolaemia, blood hyperviscosity or hypercoagulability, are wound healing inhibitors.

Hyperadrenocorticism: It is deleterious to wound healing through excess of circulating corticoids (cf infra).

Corticoids: Steroidal anti-inflammatory drugs inhibit all stages of wound healing by decreasing protein synthesis, stabilising lysosomal membranes and minimising inflammatory reactions. In high dosages, they also limit the formation of neo-capillaries, fibroblastic proliferation and slow down epithelialisation. Their deleterious effects are moreover potentiated by a nutritional protein deficiency. In practice, they do not prevent wound healing, but slow it down.

Diabetes: Diabetic animals show delayed wound healing and are predisposed to infection. However, diabetes does not seem to involve clinically relevant delays in wound healing in animals, on the contrary to what is known in man.

Hyperuraemia: It impedes wound healing through interference with enzymatic systems, biochemical ways and cellular metabolism, particularly during the first 5 days of wound healing, by inhibiting the formation of granulation tissue and the division of the epithelial cells. The apposed collagen is of poor quality or destroyed in excess, which leads to a scar lacking resistance, although its collagen content is normal.

Hepatic disease: When severe, such disease can impair wound healing, through decreased protein and coagulation factor synthesis in the liver.

Obesity: Obesity is known in man to predispose to wound infection, because of the poor vascularisation of fat.

Nonsteroidal anti-inflammatories: Their influence on wound healing is still only incompletely elucidated: they decrease inflammation, and thus would be expected to have the greatest effects during the first days of wound healing. With the clinically used dosages, they do not have any effect on scar quality.

Anti-cancer chemotherapy: Cytotoxic drugs used in cancer treatment inhibit wound healing, but their systemic administration seems to induce weak concentrations within the wound. Their deleterious effects are thus weak. On the contrary, their long-term local application can prevent wound healing.

Radiotherapy: It is, in any form, deleterious to wound healing. Fibroblasts and vascular endothelial cells are destroyed, which prevents collagen deposition and the neo-vascularisation of the wound. The irradiated wounds are dominated by ischaemia (progressive fibrosis of blood vessels), and heal slowly and with difficulty. Dividing cells are most sensitive. The tissues in constant renewal such as the digestive and urinary epithelia, or the germinal layer of the skin are thus particularly vulnerable.

Antiseptics: Antiseptics are cytotoxic. They destroy neutrophils, interfere with capillary proliferation, inhibit granulation tissue formation and epithelialisation. They reduce the mechanical resistance of the wound and predispose to infections. Their effect is volume-dependant. It is advised not to exceed concentrations of 0.05% for chlorhexidine and of 1% for povidone-iodine.

Nutritional factors: Protein depletion can worsen the effects of other deleterious factors like steroidal therapy. Vitamin A, which increases the intensity of inflammatory reactions, can on the contrary counter the deleterious effects of steroidal therapy or vitamin E intake. Vitamin E, like cortisone, stabilises cellular membranes and can delay wound healing, when given in high doses. Vitamin C is necessary for hydroxylation of proline and lysine during collagen synthesis, but dogs and cats do not rely on an exogenous supply for this vitamin. Zinc is essential to activity of certain enzymes of the fibroblastic stage, production of collagen and epithelialisation. Nevertheless, zinc supplementation does not have any clinical rationale unless in the event of a marked documented deficiency.

Wound factors

Foreign bodies: The presence of foreign bodies in a wound prolongs the inflammatory phase and delays the beginning of the fibroblastic stage. The enzymatic activity intended to eliminate the foreign bodies tends to destroy the conjunctive matrix of the wound. Sutures and surgical implants count among foreign bodies impairing wound healing.

Temperature: Wounds exposed to higher than ambient temperatures (about 30°C [86°F]) heal more quickly and show greater mechanical resistance. Conversely, cold slows down wound healing. These effects are explained respectively by vasodilatation and vasoconstriction reflexes, which increase or decrease oxygen delivery in the wound. Bandages protect the wound from cold.

Moisture: Wounds maintained in a moist atmosphere heal faster than those kept in a dry environment, as moist atmospheres facilitate the course of wound healing and immune processes.

Oxygen: Before its invasion by neo-capillaries, the low partial pressure of oxygen in the wound (about zero), does not allow protein synthesis and fibroblast proliferation. Around the capillaries, it reaches 60 to 90 mmHg, which allows fibroblastic activity. Fibroplasia is thus very dependent on the neo-vascularisation of the wound. A hyperbaric oxygen atmosphere (in a chamber) makes it possible to saturate haemoglobin with oxygen and to increase the amount of oxygen dissolved in plasma. This last point leads to a higher oxygen delivery to the avascular parts of the wound, thereby stimulating wound healing. On the other hand, such an atmosphere promotes the production of toxic free radicals derived from oxygen.

Infection: Infected wounds heal more slowly or incompletely. Infection delays, even prevents, the progression of the repair phase of wound healing. Bacteria produce collagenases which destroy the connective matrix and weaken the wound. Their toxins induce cellular necrosis and vascular thrombosis, worsening ischaemia and lengthening the inflammatory and debridement stages. They impair fibroblastic activity and interfere with the local environment, especially with the pH, which influences the enzymatic reactions of wound healing.

Skin laxity: Contraction is a major component of wound healing in dogs and cats. For a wound to contract, the surrounding skin must have sufficient laxity, for myofibroblasts to bring its edges closer.

Sutured wounds

When facing a non-healing sutured wound, in addition to systemic factors (e.g. hypoproteinaemia, hyperadrenocorticism, sepsis), surgeons must consider whether one or several of the following wound factors could be responsible.

Vascular supply: If the wound is not well vascularised, its partial pressure in oxygen may be insufficient, preventing healing.

Foreign bodies: the presence of foreign bodies, even deep in the wound and covered by granulation or healed tissues, can delay or prevent wound healing, or cause wounds to reopen.

Tension: Excessive tension on a wound makes its edges ischaemic and favours its dehiscence by direct mechanical effect.

Motion: Excessive motion will impair wound healing by impairing the formation of tissues between the edges of the wound. It can also result in intermittent tension on the wound edges.

Dead space: the presence of dead space may delay wound healing by allowing accumulation of fluid in the wound, which can apply pressure on the wound and promote infection.

Infection: The presence of infection in the wound will delay or prevent wound healing, as stated before. When assessing a wound for infection, deep samples must be obtained rather than superficial swabs of the wound, which may be irrelevant.

Tissue disease: Biopsies of the wound bed may be obtained whenever a local underlying disease could be present (e.g. residual neoplasia).

Is resecting bigger the future of surgical oncology?

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"Now that it has proved possible to resect half of the brain, an entire lung, any endocrine organ, much of the liver, any part of the digestive or urinary tract, to include the upper hemithorax in a forequarter amputation and to amputate the lower half of the body, it can be comfortably asserted that extirpative surgery has reached its final limit."

Mark M Ravitch 1910-1989

Resecting big

Surgery remains the most effective single modality treatment against cancer. More cancers are cured by surgery than by any other treatment modalities. Now this unfortunately only applies to solid, non-metastatic cancers, but such cancers represent a large proportion of all malignant tumours in dogs and cats.

William of Salicet (1210-1277) wrote "The treatment of cancer is of two sorts: firstly that the affected part be radically and totally cut away with the entire disease by means of a very sharp knife... the second type of treatment is palliative...". In the 17th century, Lorenz Heister, a German surgeon describe the concept of radical mastectomy for treatment of breast cancer in women, a principle still adhered to centuries later by surgeons such as William Halsted. These surgeons believed in radical surgeries including draining lymph nodes for treatment of cancer. They believed that radical resections should cure cancer. Metastases, if they were then believed to be a separate disease process. This was the age of radical resections, for breast cancer in particular. In the 1970s, it was shown that less radical surgeries were equally effective and radical mastectomies are nowadays rare, being replaced by more conservative surgeries, often combined with radiation therapy and chemotherapy.

The theoretical grounds justifying radical resections stemmed from the concept that tumours progressed by direct growth and local invasion into surrounding tissues. It therefore appeared logical that if more margins were taken around a tumour, any of its local extensions should be resected as well and the cancer be should be cured. This proved true to a point, initially apparently supporting this theory and leading to an era of radical surgeries. With increasing margins, however, the ratio of healthy tissues to potentially diseased tissues resected becomes less and less justifiable. Furthermore, it appears that beyond a certain margin, the excision of more tissues does not increase the number of cancers cured. Metastatic cancers, in particular, are obviously mostly beyond surgical cure. Our current understanding of cancer biology shows that cancer is a complex disease, involving the tumour, its environment and its host. The simplified concept of a tumour as an independent, isolated, locally expanding entity does not reflect the reality of the disease, and the limits of radical resections have been reached.

In veterinary medicine, even more so that in human medicine, the consequences of radical procedures have to be weighed against their sought benefits. A radical resection may not always be possible or, if so, desirable. The morbidity or debility resulting from radical procedures may not be acceptable, even if the procedure has a chance of being curative. This judgement is made, for each individual patient, jointly by the surgeon and the owner.

Resecting less

Resecting tumours with smaller margins whilst not decreasing cure rates is only possible through increased knowledge of tumour biology and careful selection of the patient. In some instances, marginal tumour resections are appropriate. In dogs, the recurrence rates of marginally resected low-grade soft tissue sarcomas (STS) of the extremities (distal to the elbow or stifle) have been reported to be 11% overall[11]. In another study, recurrence rates were dependant on the grade of the marginally resected canine STS: 7% for grade 1, 24% for grade 2 and 75% for grade 3, although the number of grade 3 STS included in this study (n=4) was too low for this figure to be reliable[12]. No recurrences were observed when wide resection was performed, indicating that clean tumour margins were predictive for non-recurrence (n=30)[12]. Another study of revision excision of incompletely excised STS on 41 dogs found recurrence and metastatic rates of 15% and 10%, respectively[13]. The presence of residual tumour was identified in 22% of resected scar tissues and it did not appear to predict recurrence[13]. When marginal resection of STS of the limbs was intentional and followed by adjuvant radiotherapy (hypofractionated protocol, 4 x 8-9Gy), recurrence rates of 18% have been observed and the only factor predicting recurrence appeared to be the delay between surgery and radiotherapy[14].

In view of these studies, marginal resection of canine low-grade STS of the extremities may be considerable, either alone or combined with radiotherapy, when a wider excision is not easily possible. In this setting, the proportion of dogs dying of causes related to their STS varies between 10% and 33%[4].

Likewise, classic recommendations for resection of cutaneous mast cell tumours in dogs involve margins ranging from 1cm for low-grade tumours to 3 to 5 cm for high-grade tumours. While this is still appropriate in many cases, the

strict application of these rules could lead to excessive resections for the smaller tumours: one study has evaluated the value of the use of proportional margins for resection of cutaneous and subcutaneous MCTs in dogs and found that resecting these tumours with lateral margins as wide as the longest diameter of the mass for tumours up to 4cm in diameter and with 4-cm margins for larger tumours resulted in complete excision of 40 out of 47 tumours[11].

More conservative resections can also be considered when neo-adjuvant or adjuvant treatments are part of the treatment plan. Wide resections aim at palliating the surgeon's inability to detect microscopic disease at a distance from the visible tumour. In other words, surgery is a good tool to remove the bulk of a solid tumour, and a mediocre tool to remove microscopic disease around it. Chemotherapy and radiotherapy are the opposite: they tend to fail in the face of macroscopic disease but are most effective at targeting microscopic disease over large portions, if not all, of the body. Combining these treatments allows the surgeon to focus mostly on the bulk of the disease, that is the visible disease.

Lastly, compartmental resections can be as effective and less extensive than en-bloc resections. Compartmental resections consist of the resection of the entire compartment containing the tumour, if it is contained in a compartment. A compartment tends to be an anatomic entity surrounded by a strong barrier against tumour infiltration, such as bone or loose connective tissues. Examples of compartmental resections include the resection of an entire muscle or encapsulated carcinomas such as anal sac carcinomas, thyroid carcinomas or mammary tumours.

The future of surgical oncology is not to resect bigger, but to resect smarter. Advancements in our knowledge of tumour biology and progresses of other modalities of cancer treatment such as chemotherapy, radiotherapy and immunotherapy allow the surgeon to tailor tumour resections precisely to each tumour (type, grade, stage, location) in each individual patient. This in turn will decrease the amount of healthy tissues sacrificed for the sake of local tumour control and limit the morbidity associated with cancer surgery.

