EERVC

EASTERN EUROPEAN REGIONAL VETERINARY CONFERENCE

6

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In collaboration with

HELLENIC VETERINARY ASSOCIATION

PROCEEDINGS

Advancing the veterinary profession
in Eastern Europe

www.eervc.vet

Welcome letter

Dear EERVC Delegate,

Welcome again to Thessaloniki, second largest city in Greece and the capital of the geographic region of Macedonia, for the 6th Eastern European Regional Veterinary Conference (EERVC).

In 2019, after EERVC in Thessaloniki we received fantastic feedback from delegates and we decided to come back 4 years later.

EERVC Board tried to follow your suggestions when considering the speakers and their topics. Speakers have been selected by recommendation and their expertise. Lectures cover all aspects of small animal medicine and surgery, as well as topics of current interest for the profession. The EERVC offers cutting-edge international speakers, the largest regional and international trade exhibition and unparalleled opportunities for professional networking during an affordable, highquality, 3 - day annual meeting.

Special sessions are dedicated to our Greek coleagues covering specific topics very much relevant for every day clinical work.

EERVC is introducing New Session – Thinking Out of the Box with... This year Mike Farrell, worldwide recognisedorthopaedic specialist, will share his insights on very common topics by widening our perspectives.

The trade exhibition at EERVC 2023 is a fantastic place to discover the newest products from industry, including the verylatest innovations and services focused on the needs of the small animal veterinarian. We recommend that you explore the trade exhibition and make the most of the veterinary industry expertise and their products. 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.

The EERVC Organizing Team have prepared lots of great opportunities for networking including Welcome Reception on Thursday, famously known EERVC Party on Friday and the Greek Night on Saturday. Do not miss none of them!

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 46 countries across the globe and we hope to see you again next year!