Advances in surgery of oral tumours

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Oral tumours are regularly encountered in dogs and cats, and our ability to treat them has increased over the last few decades. Although many oropharyngeal tumours are best treated with a multimodal approach, including various combinations of surgery, radiotherapy, chemotherapy and immunotherapy, surgery remains the mainstay of their treatment.

Tumour biology

Like for other cancers, tumour biology is the main determinant of prognosis. Only a few tumour types constitute the vast majority of tumours encountered.

In dogs, the most frequently encountered malignant tumours of the oral cavity are malignant melanomas (MM; 31 to 42% of cases), squamous cell carcinomas (SCC; 17 to 25% of cases), fibrosarcomas (FSA; 7.5 to 25% of cases) and osteosarcomas (OSA; 6 to 18% of cases). In cats, the most common oropharyngeal tumours are SCC (75% of cases) and FSA (13 to 17% of cases).

Very schematically, all malignant tumour in dogs tend to be locally invasive and require wide resection. In one study, 37 out of 120 (31%) malignant oral tumours recurred after surgical excision, with recurrence being most common with FSA (54% of cases) and least common with SCC (17% of cases)[1]. Malignant melanomas recurred in 27% of cases, but had the highest metastatic rate (30%). Even higher metastatic rates (50-80%) for MM have been reported previously. In one recent study, 9 of 13 dogs (69%) with MM had metastasis to locoregional lymph nodes[2]. Fibrosarcomas, OSAs and SCCs had metastatic rates of 21, 22% and 3%, respectively[1]. One- and two-year survival rates were respectively 50% and 50% for SCC, 29% and 12% for FSA, 9% and 0% for OSA and 5% and 0% for MM[1]. Prognostic factors for outcome with malignant oral tumours treated by curative-intent surgery include tumour type, completeness of resection, tumour size and patient age[1].

Local recurrence is a major negative prognostic factor, influenced by tumour type, size, and location, as well as by completeness of surgical excision. Wide resections, including portions of the underlying bone(s), are therefore indicated for treatment of malignant oral tumours. How wide is wide enough depends on the tumour type and size.

Tumour staging

Tumour staging is a crucial step in the management of oral tumours. It involves advanced imaging to determine the location, extension and invasion of the primary tumour (T staging), imaging, mapping and biopsy of the locoregional lymph nodes (N staging) and imaging to assess the presence of distant metastasis (M staging).

Over the last few years, it has appeared that the route of lymphatic drainage of the oral cavity is complex and hardly predictable. One study of 31 dogs with oral tumours which had their mandibular and retropharyngeal lymph node extirpated bilaterally showed that 62% of metastatic tumours would spread to contralateral lymph nodes, with 8% spreading exclusively contralaterally[2]. The aspect of lymph nodes cannot reliably be used to determine the usefulness of taking biopsies from them: a study evaluating 100 dogs with oral malignant melanoma showed that lymph node palpation and size are not reliable indicators (40% of normal sized lymph nodes were positive for metastasis) of lymph node metastasis and that cytology or histology was required for accurate staging[3]. In another study involving 37 dogs and 7 cats, clinical examination of the lymph node also appeared poorly correlated with their metastatic status[4].

This demonstrates the importance of sampling the first lymph node ("sentinel" lymph node) on the lymphatic route of drainage of the tumour. The determination of the location of this sentinel lymph node is the objective of lymph node mapping techniques, increasingly used in veterinary oncology[5, 6]. Once identified, the sentinel lymph node is best examined after excisional biopsy (typically performed at the time of surgery), although in one study, cytological examination of lymph nodes for tumour invasion appeared 100% sensitive and 96% specific, showing that fine-needle aspiration is an accurate diagnostic tool for lymph node metastasis evaluation[4].

Surgery

As discussed previously, wide surgical resection of malignant oral tumours remains the mainstay of their treatment. However, many tumours will be best treated by a multimodal approach combining surgery with various combinations or neoadjuvant and adjuvant chemotherapy, radiotherapy, and immunotherapy. Only surgery will briefly be discussed here.

Local conditions of the oral cavity (limited availability in loose soft tissues, constant movements, bacterial charge) make wide oral resections and reconstructions often challenging. A few technical specificities, such as avoiding the use of electrocautery to cut mucosal surfaces and double-layer closures, however limit the risk of complications. Brisk haemorrhage is commonly encountered during mandibulectomies and maxillectomies. Blood loss and intraoperative hypotension have been reported as the most common intraoperative complications with such procedures[7-9]. Such haemorrhage can hardly be avoided, especially in maxillectomies, as the responsible blood vessels are contained within the resected osseous cavities. It can however be anticipated and its duration kept to a minimum by a judicious order in bone sections.

Most commonly, a minimum of 2-cm margins is sought for excision of mandibular and maxillary malignant tumours. Mandibulectomies and maxillectomies can be unilateral or bilateral and rostral, lateral/segmental or caudal. Extensive mandibulectomies and maxillectomies are very well-tolerated in dogs[8-14]. Much less information is available in the literature for cats, but functional recovery has been reported to be less satisfactory compared with dogs[15]. Patient selection is therefore paramount in cats, and owners must be warned about the likelihood of acute and long-term adverse after-effects. However, owner satisfaction rates are above 80% after maxillectomy or mandibulectomy in dogs[10] and mandibulectomy in cats[15].

Over the last few decades, radical oral resections have become more widely accepted as they were found to be well tolerated. Extensive maxillary and mandibular resections, either uni- or bilateral, are regularly performed. Cosmetic consequences can be major, but functional outcomes are almost invariably good, leading to satisfactory qualities of life. In cats, however, patient selection should be stricter, as morbidity and functional consequences are typically more severe than in dogs[15], but radical resections are considerable.

The next future step after radical oral resections is replacement of the resected portions of the skull, especially of the mandibles to preserve function as much as possible and avoid side-effects of surgery, such as mandibular drift. Until recently, missing portions of mandibles were occasionally replaced with cortical autografts (rib or ulna) or bone matrices. The advent of CT imaging and 3D printing has rendered custom-designed implants more available and affordable. The use of a custom-designed titanium implant to reconstruct mandibles after resection of mandibular tumours was recently reported in a cat[16] and 6 dogs[17]. Such implants are patient-specific and currently available for clinical use in referral hospitals with access to CAD design and additive manufacturing (3D printing) technologies. Their use will likely become more commonplace in the future.

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Augmented amputations. When just the leg is not enough

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Augmented amputation is an unofficial term referring to a surgery in which a leg amputation is extended by combination with another surgical technique to seek complete resection of a tumour with sufficient margins.

Forelimb augmented amputations mostly consist of combining forequarter amputation with partial resections of the thoracic wall or with cervicothoracic hemilaminectomies for resections of peripheral nerve sheath tumours (PNSTs) of the brachial plexus invading into the vertebral canal.

Hindlimb augmented amputations mostly consist of hemipelvectomies combined with partial resections of the abdominal wall or with lumbar (hemi)laminectomies for treatment of PNSTs of the lumbar plexus.

Peripheral nerve sheath tumours of the brachial and lumbar plexuses (PNST-BLP) invading the vertebral canal

Surgical resection is the treatment of choice for PNST-BLP. The decision to combine the tumour resection with limb amputation depend on the nerve root(s) affected, the clinical presentation, the preoperative function, the presence of concurrent orthopaedic or neurologic diseases and the expectations of the owners. Resection of PNST or major nerve roots with preservation of the limb has been reported recently[1]. In this study, most dogs were improved, except for dogs with resection of the C8 nerve root. This is consistent with our clinical experience that acceptable limb function can be hoped for with most PNST-BLP, except for tumours involving the C8 nerve root. Owners may however be satisfied with the outcome in spite of poor limb function, as patients frequently otherwise improve, which is believed to be through the elimination of the pain.

PNST-BLP are almost always contained within the perineurium, which acts as a barrier. Their resection therefore only needs to be compartmental. Proximally and distally along the nerve, however, wide margins should be sought as possible. Because of low metastatic rate of PNST, complete resections are most often curative. Incompletely resected tumours will frequently recur and lead to euthanasia. Logically, tumour-free margins have been found to be the only prognostic factor for PNST-BLP[1]. Tumours which as sufficiently distant from the spinal cord will therefore be associated with excellent survival times whereas tumours extending to the spine carry more guarded prognoses.

The surgical resection of tumours invading into the intervertebral or vertebral canal can be challenging technically. The tumour is identified by inspection and palpation of the brachial plexus, and dissected proximally to the spine. For the lumbar plexus, this may require partial resections of the ilium[2, 3]. The portion of the tumour located inside the vertebral canal must then be approached and dissected, which is achieved through a lateral approach to the cervical or thoracic spine for PNST of the brachial plexus, and either through a lateral or a dorsal approach to the lumbar spine, depending on how far cranially the tumour extends, for PNSTs of the lumbar plexus. The greatest margins proximally will be achieved by performing a durectomy around the origin of the affected root and visualising and distracting the rootlets away from the spinal cord itself. Commonly, the presence or absence of invasion of the spinal cord can only be ascertained after opening of the dura mater. In cases where the rootlets are infiltrated, only minimal margins can be obtained proximally (1-2 mm or less), but this does not always signify that the resection will not be complete. In addition, precise pathological assessment of the margins at the level of the sectioned rootlets can be difficult, even if they are cautiously fixed and inked. Dissection of more invasive tumours can be carried out microsurgically within the spinal cord, although this obviously carries a much greater risk of postoperative neurological deterioration.

Recovery from surgery is straightforward for cases without durectomy but can be more protracted for cases with extensive tumour manipulation or dissection within the spinal cord. Cases in which the spinal cord is significantly manipulated can take weeks to months to stand and walk without assistance, or may not recover. Most dogs will however recover similarly to dogs having had spinal surgery and/or amputation, depending on the type of procedure they underwent.

Forelimb amputations with thoracic wall resections

Forelimb amputations combined with chest wall resections can be required for tumours of the proximal forelimb or of the axilla/chest wall. The portion of thoracic wall to resect usually consists of the first few ribs, with or without a portion of the sternum.

The thoracic wall resection part of the surgery generally start with an intercostal thoracotomy at the caudal boundary of the planned resection. This thoracotomy allows verification of the macroscopic intrathoracic extension of the tumour, to ascertain that it is not greater than assessed on advanced imaging. Ribs are then sectioned with an oscillating

saw or rib shears, along the line of the ventral or dorsal boundary of the planned resection. Between each rib section, the intercostal muscles are cut and the intercostal artery and vein are cauterised with uni- or bipolar electrocautery. Once this ventral or dorsal section has been carried out, the costal flap can be slightly elevated to assess once more the macroscopic extension of the tumour and verify that the next planned section line is appropriate. The next section line is then performed (ventral/dorsal or caudal/cranial) and, once more, the tumour position and extension is checked by elevating the costal flap further. The remaining section line is then performed and the costal flap is freed. It is lifted gently and the presence of any adhesions of the flap/tumour with intrathoracic structures (diaphragm, lungs) is evaluated. When the tumour is adherent to a lung lobe, a partial or complete lung lobectomy. Occasionally, adhesions of the tumour with the pericardium necessitate to perform a partial pericardectomy. In all such cases, adhesions between the tumour and intrathoracic structures are not detached to avoid dissemination of tumour cells in the surgical field and chest. The adhered organ is partially resected en-bloc with the tumour whenever possible.

A chest drain is then placed under direct visual control and intercostal nerve blocks are performed on resected rib spaces and 2 to 3 spaces cranially and caudally to them.

The reconstruction of body wall defects must use autologous tissues as often and as much as possible to reduce the risk of postoperative complications[4]. The utilisation of synthetic meshes only to reconstruct defects in the thoracic wall was associated with 12.8 times more complications and the combined use of meshes and autologous tissues with 3 times more complications, both compared with the exclusive use of autologous tissues[4]. In many cases, a muscle flap using the latissimus dorsi can be used to cover thoracic wall defects. To perform such a flap, the cranioventral insertion of the muscle on the humerus is left intact and its caudodorsal insertion is on the lumbar fascia is sectioned as caudally and as dorsally as possible to elevate the muscle, which is then transposed and sutured to the edges of the thoracic wall defect, thereby covering it. Other muscle flaps, using nearby muscles such as pectorals, or lumbar fascia grafts can also be used to cover the parietal defect. Lastly, when all sources of autologous tissues are insufficient to entirely cover the body wall defect, synthetic implants such as meshes, either non-absorbable (e.g. polypropylene) or absorbable (e.g. polydioxanone), can be used. Ideally, intracavitary organs should be prevented to come into contact with the mesh by interposing autologous tissues. The greater omentum is most commonly used for this purpose. It is easily transposed and brought to the parietal defect, directly for abdominal wall defects and either through a retrocostal or transdiaphragmatic approach for thoracic wall defects.

The addition of rigid implants such as lubra plates is extremely rarely needed for support of thoracic wall reconstructions of defects of up to 6 ribs. However, the use of such implants or of surgical cement (polymethylmetacrylate; PMMA) may be required to rigidify and stabilise the rib cage after sternal resections. When reconstructing thoracic wall defects of up to 6 ribs without any rigid implants, the reconstruction results in a soft portion of thoracic wall and paradoxical movements of this portion during respiration in the immediate postoperative period. However, as the tissues heal and get more fibrotic, this portion of the wall progressively rigidifies and these paradoxical movements markedly decrease or completely resolve over a few weeks after surgery.

Amputations with hemipelvectomies and abdominal wall resections

The term "hemipelvectomy" refers to partial resections of the pelvis. It can be combined with hindlimb amputation ("external hemipelvectomy") or not ("internal hemipelvectomy"). A classification of hemipelvectomies in 6 types has been described[5] (Figure 1). Hemipelvectomies are most commonly performed for resection of tumours, but can also be indicated for treatment of malunion of pelvic fractures causing functional abnormalities[6].

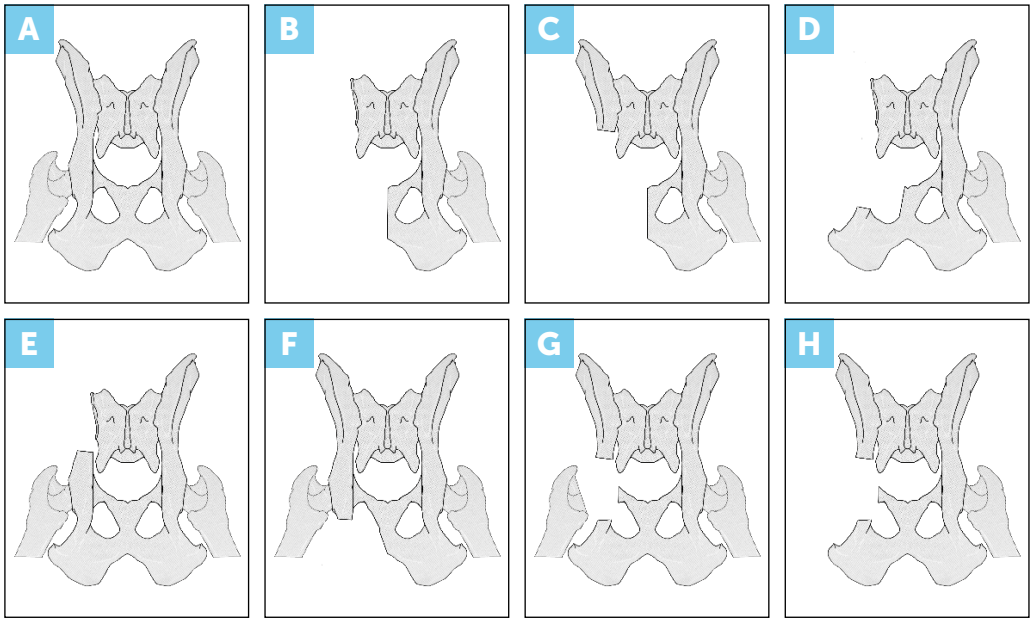

Figure 1: Classification of hemipelvectomies (A) Normal pelvis; (B) Total external hemipelvectomy; (C) caudal external hemipelvectomy; (D) cranial external hemipelvectomy; (E) cranial internal hemipelvectomy (iliectomy); (F) caudal internal hemipelvectomy (ischiectomy); (G) Middle internal hemipelvectomy (acetabulectomy); (H) Middle external hemipelvectomy (acetabulectomy).

The surgical technique has been well described elsewhere[5, 7]. Provided appropriate technique is used, intraoperative complications are infrequent, with haemorrhage being the most common: in one study substantial haemorrhage occurred in 7 of 84 dogs, and 2 required blood transfusion[8]. Care should be taken to protect intrapelvic organs from iatrogenic damage. Similarly, attention should be paid not to leave bone prominences which are poorly covered with soft tissues, as this would favour the development of pressure sores postoperatively. Postoperative complications are also uncommon, being dominated by wound and abdominal wall complications (dehiscences and hernias)[8].

Cranial hemipelvectomies including parts of the pubic rim or ilium may need to be combined with partial resections of the abdominal wall, depending on the indication for resection. The abdominal wall is partially resected en-bloc with the pelvis, at the time of the ventral approach to the pubis and/or ilium.

When a portion of the abdominal wall is resected, the resulting parietal defect can be reconstructed using parts of the thigh muscles if they can be spared, a synthetic mesh, or a combination of both. Autologous tissues must be used as often and as much as possible to reduce the risk of postoperative complications. If the caudal pelvis can be spared, the caudal thigh muscles (e.g. semi-membranosus and semi-tendinosus) can be preserved and transposed cranially to cover the abdominal wall defect. They are sutured simply to the remaining abdominal wall muscles.

When all sources of autologous tissues are insufficient to entirely cover the body wall defect, synthetic implants such as meshes, either non-absorbable (e.g. polypropylene) or absorbable (e.g. polydioxanone), can be used. As much as possible, abdominal organs should be prevented from coming into contact with the mesh by interposing autologous tissues between the peritoneal cavity and the mesh. The greater omentum is most commonly used for this purpose, as it is easily transposed and directly brought to the parietal defect. If the omentum is insufficient, muscle flaps (e.g. transverse abdominis muscle) can be used. Bone tunnels can be made in the remaining portions of the pelvis to anchor sutures. Repair of defects of the pelvic diaphragm is not mandatory[7], but should be carried out if easily possible with autologous tissues.

Regardless of whether hemipelvectomies are combined with resections of portions of the abdominal wall, the functional outcome is typically excellent, equivalent to that of a similar patient undergoing hindlimb amputation. The considerations around the propriety of performing surgery on an individual patient with regards to postoperative function are therefore similar for hemipelvectomies and conventional hindlimb amputations.

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Liver surgery: lobectomies

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General considerations

Anatomy

In dogs and cats, the liver is mostly contained within the costal arch. Its cranial surface lies against the diaphragm and its caudal surface is related to the stomach, pancreas, right kidney, duodenum and sometimes spleen. In these species, the liver has 6 lobes: the *right lateral*, *right medial*, *quadrate*, *left medial*, *left lateral* and *caudate* lobes. The caudate lobe is further subdivided in two processes: the *caudate* and *papillary* processes. The gallbladder lies between the quadrate and right medial lobes and can be punctured by inserting a percutaneous needle to the right of the tip of the xiphoid process. The bile produced by each liver lobe is drained through the corresponding *hepatic duct*, which empties in the *(common) bile duct* (or *ductus choledochus*). The bile accumulated in the gallbladder reaches the bile duct through the *cystic duct*. The bile duct empties in the duodenum at the level of the *major duodenal papilla*. In dogs, the bile duct and the (major) pancreatic duct often open side by side on the papilla, whereas in cats, they often share the same opening.

The liver is tethered to the diaphragm by reflections of its serosa, the coronary, right triangular and left triangular ligaments. The latter are expansions of the coronary ligament and can safely be sectioned to help in mobilising the right lateral and left lateral liver lobes.

The caudal vena cava courses through the right half of the liver. Consequently, the right hepatic veins are shorter than the left. In other words, the hili of the right and central lobes are closer to the caudal vena cava than those of the left lobe. This is one of the reasons why left lobectomies are technically easier than right or central ones.

The portal vein collects the venous blood from all unpaired abdominal organs (stomach, pancreas, spleen, intestines), except for the caudal portion of the rectum. It enters the liver on its caudal (visceral) surface. In the dog, it then divides in a smaller right and larger left branches. The right branch supplies the caudate process of the caudate lobe and the right lateral lobe. The left branch gives off branches to the right medial lobe, to the papillary process of the caudate lobe and then divides in 3 branches for the quadrate, left medial and left lateral lobes. This pattern seems to be rather consistent among dogs. In the cat, the portal vein is reported to divide into right, central and left branches. However, its anatomy has been much less studied in this species and data pertaining to the accuracy and variability of this pattern are lacking.

Perioperative considerations

The liver has numerous metabolic functions which can be impaired when it is diseased. Of particular relevance for the surgeon is the fact that most animal with liver disease have abnormal concentrations of coagulation factors and prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT). However, despite these abnormalities, animals with naturally occurring liver disease most often show no increased tendency to bleed (diathesis).

Hypoalbuminaemia and hypoproteinaemia are also frequently associated with liver disease and are important risk factors for complications of wound healing and poor postoperative recovery.

Therefore, prior to surgery, it is important to assess the albuminaemia, glycaemia, haematocrit, natraemia, kalaemia, chloraemia, and to evaluate the clotting function (mucosal bleeding time, PT, aPTT). Appropriate preoperative goals are to maintain albuminaemia above 20 g/l and the haematocrit above 25%. This is sought through administration of blood products as required. Also, preoperative parenteral administration of vitamin K1 (0.2-7 mg/kg SC q8h, no intravenous or intramuscular administration) for 24 to 48 hours before surgery is often judicious, as absorption of this vitamin is frequently impaired with biliary obstructive diseases.

Surgical approaches

The liver is most commonly approached through a median coeliotomy extending from the xyphoid process cranially to the umbilicopubic area. This allows performance of most hepatobiliary surgeries. However, this approach is sometimes found to be inadequate, either because of too little exposure of the liver or insufficient room to manoeuvre bulky instruments such as staplers. The exposure of the liver and surrounding structures can then be increased by a number of additional incisions. Unilateral or bilateral paracostal incisions can extend from the cranial portion of the median coeliotomy incision. Exposure of the diaphragmatic surface of the liver can be improved by extending the median coeliotomy cranially to the thorax (caudal median sternotomy). To avoid a sternotomy while still making the

liver mobilisation easier, the diaphragm can be incised (phrenotomy) to create a pneumothorax. This results in the diaphragm losing most of its concave shape and in the liver being more greatly mobilisable caudoventrally. When the procedure is complete, the diaphragm is closed routinely and the pneumothorax drained.

Minimally invasive hepatobiliary surgery

A number of hepatobiliary surgeries can be performed with a minimally invasive approach (laparoscopy). The easiest procedures are liver biopsies and laparoscopically-assisted percutaneous cholecystocentesis for bile collection. As the surgeon gains experience, more technically challenging procedures, such as cholecystostomies or cholecystectomies, can be attempted. Also, laparoscopic attenuation of portosystemic shunts has been described.

The detailed description of minimally invasive hepatobiliary surgery is beyond the scope of this text and the interested reader is referred to the relevant literature.

Surgical techniques

Liver biopsy

Liver biopsies can be performed using several techniques depending on the position of the tissues to be sampled. In case of diffuse disease, biopsies are preferentially taken from the edges of the liver. However, it is important not to take tissues only from the very edge, are they are more likely to be affected by fibrosis which can hamper accurate diagnosis of the actual liver condition.

The guillotine method consists of placing a ligature around a portion of a liver lobe and to crush the liver parenchyma while tightening it. A small portion of liver is left between the ligation and section sites to avoid slippage of the ligature. If the ligature tends to slip off the liver lobe when it is tightened, small indentations can be made with scissors on the liver edges to overcome this difficulty. Large liver samples can be obtained through this method with minimal haemorrhagic risk.

Alternatively, or if a discrete lesion away from the liver edges is to be biopsied, a punch or wedge biopsy can be taken from any area of the liver. Avoiding penetrating more than half of the thickness of the liver lobe decreases the risk of injury to a major hepatic vessel or duct as these run closer to the concave surface. If haemorrhage is significant, haemostasis is sought by digital pressure, maintained for 3 to 5 minutes, by application of haemostatic sponge (e.g. gelatine foam, Gelfoam®) or by suturing the wound, in a mattress or cruciate pattern. In the latter case, a large diameter suture should be used with minimal tension as the liver parenchyma is highly friable. The aim of such suture is not to perfectly appose the edges of the wound but rather to increase the pressure on the wound enough to promote spontaneous haemostasis.

Liver lobectomy

Liver lobectomies can be partial or complete. Considering the extreme potential for regeneration of the liver, when partial lobectomy is indicated, it can be easier and safer to perform a complete lobectomy, especially for left lobes.

A partial liver lobectomy consists of the excision of only a portion of a hepatic lobe. The liver capsule is sharply incised along the desired line of section. The hepatic parenchyma is then bluntly dissected either with a blunt instrument or fingers. Large vessels and duct encountered are ligated, clipped or sealed. Minimal self-resolving haemorrhage is often present on the section surface of the liver parenchyma after completion of the procedure. If deemed necessary, topical haemostatic agents (e.g. fibrin, cellulose, collagen or gelatine sponges) can be placed on the cut surface of the liver to promote haemostasis. Alternatively, partial liver lobectomies can be performed with automatic staples (e.g. TA staplers).

A complete liver lobectomy consists of the excision of an entire hepatic lobe. This is achieved by dissection and ligation of the lobar artery, vein and duct at the level of the lobe hilus. In small dogs and cats, mass ligation can be used for excision of the left lateral or left median lobes, but isolation and separate ligation of these structures is recommended for other lobes or in medium-size and large dogs. Alternatively, a stapling device (e.g. TA stapler) can be used to permanently occlude these structures without the need to dissect and isolate them. In either case, the lobe to be excised must be mobilised and freed from any attachments by transecting its ligaments (triangular, hepatorenal) or separating it from the gallbladder as necessary. Once the vascular and ductal isolation is performed, the liver lobe can be safely transected.

The hilus of the liver lobe(s) to be resected may not be readily apparent and may need to be isolated. The inside of a Poole suction tip can be used for dissection of the liver parenchyma away from large vascular and biliary structures.

As a rule, liver lobectomies are easier to perform on left lobes rather than on central and right lobes. The main reason is that the vascular pedicle of the left lobes is longer, which makes isolation of their hilus easier.

Surgery is ideally planned on advanced imaging, CT angiogram especially. In most cases, it will allow precise preoperative determination of the extent of the resection and its proximity to the hilus of the liver lobe(s) to resect. The surgeon can therefore prepare appropriately (time and material resources, availability of blood products, etc.) according the expected technical difficulty of the procedure.

When resecting tumours of the right division of the liver extending close to the porta hepatis, it is prudent to prepare for the vascular exclusion of the liver, by placing Rummel tourniquets around the ventral boundary of the epiploic foramen ("duodenohepatic ligament", containing the portal vein and hepatic artery), as well as around the caudal vena caudally and cranially to the liver (which is most easily achieved in the chest, through a phrenotomy). The tourniquets are kept loose and only tightened if a major vascular breach occurs, which most commonly occurs in the vena cava during elevation of the tumour and section of the hepatic veins of the right lobes of the liver (caudate process of the caudate lobe, right lateral lobe).

Another relevant notion is that tumours of the central division of the liver (right medial and quadrate lobes) typically require resection of the entire central division. If the tumour is adherent or invading into the gallbladder, a cholecystectomy is performed en-bloc with the central division resection. If not, the gallbladder can be elevated and preserved. After resection of the central division of the liver, it is fixed to the diaphragm with sutures (cholecystopexy).

Liver surgery: portosystemic shunts

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Portosystemic shunts are abnormal vessels allowing communication between the splanchnic and systemic circulations. They are either congenital or acquired, single or multiple, extrahepatic or intrahepatic.

Diagnosis

Portosystemic shunts (PSS) take blood away from the liver, making underfed and causing hepatic underdevelopment, atrophy and fibrosis, the end-stage of which can be live failure. They also let blood reach the systemic circulation without having been filtered and devoid of many neurotoxic substances by the liver.

Clinical signs associated with HE can be broadly separated in neurological, gastrointestinal and urinary. Neurological signs include depression, listlessness, ataxia, pacing, circling, head pressing, cortical blindness, seizures and coma. They have been classically described as correlated with meals, but it has been shown to only be the case in 25% to 50% of patients. Gastrointestinal signs occur in about 30% of canine cases and include anorexia, vomiting and gastrointestinal bleeding. In cats, ptyalism is a very common clinical sign, present in 75% of cases. Urinary signs include dysuria, stranguria, pollakiuria and haematuria and are associated with ammonium urate crystalluria.

Clinical pathology changes most commonly encountered in animals with PSS include mild to moderate microcytic normochromic nonregenerative anaemia, elevated alkaline phosphatase (ALP) and alanine aminotransferase (ALT) activities, hypoalbuminaemia, decreased blood urea nitrogen (BUN), hypocholesterolaemia and hypoglycaemia. Coagulation times are almost consistently prolonged in affected dogs, these abnormalities are infrequently clinically significant. Urinalysis abnormalities include hyposthenuria, ammonium biurate crystalluria and signs of secondary urinary tract infection. The most common laboratory tests used for diagnosis of liver dysfunction include bile acids stimultation test (BAST) and plasma ammonia levels.

Survey radiographs are of limited value in the diagnostic of PSS. Portovenography, either jejunal or transplenic, can be performed pre- and/or intra-operatively and is very sensitive and specific for PSS detection. Ultrasound is still widely used for assessment of PSS, with 74% to 95% sensitivity and 67% to 100% specificity. Scintigraphy is quite sensitive for detection of PSS, but cannot discriminate between EHPSS and IHPSS, nor can it give any information of the number of shunts. Computed tomographic angiography has become the gold-standard for characterisation of PSS[1], as it is safe[2], non-invasive, more accurate than portographies[3] and ultrasound[4], and allows precise characterisation of the shunt morphology[5].

Treatment

Surgical attenuation of PSS is the current treatment of choice, as it has been shown to result in better survival rates and fewer clinical signs than medical treatments[6, 7]. Increasingly, interventional procedures are also available for treatment of PSS, with good results[8-10]. The principles of interventional radiology management of PSS will not be covered here. A recent short review is available elsewhere[11].

Medical treatment

A medical treatment can be used to decrease the clinical signs and optimise patients prior to surgical correction of operable CPSS, or for long-term management of multiple acquired or inoperable CPSS.

It aims at decreasing the clinical signs associated with HE by reducing the amount of neurotoxic by-products of protein metabolism. It is therefore based on the administration of a low-protein diet, antibiotics to decrease the number of ammonia-producing bacteria in the digestive tract, lactulose to decrease the production and absorption of ammonia, and gastroprotectants and antacids to prevent or treat gastrointestinal ulcers and bleeding. Seizure control is sought through administration of phenobarbital, potassium bromide, gabapentin, or propofol. Levetiracetam is another anticonvulsant commonly used to prevent or control seizures in PSS patients[12], which the author routinely prescribes to patients for a few days before surgery at 10-20mg/kg TID.

Surgery

Identification of the shunt

Most PSS are found to terminate on the caudal vena cava at the level of the epiploic foramen, which should therefore be inspected first. Any blood vessel found to enter the caudal vena cava between the renal and phrenico-abdominal

veins and the liver should be considered as potentially being a PSS. Blood flow turbulences are often visible in the caudal vena cava or shunt vessel, which further supports the shunt identification. If no abnormal vessel is found through the epiploic foramen, the omental bursa must be opened by tearing the superficial leaf of the greater omentum. This allows inspection of the tributaries of the portal vein. Most often, shunting vessels originate from the gastrosplenic vein in dogs and left gastric vein in cats. Portoazygos shunts are found as abnormal vessels penetrating the diaphragmatic crura or aortic hiatus. Occasionally, shunts cross through the diaphragm at the oesophageal hiatus. If no abnormal vessel is found, the presence of an IHPSS should be evaluated. This is done by identifying the left hepatic veins cranial to the liver for the left lobe, or branches of the portal vein caudal to the liver for the right and centre lobes. Temporary occlusion of any of these veins communicating with the shunt results in immediate signs of portal hypertension. Acute or gradual occlusion of this vessel is then carried out. In addition, any dilation or abnormally soft, fluid-filled consistency of a liver lobe should raise the suspicion of the presence of an IHPSS passing through it.

Shunt occlusion

Two types of occlusions are used for PSS attenuation: acute and gradual.

Acute surgical attenuation consists of completely or partially ligating the abnormal vessel. In many cases, complete ligation is not possible without life-threatening portal hypertension. Partial occlusion may result in persistent shunting and necessity for a second surgery to ligate the shunt further. Acute attenuation always carries a risk of postoperative portal hypertension, which may cause death or necessitate reintervention to remove the ligature.

Gradual attenuation of a PSS aims at giving time for the intrahepatic portal vasculature to develop as the PSS is progressively attenuated, thereby decreasing the risk of portal hypertension, and can be achieved with ameroid constrictors, cellophane bands or hydraulic occluders. A recent study found more frequent residual shunting after cellophane attenuation than ameroid constrictor placement, although complication rates and clinical outcomes were similar[13].

The author currently prefers cellophane banding over other techniques. Cellophane bands placed around shunt vessel induce inflammation around the vessel, leading to its occlusion. The rate of occlusion is therefore dependant on the amount of inflammation induced. They are reported to induce complete occlusion of the PSS within 6 months. Cellophane can be used for shunt vessels of any size, as well as for EHPSS and IHPSS. In early reports, it was advocated to attenuate shunts intraoperatively to less than 3mm of diameter for complete occlusion to occur, but more recent evidence suggest that no attenuation is necessary to achieve long-term complete occlusion, regardless of the shunt size[14], which avoids the risk of inducing portal hypertension. The cellophane band is therefore just applied around the shunt vessel and secured with 3 or 4 vascular clips.

Postoperative care

If any attenuation has been induced surgically, the patient is monitored for signs of portal hypertension, which may warrant reintervention to relieve the shunt occlusion.

Postoperative hypothermia and hypoglycaemia are frequent and must be actively monitored, and promptly addressed. Postoperative seizures occur in 3% to 7% of dogs and 8% to 22% of cats after PSS attenuation, typically up to 4 days after surgery. Recently, one study reported that 11% of 253 dogs had postattenuation neurological signs (PANS)[15]. Treatments include midazolam, propofol, barbiturate or levetiracetam administration.

Once discharged from the hospital, animals are maintained on a low-protein diet, antibiotics, lactulose and gastrointestinal protectants. Bile acids levels are monitored 1, 3 and 6 months after surgery. In the absence of clinical signs of HE, antibiotics are stopped 1 month after surgery and lactulose administration is discontinued a few weeks later. Approximately 3 months after surgery, if tolerated, the diet is progressively returned to normal.

Prognosis

Both short- and long-term, dogs with CPSS treated surgically have better survival rates and less persistent clinical signs than those treated medically[6, 7]. In dogs, reported mortality rates range from 2% to 32% after EHPSS surgical attenuation and from 0% to 27% after IHPSS surgical attenuation. Good to excellent outcomes in surviving dogs are reported in 84% to 94% for EHPSS and 50% to 100% for IHPSS.

In cats, perioperative mortality ranges from 0% to 23%. Good to excellent long-term outcome is reported in 33% to 80% of surviving cats.

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Nurse Stream

Nicola Ackerman (UK)

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(Nurse Stream)

Nicola joined the Veterinary Hospital Group as a Veterinary Nurse at our Plympton Veterinary Health Centre in 2002, progressing to Head Veterinary Nurse of the practice in 2004 and now Senior Medical Nurse at the Veterinary Hospital. Nicola also works as one of the emergency night team. Nicola has worked in the veterinary industry since 1994. In 1999, she graduated from Hartpury College with an Honours Degree in Equine Science, specialising in nutrition. She has subsequently gained post-graduation certificates in small and exotic animal nutrition and in emergency critical care. Nicola's interests are in medical nursing, nutrition and emergency care; and she helps to run the nurses' clinical team alongside eight other nurses. These clinics offer advice on nutrition, preventative healthcare and the care of puppies and kittens. She is also a clinical coach, training our student veterinary nurses in the practice. Nicola has written textbooks on Companion Animal Nutrition for veterinary nurses and technicians, and The Consulting Veterinary Nurse, a book on nursing clinics. Nicola sits on boards for the Veterinary Medicines Directorate and the Editorial Board for the Veterinary Nursing Journal. Nicola has lectured internationally in Russia, Eastern Europe, Australia, Ireland and most recently, the USA. Nicola is the only veterinary nurse in the UK that holds the Veterinary Technician Speciality (VTS) in nutrition. Nicola has won several awards, The Blue Cross BVNA Welfare Award in 2010, The SQP Veterinary Nurse of the Year in 2011, The SQP Mastermind Award in 2012, and the SQP Nutritional Advisor Award in 2013. In 2012, Nicola won the prestigious award of the CAW Professional Development Award for outstanding service to the veterinary nursing profession. In the same year, she was made an honorary member of the British Veterinary Nursing Association. At home, Nicola has a three-legged cat called Henry and a Border Terrier cross called Splat.

General: the role and importance of veterinary nurse

Nicola Ackerman (UK)

The role of the veterinary nurse has evolved greatly, standing now as a fee earning regulated professional in some countries. Nurses have a vital role to play in the veterinary practice not just as veterinary assistants but in the role as consulting nurses, not limited just to the offering of advice to clients, but including the performing the groundwork in collecting data parameters (blood tests, urine sampling, radiography, complex diet and behavioural histories) in order for the veterinary surgeon to then interpret the collected data and make a diagnosis, the undertaking of preventative healthcare for animals, post-operative appointments, and wound management.

One of the roles of the veterinary nurse is to ensure that the client has good compliance with the recommendations given by the veterinary surgeon. In some cases this can refer to medications, and the nurse can discuss with the owner that they are able to administer the medications that their pet has been prescribed. In some cases a different format of medication, liquid instead of tablets, can be of use. In these cases referral back to the veterinary surgeon is required as the client will require a different medication to be prescribed. Many owners do appreciate guidance on the administrations of medications, whether this is verbally or with leaflets. In regards to nursing clinics they are best utilised when the veterinary surgeon offers all newly diagnosed patients an appointment with the nurse in order to discuss all aspects of care for that patient.

Laboratory work, the emergency database and beyond

Nicola Ackerman (UK)

The emergency database is the same for all critical care patients that are presented to the practice. The database includes;

- Packed Cell Volume (PCV), alongside a refractometer total solids (TS) or total protein (TP).`
- Glucose
- Blood urea nitrogen
- Evaluation of a blood smear

- Increase in PCV and TP = dehydration
- Decrease in PCV and TP = aggressive IVFT, haemorrhage.
- Decreased PCV and normal TP = possible increased destruction of RBCs.
- Increased PCV and decreased TP = dehydration with protein loss, e.g. HE.

These values will help the clinician towards the IVFT requirements.

In many cases a full haematology and biochemistry are run on the in-house analysers from the start. Additional tests can include species specific pancreatic lipase test, saline aggluntination tests, blood gas analysis, clotting times and lactate. These can be performed in house if equipment is available. In emergency situations the most useful are clotting times and saline aggluntination tests.

In-house cytology ears and skin

Nicola Ackerman (UK)

Cytology is important in the evaluation of otitis externa, it allows targeting of therapeutics and thus permits accurate monitoring of response to these medications, (Angus, 2004). Samples for cytology can be obtained either via a swab or gloved finger, the material is rolled onto the microscope slide. Diff-Quik should be used for microscopic examination, (Angus, 2004).

Samples should be viewed under the x400 dry field and X1000 oil immersion lens of the light microscope. A semi-quantitative system of assessing yeasts and bacteria number in the sample can be instigated. Recommendations are made that samples with greater than 5 yeasts per high power dry field (HPDF) (x400 magnification) and greater than 25 bacteria per HPDF (>12/HPDF for yeast and >15/HPDF for bacteria in cats) being considered significant, (Ginel *et al.,* 2002).

Shaw (2016) stated opinions surrounding the value of bacterial culture and selectivity testing in otitis externa is divided. This is due to the higher concentrations of the antibiotic being achieved *in vivo* over coming apparent *in vitro* bacterial resistance in cultured samples. Shaw (2016) has indicated certain circumstances when culture and selectivity should be performed:

- If rod-shaped bacteria are seen on cytology
- When the patient has had multiple previous courses of antibiotics
- If there has been poor response to previous treatments
- If systemic treatment is indicated.

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In-house urinalysis (including microscope analysis)

Nicola Ackerman (UK)

Before urinalysis can be started it is important to know a few details:

- How was the sample collected – voided, cysto, via catheter.
- What was it collected in – sterile urine sample pot, jam jar.
- When was the sample collected?
- How was it stored, from time of collection to time of urinalysis.

Commercial Multistick analysis.

- Bilirubin: Dogs negative to +1, cats negative.
- Blood: Negative; positive results may be caused by trauma induced by collection method.
- Glucose: Negative.
- Ketones: Negative.
- Nitrite: Test pad unreliable in cats and dogs.
- pH: 5.5-8.5
- Protein: Negative; trace to +1 in highly concentrated samples.
- Specific Gravity: Test pads unreliable in dogs and cats.
- Urobilinogen: Negative
- White cells (leukocytes): Test pad unreliable in cats and insensitive in dogs.

Urine specific gravity measurement is vital in telling you how concentrated a sample is. Urine SG can be vital to aid in prevention and dissolution of stones and crystals. Need to get the urine specific gravity as low as possible in these cases and can be more significant than the pH level. Always use refractometer.

Sediment Analysis Normals.

- RBCs/hpf : 0-5 (Feline and Canine)
- Casts/lpf : Occasional hyaline (Feline and Canine), no others should be seen.
- Epithelial Cells/hpf : Occasional
- Fat Droplets /hpf: Uncommon in dogs, common in cats.
- Bacteria /hpf: Negative
- Crystals/hpf: Variable

Nutrition: for gastrointestinal cases

Nicola Ackerman (UK)

The causes of many gastrointestinal disorders in dogs can be difficult to initially identify. Treatments initially start based on the clinical symptoms, which do tend to resolve over a couple of days. In situations where clinical symptoms persist (vomiting, diarrhoea and weight loss) a diagnosis may be required in order to accurately treat the patient, (Table 1). Electrolyte imbalances can quickly develop in animals with severe diarrhoea, with oral hydration or intravenous supplementation being provided when required, intravenous routes being required if the animal is vomiting or clinically dehydrated.[1]

The gastrointestinal system requires nutrition, and therefore requires to be fed, even when the disease / disorder still persists. With there being numerous gastrointestinal disorders and with each individual reacting differently to different diets, it is important to obtain a full nutritional / diet history from owners about their pets. Talking to the owner and finding out what the pet has traditionally ate, how well does the pet eat, does it only eat a home cooked diet or a specific flavour of food is not only important to find out whether the gastrointestinal symptoms are related to what the pet is being fed (or dietary indiscretion), but also where to go to next in the recommendation of a new diet.

Dietary Management

Dietary manipulation can aid in a number of nutrient responsive conditions, but it can be a process of elimination to find the one that suits the individual the best. What may have suited one animal may not suit another. Some animals may require a combination of diets; some may have concurrent conditions which mean that the normal recommended diet may not be suitable, or even cause more problems. Many diets aimed at conditions affecting the gastrointestinal system work on the bases of manipulation of fat content, fibre content, digestibility or novel protein source (Table 2). Monitoring of the animal whilst dietary change is occurring is important, weight, body condition, faecal quality and output, and the monitoring of blood parameters (Folate, B12) can all indicate the success of nutrition. Gaining a diagnosis from the veterinary surgeon is an important starting point; though there are many occasions where nutrition can also be used as a diagnostic tool (for example dietary sensitivities).

For those cases that are suffering from severe unretractable vomiting for over 48hours total parenteral nutrition must be provided, alongside very small amounts of nutrition being given by mouth (microenteral nutrition), and the necessary medications prescribed by the veterinary surgeon[2]. The use of micro-enteral nutrition has shown to improve prognosis of many cases that were traditionally starved. Dietary therapy for dog's suffering from acute pancreatitis was traditionally nil-by-mouth, until the clinical symptoms ceased, and in some practices this could be up to five to seven days. Evidence has shown that nil-by-mouth in these cases has little benefit to the animal. The oral nutritional support is required to prevent gastroduodenal ulceration, bacterial translocation from the gut and septicaemia. Small amounts of watered down baby rice or cottage cheese can be used before moving onto a commercial low-fat, highly digestible diet, oral hydration fluids can also be utilised[2].

Primary causes of chronic diarrhoea	Secondary causes of chronic diarrhoea
Infectious Endoparasites, enteropathogens, small intestinal dysbiosis	**Exocrine Pancreatic Disease** Exocrine pancreatic insufficiency Chronic pancreatitis
Inflammatory Idiopathic inflammatory bowel disease	**Hepatic Disease** Liver failure
Neoplastic Intestinal lymphoma Other	**Kidney Disease** Chronic kidney disease
Mechanical Sliding intussusception	**Adrenal disease** Hypoadrenocorticism
Toxic	**Thyroid Disease** Hyperthyroidism in cats Hypothyroidism in dogs
Other rare conditions	**Cardiovascular disease** Central nervous system disease

Table 1: Causes for chronic diarrhoea.[3]

Diet Type	Dietary Characteristics
Novel protein source	Contains one protein and one carbohydrate source that needs to be novel to the animal.
Hydrolyzed protein diet	Contains protein that has been broken down into smaller peptides or amino-acids. The diets differ in degree of hydrolization, and protein source.
Easily digestible diet	Low-residue diet will contain a good source of prebiotics.
High Fibre diets	Useful with fibre responsive colitis.
High fat/low carbohydrate or moderate fat/ moderate carbohydrate diet	Mechanism of action unknown, chosen diets needs to digestible.

Table 2: Dietary types that may be effective that may be effective for a dietary trial with chronic diarrhoea in cats and dogs.[3]

In human medicine there is a continuing bank of evidence indicating that "feeding through" diarrhoea with an appropriate diet can be beneficial. Comparisons can be difficult, as many cases of diarrhoea in man tend to be secretory, whereas osmotic diarrhoea is more common in dogs and cats. The advantages of "feeding through" include maintaining mucosal health, reducing the risk of bacterial translocation, and aiding in the "flushing out" of the causal factor. Feeding through should not be used in animals that are vomiting or severely dehydrated. With animals that are vomiting or the GIT is not functioning, the animal's nutritional requirements should be met through parenteral nutrition. The obvious disadvantage of "feeding through" is the risk of "accidents" in the house, and the increase in faecal volume. Whether food is withheld or not, unlimited access to water must be maintained at all times. The use of oral rehydration solutions containing simple sugar, soluble fibres, peptides and electrolytes should be advocated in these cases. When using this method feeding a diet, which won't cause an inflammatory reaction in the future is important. Dietary antigens can cross the compromised gastrointestinal mucosa and set up a hypersensitivity reaction. Use of a novel protein and/or carbohydrate source should be recommended. Once the animal is then well, and transferred to its original diet, it is unlikely to have any reactions to the original protein source.

Dietary transitions are as important as the diet itself. When the gastrointestinal system is dysfunctioning transitions may need to be over a longer period of time. Palatability of the diet can be affected by the animal feeling ill, nausea being the biggest cause. Treatment to correct any factors of illness that effect palatability is important, alongside correction of any hydration issues.

Pro- and Pre-biotics

Pro- and Pre-biotics are widely used in the treatment of gastrointestinal disorders. Prebiotics are substances that are able to alter the gastrointestinal flora in a manner to benefit the microorganisms, these are normally types of fibres (e.g. Manno-oligosaccharides, Fructo-oligosaccharides) or amino acids like glutamine. Probiotics however, are a live microbial feed supplement, which benefits the host animal by improving the gastrointestinal microbial population. Probiotics generally used are comprised of lactic acid bacteria such as *Lactobacilli, Streptococci* and *Bifidobacteria.*

Pharmaceuticals

Many different pharmaceuticals can be utilised in the treatment of different gastrointestinal problems that can be seen in veterinary practice. It is important when conducting nursing clinics to read the clinical history and to make note of the medication regimes that the veterinary surgeon has prescribed for the animal. In some chronic cases drug dosages are tapered to effect and therefore support from the veterinary nurse may be required in order to help clients achieve this.

Vitamin B12 (cobalamin) injections are commonly used in animals with low blood cobalamin, which is commonly seen in animals with gastrointestinal problems. Weekly injections in some cases may be required for a number of weeks, and this is a role for the veterinary nurse to undertake. Oral supplementation is possible in some cases, and there are now nutritional supplements which contain Vitamin B12.

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Feeding peri-operatively

Nicola Ackerman (UK)

Historically owners were advised, 'no food or water after 8pm'. Potentially the animal can go without water for >12 hours. Water on an empty stomach will be out of the stomach within 20-30 minutes. Remove water at time of pre-med, schedule your procedures, and administer pre-meds accordingly.

Once sufficiently recovered, offer water and then food. Most cats won't drink as they derive their water from wet food. Always feed wet diet, due to increased water content and we want to ensure correct hydration levels. Increased palatability with moist diets.

Avoid any vomiting. Diet that promotes good gastric emptying times. Supplies the pet with the nutrients required. Easily digestible diet, with good palatability.

What Diets to Use?

This really does depend on a few factors:

- The clinical status of the patient,
- What route the nutrition is being going by?
- Is the animal eating?
- Is the animal going to take enough nutrients in by this route?
- Is the animal able to absorb these nutrients?

Nutrition for urinary cases: does diet make a difference

Nicola Ackerman (UK)

Feline urinary tract issues may result from a number of different aetiologies including infection, neoplasia, urolithiasis, neurological disorders, anatomic abnormalities and inflammatory conditions. The name Feline lower urinary tract disease (FLUTD) may not be wholly representative of the condition, the role that stress has on the urinary system is starting to become more fully understood, with this psychological aspect involvement the brain and neurological system also needs inclusion. Of the feline patients seen in first opinion practice approximately 7% present with urinary disorders. With increases of the prevalence of risk factors such as obesity there is the potential that there will be more cases being presented.

Age	Most commonly seen in cats between one and ten years.
Gender	Males and females have a similar risk of non-obstructive FIC. Prevalence of urethral obstruction is more common in males
Neuter Status	Neutering in both males and females is associated with an increase in risk.
Food	An increase in dry food consumption can increase risk factor.
Weight	Excessive weight (obesity) will increase the risk of FIC.
Water Consumption	A decrease in water consumption can greatly increase the risk.
Activity Levels	Animals that have a more sedentary lifestyle are more likely to develop FIC.
Weather Conditions	Veterinary practices are more likely to see an increase in FIC cases when the weather is poor. Possibly due to cats unwilling to urinate outdoors in wet weather.

Table 1: Risk factors associated with increases in FIC cases.

Urine is a composite of a complex solution of both organic and inorganic ions. Crystals can grow and form when an imbalance occurs in this complex solution. There are several reasons that can cause these imbalances. Diet, decreased water consumption, urine pH alterations or relative lack of inhibitors of crystallisation can cause the solubility of a particular crystal to be exceeded. This result is crystal aggregation and growth. Clinical signs of FIC include haematuria, proteinuria, dysuria, polakiuria and/or urethral obstruction.[1] A full diagnostic work up is recommended in all cases, including blood work and imaging, (Figure1). Radiography should be included in all cats presenting with urethral obstruction.

It is recommended that all cases are given advice on all aspects of husbandry. Dietary manipulation can aid in reducing the risk factors of uroliths, but there are many other factors that need to be taken in to consideration and addressed. Utilisation of the veterinary nurse is highly recommended as conveyance of this information can be extremely time consuming, and the nurse is better placed to undertake these clinics. Having clear indications of what you would like the veterinary nurse ot cover in each type of clinic can be very useful to some nurses. The aims of the nurse clinic would be to include:

- A full history of the environmental factors needs to be taken for the cat, this includes other pets in the household, any changes at home (builders, new baby) and give advice regarding these factors. Discuss strategies to reduce any stressors for the cat.
- Dietary manipulation
- Increasing water consumption
- To aid the animal in order to obtain an ideal body condition score if required
- Ensure compliance with the home care plan drawn up the veterinary surgeon, (administration of medications, bringing in repeat urine samples).

Recommendations should be given to clients about preventative measures in all cats. There are clear risk factors associated with FIC, some cannot be helped, and age, breed and gender, others, such as lifestyle and obesity can. Neutering does play a significant impact on the risk of bladder stones, the risk of oxalate increasing seven fold, struvite 3.5 fold.[2] Educating the owner to ensure an adequate water intake, and limiting weight gain post neutering is vital.

Feeding a cat with FIC

The choice of diet is dependent on two factors, the body condition of the animal and results of the urinalysis. Correct identification of the type of crystals present (if any) and the pH of the urine is necessary. Use of a diet that promotes urinary health tends to be aimed to prevent struvite formation. Use of these diets in cats with a predisposition to calcium oxalate uroliths may increase the risk of urolith formation. A full dietary history of the cat is required, including any treats, supplement (especially if containing calcium) and whether or not the owner gives the cat milk. Both treats and processed human food (processed meats) are high in mineral levels, such as phosphorous, and should be avoided.

Use of a moist diet is preferable, as is *ad libitum* feeding. This might not be possible if the cat is overweight with this feeding scenario. When any animal consumes food, gastric acid is secreted and creates a temporary net acid loss from the body, and alkalisation of the urine. This is referred to as the postprandial alkaline tide. The alkaline tide is caused by secretion of bicarbonate into the blood by parietal cells of the stomach. A transient bicarbonisation is produced and increase urinary pH. Acidifiers in the diet will offset this increase in pH. If the diet is offered free choice (*ad libitum*), the cat will eat little and often. These feeding habits result in a smaller but more prolonged alkaline tide. This can reduce the likelihood of struvite precipitate formation.

Recommendations should be given to clients about preventative measures in all cats. There are clear risk factors associated with FIC, some cannot be helped, and age, breed and gender, others, such as lifestyle and obesity can. Neutering does play a significant impact on the risk of bladder stones, the risk of oxalate increasing seven fold, struvite 3.5 fold.[3] Educating the owner to ensure an adequate water intake, and limiting weight gain post neutering is vital.

Reducing stress in cats

The influence of behavioural responses in the cat have been widely linked to the occurrence of FIC in cats. Clients need to be made aware of this link and given appropriate advice in order to help their cat. Many cats can be presented to the veterinary practice for behavioural problems with inappropriate urination, medical issues needs to be ruled out prior to instigation of behavioural treatments. Any of the following behavioural traits can be indicators of stress.

- Food intake disorders (anorexia or over-feeding)
- Overgrooming (bald areas) or undergrooming (matted or soiled fur)
- House soiling, inappropriate urination or defecation.
- Decreasing levels of activity, increased resting or feigned sleep.
- Appearing withdrawn (reduced desire to play or interact), hiding.
- Extreme vigilance and heightened startle response.
- Defensive aggression towards people and other cats in the household, e.g. hissing.
- Increased dependency or social withdrawal (dependent on personality type).
- Changes in patterns of behaviour, e.g. spending a more significant amount of time indoors, irrespective of normal seasonal changes.
- Urine spraying.

Helping the client to understand these sometimes very subtle signs can be very difficult for clients. In multi-cat households the presence of other cats can be the main cause, and removal of the cause is impossible. Owners need to be supported in order to make changes to the household to help the stressed family member. There needs to be sufficient resources in the household in order to reduce competition for them. This means that more litter trays, food bowls and water bowls are required than cats within the household. All of these resources need to be separate from one another, as cats do not like to eat, drink or eliminate in the same area. Also take into consideration the type of cat litter that is utilised, as cats do have preferences. Multimodal environmental modifications (MEMO therapy) was found to be exceptionally useful in cases of FIC[5]. MEMO involves gaining a full thorough environmental history. A detailed client history form, alongside additional client and veterinary resources can be found online at http://indoorpet.osu.edu/veterinarians/research/index.cfm.

Stress and anxiety modification supplements

There are several commercially available nutritional supplements and diets that contain specific nutrients and dietary ingredients that can aid in reducing stress and anxiety. These include L-tryptophan and milk protein hydrolysate (MPH). Tryptophan is an essential amino acid that is a precursor of serotonin in the brain. Trytophan has shown to decrease anxiety, stress-related behaviours and house-soiling when placed in the diet after eight weeks.[6] MPH is a source of peptide which exhibits many biological effects, including a positive effect on the management of anxious disorders in cats,[7] and acts as an anti-depressant in dogs.[8]

Further reading

Guidelines for achieving the environmental needs of cats have been published by the International Society of Feline Medicine and the American Association of Feline Practitioners[5].

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Care of the diabetic patient

Nicola Ackerman (UK)

Diabetes mellitus is a complex disease, with stabilisation of blood glucose levels being affected by confounding disease processes, efficacy of the primary disease control treatment, diet and exercise programme and weight control. Thus a full history of the animal, including all these factors must be taken. There are several possible causes of diabetes mellitus, including pancreatitis, obesity, drugs (glucocorticoids, progestins), concurrent illness (hyperadrenocorticism, acromegaly), genetics, immune-mediated insulitis, infections and Islet amyloidosis. Obtaining an ideal body condition score in both cats and dogs is required. Obesity increases the risk in cats by fourfold. Obese diabetic animals may have difficultly losing weight. Stabilisation of the diabetes is the initial aim, followed by a conservative weight loss programme.

Protocols for nursing diabetic clinics

Having a protocol for the diabetic clinic can be useful. Having a checklist to run through can aid the veterinary nurse in ensuring that all points have been covered, and specific notes can be added where greater clarification is required by the owner.

1. All newly diagnosed diabetic cases should be discharge by the Diabetic care nurse, with a 30-45 minute appointment allocated.
2. Subjects to discuss with owner include, how to give injections, storage of insulin, disposal of sharps and monitoring of the animal. This includes polydipsia and polyuria, appetence levels, lethargy, activity levels, how to identify hypoglycaemic episodes. The treatment of hypoglycaemic episodes and what to do if the owner is worried at any point should be covered. Symptoms of hypoglycaemia include, but don't necessarily mean that all will be noted but the owner:
    - Polyphagic
    - Weakness/lethargy
        - Disorientation
        - Ataxia
        - Strange behaviour, e.g., aimless wandering (sometimes noted as being vacant), searching for food, licking lips
        - Severe neurological signs, e.g., collapse, convulsions, loss of consciousness and eventually death
3. If required the process of home monitoring can be discussed, and the owner shown how to use a glucometer. A second appointment can be made to cover this subject if the owner wants to have two consultations as it can be a large amount of information to take on board in one session. Having client literature or DVDs on this subject can be useful for the client to take away and view initially prior to having the second nurse consultation.
4. Discuss how the diabetes stabilisation programme works. Explain why the insulin levels are only increased once every 7-10days in small increments followed by glucose curve until correct dose reached. Explain to the owner that it can take a long time, so that they are not disheartened if it does take a while to stabilise.
5. Discuss exercise regimes and feeding levels and timings. It can also be useful to discuss what to do if the animal is unwell, or has not eaten all of it's diet. Again, it can be a little over whelming for owners with newly diagnosed animals to have all of this information. Splitting up of the information into two consultations a week apart can prove to be useful.
6. Discuss the type of diet the animal is receiving. If the pet is already receiving a "good" diet, then it can remain on the diet. If not, this includes semi-moist diets; the animal's diet does need to be changed. Semi-moist diets are higher in simple sugars and can cause higher post-prandial hyperglycaemic spikes than any other diets. Ideally the pet should transition onto a diet specifically designed for diabetics as this can have several benefits.
7. Ensure that the owner has business card/contact details of the diabetes nurse in charge of the case. Having a named nurse can greatly increase compliance, and ease any worries that the owner may have. Ensure that the owners are aware that in an emergency not to wait until the diabetic nurse is next on duty, but to phone the practice as soon as possible. The use of e-mails can be just as helpful as a phone number in order to contact the diabetic nurse.
8. Fill out diabetes care sheet, and explain to the owner how to fill out the diabetes diary. This is very helpful if more than one person is caring for the animal, so that the pet isn't accidentally injected more than once. Having written instructions is very important with all new cases.
9. The diabetes nurse in charge of the case should contact the owner for the first couple of days to ensure that the owner is happy with injecting insulin. If not, the owner and pet can come to the practice for the first few injections with the nurse present to aid if required.

Blood vessels access

Nicola Ackerman (UK)

The type and insertion site of catheters will depend on the reason they are being placed, what they are to be used for, disease processes present for example a jugular catheter may not be suitable for a coagulopathic patient, what will be administered through it, how long it needs to remain and place and the technical ability of the person placing it.

Peripheral catheters

Reasons to place peripheral catheters:

- Inexpensive and less technically challenging
- Well tolerated by most patients
- Easily accessible for quick catheterization
- Generally minimal restraint required compared to central venous catheter placement
- Fewer significant complications compared to central venous catheters

Sites for insertion include:

- Cephalic and accessory cephalic
- Medial and lateral saphenous
- Auricular – especially useful in rabbits and Bassett Hounds
- Dorsal common digital veins.

The lateral saphenous vein is larger than the medial saphenous vein in the dog and vice versa in the cat.

Over the needle catheters are the most commonly used type for peripheral placement and can also be placed as a quick and easy method of central catheter placement in the cat. They are inexpensive, easy to place and are suitable for short to medium term. Over the needle catheters can be left in place for 48 to 72 hours. There are also relatively few complications associated with placement of these catheters. They comprise a needle with a closely fitting catheter over the needle and bonded to it. A wide variety of materials, lengths and gauges are available.

It should be noted that fluid flow through a catheter is related to the length and radius of a catheter. Catheter radius(r) has the greatest effect with flow related to r^4 therefore halving the diameter will result in a 16 fold decrease in flow.

Equipment required for the placement of a venous peripheral catheter, Figure 1:

- Alcohol hand rub
- Non-sterile gloves
- Clippers
- 2% chlorhexidine gluconate solution
- Lint free swabs
- Sterile applicator containing 2% chlorhexidine gluconate in 70% isopropyl alcohol
- Intravenous catheter the appropriate size for the patient
- T-connector or bung – if a T-connector is used this should be flushed with saline or heperanised saline in an aseptic manner prior to catheter placement
- Tape to secure the catheter
- Syringe and needle filled with saline or heparinised saline

Placement of peripheral catheters:

1. Apply alcohol hand rub or wash hands thoroughly using the WHO hand hygiene method
2. Don non-sterile gloves
3. Clip and aseptically prepare a large area of skin over the insertion site (2% chlorhexidine gluconate in a back and forth motion with lint free swabs followed by sterile application of 2% chlorhexidine gluconate in 70% isopropyl alcohol)
4. Remove gloves and apply alcohol hand gel again
5. An assistant should raise the vein.
6. The catheter is then introduced through the skin and into the vein until a flashback of blood is seen.
7. The catheter and stylet should be advanced an additional few millimeters to ensure that the end of the catheter is safely within the vein.
8. The catheter can then be advanced off the stylet into the vein.
9. The stylet is removed and an injection port or T-connector is secured to the catheter.
10. The catheter should be securely taped in place and bandaged accordingly.

Figure 1: Placement of peripheral catheter.

Bandaging techniques

Nicola Ackerman (UK)

Wounds

Definite wound management may need to be delayed as the treatment of life-threatening injuries takes priority. Emergency management should prevent any additional injury and minimise contamination. Open wounds may be covered with a sterile dressing until the patient is stabilised. Many patients may be in pain from their injuries, so appropriate analgesia is important. Fractious patients may require sedation or general anaesthesia for wound evaluation to be performed.

Wound classification

The following parameters can be used to classify wounds:

- Aetiology
- Nature and extent of the skin deficit
- Degree of bacterial contamination
- Extent of the trauma to the surrounding tissues

Types of wounds

Abrasions

Abrasion wounds are the result of friction applied approximately parallel to the external surface of the skin. This friction usually results in the removal of variable amounts of the epidermis, dermis and hypodermis. In small animal practice these wounds are commonly seen as a result of road traffic accidents for example where the animal has become trapped between the road surface and the moving vehicle. Such wounds are consequently frequently heavily contaminated bacteria and the frictional nature of the injury means that the bacteria and debris from the road surface are deeply embedded within the upper layers of the wound. Abrasion wounds may also be seen as a result of poorly fitting casts and bandages, or from the abnormal wear of the patient's pads following prolonged contact with rough surfaces or due to a patient weight bearing on areas other than the pads.

The effective debridement of these wounds is of paramount importance. As previously mentioned the debris from the debriding road surface is often deeply embedded within the wound combined with the fact that abrasion wounds frequently result in an extensive tissue deficit. These wounds are often located on the distal limbs resulting in reconstruction being challenging with skin grafting or open wound management being the only options for closure.

Degloving wounds

Degloving injuries are caused when the skin is torn from the underlying tissues, usually from a limb.

Mechanical degloving occurs where the overlying tissue is torn from the sub dermal plexus, e.g. following road traffic accidents. Physiological degloving occurs when the skin is sheared from the subcutaneous tissues therefore resulting in damage to the local blood supply and ischemia of the area, this results in necrosis and sloughing of the skin over the following days. Secondary bacterial contamination frequently occurs with this physiological sloughing.

Avulsion injuries

Avulsion injuries refer to the forcible separation of tissues from their underlying attachments. Avulsion injuries frequently occur following dog bite wounds or road traffic accidents where the skin and subcutaneous tissue is avulsed from the mandible, resulting in the exposure of the underlying bone.

Shearing

Shearing injuries have a similar aetiology to degloving wounds, they represent a combination of degloving and abrasion injuries and are frequently seen following road traffic accidents, with the wounds usually located on the patient's distal limb, particularly on the medial aspect of the carpus, phalanges and tarsometatarsal joint.

Shearing injuries tend to be deeper than abrasion injuries and may involve the underlying joints. Like abrasion injuries, large areas of tissue may be involved and will be heavily contaminated with foreign material, e.g. gravel and bacteria.

Shearing wounds tend to be extensive, deep and as a result a prolonged period of open wound management is often necessary. There may also be concurrent damage to the underlying joints and supporting soft tissue structures (tendons and ligaments) which may require external support of the joint during this period and ultimately prosthetic and replacement of ligaments.

In severe cases, salvage of the joint is not possible and therefore arthrodesis (surgical fusion of a joint) must be performed. In more severe cases, salvage of the limb is impossible and amputation will be necessary.

Incisional

These wounds are most commonly seen in practice as intentional surgical wounds but they can also by trauma. These wounds may be caused by a sharp object, e.g. piece of glass or a metal shard moving in a plane parallel to the skin surface. These wounds typically have clean, regular edges, which will gape open because of the inherent elasticity of the adjacent skin.

There is often relatively little involvement of the skin, either side of the wound, but the incision itself may be long and there may be extensive damage to the deeper tissues, e.g. muscle and tendons, nerves and blood vessels, which may not be detected on first inspection. This highlights how important it is to surgically explore these wounds for signs of further damage.

Contamination of such wounds is likely to be less than for abrasions. In addition sharp trauma results in more bleeding, which will have an irrigating effect, thereby reducing contamination.

These wounds may be suitable for debridement and primary closure. However, delayed primary closure may be preferable if the wound is more than a few hours old or contamination is a concern.

Bandages and dressings

The ongoing management of the wound to allow secondary closure, delayed primary closure or second intention healing involves protection of the wound surface by bandaging.

Bandaging aims to achieve the following:

- Immobilisation of the wound surfaces, ensuring that the capillary buds and migrating epithelial cells are not disrupted and therefore maximising the rate of wound healing;
- Protection of the wound from trauma and contamination (including self-trauma and bacteria migrating through the dressing onto the wound);
- Pain relief for the patient;
- First aid – bandaging of a wound may be a temporary first aid measure to protect the wound from further contamination and aid haemostasis while a trauma patient is stabilised. The wound should be covered with a non-adherent dressing and an absorbent secondary layer. At this stage, ointments, antiseptics or wound powders may only serve to cause chemical damage and complicate debridement later on.

The most important layer of the dressing in terms of wound healing is the primary contact layer which should be chosen according to the condition of the wound. In the early stages, if the wound is still producing exudate and necrotic debris, debriding dressings are indicated. As the wound improves and granulation tissue is evident, a semi-occlusive non-adherent dressing may be used which may be used which will allow exudate to be drawn away from the wound into the secondary layer of the bandage, while keeping the wound surface moist and protected. New tissue is not damaged on removal. Petroleum gauze products allow excess fluid through, but may allow slow epithelialisation. Smooth non-adherent dressings, such as Melolin (Smith & Nephew), may be used as the exudate reduces.

Occlusive dressings are indicated once there is no infection and the wound is healing well. They keep the wound bed moist and warm and protect the new epithelium from abrasion. The hydrocolloids are a suspension of starch polymers in an adhesive matrix. They absorb fluid from the wound and form a moist gel. The edges of the dressing overlap with normal skin and form a seal, so that secondary dressing layers are not needed. This stimulates granulation tissue, allows rapid epithelialisation and also has some analgesic effect. Hydrocolloid dressings may prove expensive if dressing changes are frequent, but can be left in place for up to five days. These dressings will cause maceration of the tissue if the wound is exudative and they do not allow debridement. Furthermore, the adherence of the dressing at the wound edges may 'splint' the wound and prevent contraction. Intrasite gel (Smith & Nephew) is a hydrocolloid gel that may be used in a concave wound to allow the advantages of the moist environment but without being completely occlusive. The gel should be covered with a non-adherent dressing and a secondary absorbent layer.

Alginate dressings (e.g. Kaltostat; BritCair) also form a gel after absorbing wound exudate, and encourage epithelialisation in the same way. As they are not occlusive, they may be used as an alternative to the hydrocolloids if there is any doubt as to the state of the wound. Kaltostat may be useful for the transition from debriding dressings to hydrocolloids in the management of open wounds. The wound should be irrigated with sterile saline to remove the dressing.

All of these primary layer dressings are only as good as the bandage holding them in place. They must be changed regularly. It is important that the owner appreciates that if the bandage becomes wet it should be changed immediately.

Generally bandages are composed of three basic component layers:

- Primary (contact) layer
- Secondary (intermediate) layer
- Tertiary (outer) layer

Primary layer

This involves the various dressings available for use as the contact later.

Secondary layer

It is essential that all layers of a bandage are correctly and meticulously applied in order to avoid the common complications that can arise from inadequate, unskilled or incorrect application. The role of the secondary layer in wound management, in addition to providing support and comfort, is absorption. It acts as a 'trap' for exudative fluids from the wound; evaporation from this layer helps to prevent bacterial strikethrough. To aid its absorptive role this layer needs to have good capilliarity and should be thick enough (single or preferably multilayered) to collect the fluid and pad the wound. The intermediate layer must be in close contact with the primary dressing but it should not be applied so tightly as to limit exudate absorption. Suitable materials are hospital quality absorbent cotton wool or synthetic materials.

Tertiary outer layer

The outer layer serves to hold all the other layers of the bandage in place. In a multi-layered bandage (e.g. modified Robert-Jones), intermediate layer of conforming gauze and absorbent material may be used prior to applying an outer covering such as an adhesive wrap or preferably a self-adhering dressing. It is important that the outer layer allows evaporation of fluid but minimises external fluid absorption. Plastic bags which may be placed over the distal dressing should only be left in situ for a minimal period to prevent excessive fluid retention, with the increased risk of bacterial strike though and tissue maceration.

Industry Symposium

The tiny helpers in dermatology: extensively hydrolyzed protein-based diets for adverse food reaction

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Skin issues continuously represent one of the most frequent reasons for consulting a veterinarian and dermatology still has, despite a fast development on the field, this mysterious side that sets it apart from many other veterinary clinical disciplines. Finding the diagnosis and management for a certain condition can still create frustration and disappointments. A veterinarian is fighting daily many battles with different dermatological conditions; and to be able to wave the flag as the winner needs allies. Recent research works in dermatology have showed a steep acceleration and revealed fascinating insights, mixing immunology, histopathology, pharmacodynamics, internal medicine... Still, Nutrition continues to hold a significant role, reinforced by more and more robust science, lastly. When it comes to the diagnosis and management of adverse food reaction (AFR), more and more data substantiate the efficacy of extensively hydrolyzed protein-based diets. But which dietary strategy is good enough? Studies have shown that diets commonly used in AFR can be unreliable and contain proteins that are not declared in labeling text. Elimination diets must be free of the suspected allergens, throughout major protein source being either novel (no need to be exotic, but needs to be new to the individual pet) or hydrolyzed enough (or both). No ancillary protein should be brought by this food, be it via other formula compounds (carbohydrates, palatability enhancer...) or via cross-contaminations, hence the importance of Quality controls during manufacturing[1].

In Royal Canin, there is a focus on 3 key parameters to ensure the purity of extensively hydrolyzed diets: full characterization of raw materials used in the formula, fit-to-purpose industrial equipment and cleaning processes and adapted analytical measures to validate each production. The analyses performed on Anallergenic™ showed that no cross-contamination from ancillary protein was detected and confirmed that the protein source for these diets was extensively hydrolyzed[2].

In several countries studies have been performed to confirm the clinical efficacy of Anallergenic™ diets in the diagnostic and management of Adverse Food reactions, including in some difficult cases. The results obtained showed excellent efficacy in the management of chicken-allergic dogs[3] and complex or refractory AFR cases.

Royal Canin Anallergenic™ diets are formulated with very low molecular weight feather protein and purified corn starch instead of classical entire cereals and can be useful allies of the veterinarian during complex and sometimes extremely long and exhausting dermatology battles (elimination trial phase of AFR diagnostic procedure, management of complex or refractory cases of cutaneous AFR).

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Get the hang of it: analgesia and anasthesia with opioids

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Analgetics and anaesthetics are an important component of anesthesia and pain management. The choice of medications, dosages and use alone or in combination has significant influence on anesthetic induction and maintenance. Preanesthetic medication and analgesia can reduce the dosage of anesthetics for induction by 25-90%. This is an advantage for reducing the cost of anesthetics. However failure to recognize this can result in anesthetic overdose and complications.

Preanesthetic use of analgesics is an important step in desirable pain management. Often it is a key factor in preventing perioperative pain.

The use of tranquilizers, sedatives and analgesics alone or in combination will be discussed in this lecture. Their use in combination is referred to as multimodal analgesia or as part of balanced anesthetic management. This results in more effective management of patients requiring special medical procedures or surgical patient needs.

One Health symposium

Saturday, October 5, 2019, Thessaloniki, Greece
Grand Hotel Palace, Room Kallipatira
Organized by: Pan-Hellenic Veterinary Association &
The Royal Institute of International Affairs, Chatham House

	Key Note Speakers	
14.50–15.00	**Athina Trachili**, *(DVM) – President of Hellenic Veterinary Association & Vice President of UEVP (Union of European Veterinary Practitioners)*	**Welcome**
15.00–15.15 15.15–15.20	**Professor Theo Kanellos,** (*BVetMed, MSc, PhD, MBA, Hon DVM&S, MRCVS) – Director, Business Development and Alliances, Zoetis International* *President of the One Health Committee of HVA* Q & A	*Sustainability of One Health solutions through effective innovation*
15.20–15.35 15.35–15.40	**Christos Zafeiridis,** *(DVM) – Official Veterinarian, Ministry of Rural Development & Food* Q & A	*Antimicrobial resistance and healthcare-associated infections/ Country visit (Greece) to Germany*
15.40–15. 55 15.55–16.00	**Professor Dr Nikos Papaioannou** – *Rector of AUTH* Q & A	*Pioneering One Health Education*
16.00–16.20	**Coffee break**	
16.20–16.35 16.35–16.40	**Professor Isaac A.O. Odeyemi** *(DVM, MSc, PhD, MBA, MCMI) – Head Outcomes Research, International Centre of Excellence Zoetis* Q & A	*One Health Economics: What are the challenges and opportunities*
16.40–16.55 16.55–17.00	**Dr Victor J Del Rio Vilas, DVM, MBA, MSc(Epi), PhD, MRCVS)** *– Chatham House Consultant* Q & A	*Vets and Global One Health*
17.00–17.55	**Panel Discussion** **Prof Theo Kanellos** (*BVetMed, MSc, PhD, MBA, Hon DVM&S, MRCVS) – Director, Business Development and Alliances, Zoetis International* *President of the One Health Committee of HVA* **Prof Isaac Odeyemi** *(DVM, MSc, PhD, MBA, MCMI) – Head Outcomes Research, International Centre of Excellence Zoetis* **Dr Katsimboulas Michalis,** *(DVM, PhD, SRS) – Staff Research Scientist – Assistant Professor Level, Experimental Surgical Unit, Center of Clinical, Experimental Surgery and Translation Research Biomedical Research Foundation of the Academy of Athens* **Dr Valiakos George**, *(DVM, MSc, PhD) – Assistant Professor Laboratory of Microbiology and Parasitology, Faculty of Veterinary Medicine, School of Health Sciences, University of Thessaly* **Coordinators** **Dr Stefanos Kladakis,** *Lietenant Colonel DVM -C'Army Veterinary Companion Animal Veterinary Society (HCAVS)*	*Presentation of questionnaire results* *Antibiotics in Pet Clinics* *Discussion*
17.55–18.00	**Eleni Pavlidou**, *DVM, MBA, Chatham House Consultant, Asclepius One Health Platform*	**Wrap up**

Tsipianitis Efstratios-Erricos

Dr Tsipianitis Efstratios-Erricos, he graduated from the Veterinary Faculty of Aristotle University of Thessaloniki in 1997 and 1999 and he completed the postgraduate program at the Surgical Clinic of the Veterinary Faculty of Aristotle University of Thessaloniki. Until 2007 he worked as a freelance professional with the surgical, orthopedic and neurosurgery of pet animals in clinical clinics in Greece and since 2007 he maintains the specialized Surgery clinic Vet Surgery in Holargos, Attica. He has been trained in specialized techniques in Orthopedic and Neurosurgery at Ohio State University, North Carolina State University, SCIVAC, ESVOT, AOVET, IEWG. He is a member of the National Veterinary Association (PEC) ELEKZZ, Chairman of the Hellenic Society of Orthopedics and Neurosurgery, OMON and other Hellenic (founding member of EKEOT, CSR) and foreign (ESVOT), AOVET, IEWG) Scientific Veterinary Societies. It monitors the evolution of Orthopedic and Neurosurgical of Science and participates in national and international Veterinary Scientific Conferences. As a member of the One Health Committee of the Hellenic Veterinary Association (HVA), he participated in the Organizing Committee of the 1st Greek One Health Forum in Greece.

Professor Theo Kanellos

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Theo Kanellos qualified as a veterinarian from the Aristotle University of Thessaloniki in Greece and has been awarded an MSc in microbiology and PhD in molecular medicine from the University of London. He also has a business diploma from the Ecole Supérieur de Commerce de Paris (ESCP). During his career he worked as a clinician, an academic, a governmental official and for the last seventeen years as part of the management within the Pharmaceutical Industry where he has held several strategic roles. He has managed research laboratories, business development transactions, scientific and multi-functional alliances teams and programmes in several organisations that have led to the spinoff of biotechnology companies, the award of significant scientific grants, the founding of major strategic partnerships and the registration and licensing of successful commercial products and services. In his current role in Zoetis he establishes business transactions and entrepreneurial partnerships with companies, venture capitalist groups, universities, and governmental institutions, internationally. He holds a visiting professorship at the School of Health and Medicine at the University of Surrey and he is a board member in several organisations including the Global Alliance for Livestock Veterinary Medicines in Africa, The Global Antimicrobial Research Innovation Fund, Action Group of the One Health Platform etc. He is ad hoc advisor in several EU and national scientific and veterinary organisations. He is the author of over 40 peered reviewed papers and his articles, presentations and interviews have also featured in many trade and public media.

Michalis Katsimpoulas, DVM

PhD, Staff Research Scientist (Assistant Professor Level) Center for Experimental Surgery, Biomedical Research Foundation, Academy of Athens

Michalis is Designated Veterinarian at Laboratory for Experimental Surgery and Surgical Research of the Medical School NKUA. He is also Staff Research Scientist (Assistant Professor Level) at Center of Clinical, Experimental and Translational Research, Biomedical Research Foundation of the Academy of Athens (BRFAA), and Partner and Senior Surgeon at "Attikon Animal Hospital".

Lieutenant Colonel Stefanos Kladakis, DVM

C' Army Veterinary Hospital, Thessaloniki, Greece

President of Hellenic Companion Animal Veterinary Society (HCAVS)

Stefanos graduated from Aristotle University of Thessaloniki, Greece and received post-graduation studies in Small Animal Surgery in Greece and USA.

Currently he serves as Head of Veterinary Clinic at C' Army Veterinary Hospital of Thessaloniki, Greece. He also works in private practice as a referral veterinary surgeon focused in small animal surgery.

He is an invited speaker in national and international conferences, seminars and labs, an active member of several national and international veterinary associations and currently the President of the Hellenic Companion Animal Veterinary Society (www.hcavs.gr).

Professor Isaac A.O. Odeyemi

DVM, MSc, PhD, MBA, MCMI

Isaac.Odeyemi@Zoetis.Com

Currently, Senior Director and Head of Health Economics and Outcomes Research in Zoetis Pharmaceuticals Centre of Excellence, International Operations, Dublin. Also, a Visiting Professor of Health Technology Assessment and Health Policy, Faculty of Health, Psychology and Social Care, Manchester Metropolitan University, United Kingdom.

Has over 30 years global human and animal healthcare experience with specialization spanning clinical practice and research in public health, economics of health care financing, health policy and market access. Over 20 years in senior management positions in global pharmaceutical industries as well as advising national health organisations in health technology assessment.

A member of the Chartered Management Institute of the UK, as well as several health economic professional bodies, including iHEA, ISPOR international and the ISPOR Animal Health Special Interest Group.

Research interests include developing methodologies in optimising patient and market access to healthcare interventions, concepts in quantifying welfare and quality of life value propositions in animal health and the use of real-world evidence (Big Data) in the human-animal health interphase.

Eleni Pavlidou

DVM, MBA

She is Secretary of One Health Committee Hellenic Veterinary Association and President of the Executive Board of Asclepius One Health platform. Consultant of The International Institute of Royal Affairs, Chatham House, UK, in Southeast Med region for One Health. She is a member of Hellenic Veterinary Association (HVA) and Secretary of One Health Committee of HVA. With the One Health Committee of Hellenic Veterinary Association organized the 1st Hellenic One Health Forum, on 13th of December, 2018, in Greece. For 3 years she was Product Manager for CA, Boehringer Ingelheim. Since 2000, she was the Head of Regulatory Affairs and Technical Manager of Zoetis Hellas for Greece & East Balkans & Malta, and as the global alliances such planning, monitoring, preparation, review and coordination of independent projects such Bio-Surveillance, One Health and contacts with key Health Authorities and Research Institutes, Universities around the world with development and monitoring clinical studies, helped Zoetis achieve the company's evolution and expand to new areas (i.e. Aquaculture, Digital Medicine). Strong relationship with the Animal Market, working for 1.5 years outside of Greece, knowing how to motivate the team and executed action plans to drive results having a very strong and positive development to the marketing activities, responsible for the technical training of individuals in the sales team and new employees. She holds a Doctor of Veterinary Medicine degree from Aristotle University in Greece, with an MBA, a Certificate of Continuing Professional Development concerning Regulatory Affairs for Veterinary Medicine in London, a Certificate of Attendance of Marketing Course and a Leadership through Influence course Emotional intelligence course.

George Valiakos

DVM, MSc, PhD

George is Assistant Professor, Laboratory of Microbiology and Parasitology, at the University of Thessaly.

He gained a DVM in 2005, a MSc in 2012 and a PhD in 2015.

Victor Del Rio Vilas

DVM, MBA, MSc (Epi), PhD, MRCVS

Victor is currently at the Dept of Epidemiology, School of Veterinary Medicine, University of Surrey (UK), and at the Centre on Global Health Security at Chatham House, London. Until January 2018 he worked at the World Health Organization (WHO-Geneva) on the development of WHO's epidemic vulnerability evaluation framework. Until November 2016, Dr Del Rio was a consultant with the Pan American Health Organization (PAHO/WHO), based in Rio de Janeiro (Brazil) with regional responsibilities. In that capacity, Dr Del Rio advised Ministries/Departments of Health across the region on epidemiology, surveillance and control measures for a number of diseases such as rabies, leishmaniasis, yellow fever and on zoonoses programmatic issues. He also contributed to WHO's global response to the Ebola Virus Disease outbreak in Liberia in 2015; previously worked in Uzbekistan implementing the Biological Threat Reduction Program (Defense Threat Reduction Agency, US DoD), and as veterinary advisor and epidemiologist for UK´s Department for Environment, Food and Rural Affairs (Defra) and the Veterinary Laboratories Agency.

Christos Zafeiridis

Official veterinarian at the Department of Veterinary Drugs, Residues and Veterinary Supplies, Directorate of Animal Welfare, Drugs and Veterinary Applications, General Directorate of Veterinary Services, Ministry of Rural Development & Food, Athens (Greece).I have been working as a Veterinarian for 18 years (12 of which as an Official Veterinarian and for 6 of which as a Veterinarian Expert representing Greece at the European Commission and at the Council of the European Union).

Food safety (including Antimicrobial Resistence)– policy and legislation, are my areas of strength that. Specifically my main tasks are:

- Surveillance of the implementation of Council Directive 96/23/EC on measures to monitor certain substances and residues thereof in live animals and animal products.
- Member of the National Interministerial Committee for the issuing and implementation of the National Action Plan for tackling Antimicrobial Resistance in the context of the “One Health” concept.
- Member of the Working Group for the Implementation of the EU-JAMRAI [European Union Joint Action on Antimicrobial Resistance (AMR) and Healthcare-Associated Infections (HCAI)] on the Veterinary Sector.
- Special Scientific Advisor, on the Veterinary Issues, to the Minister’s of Rural Development and Food Cabinet.
- Instructor at the Public School of meat professions (Athens).

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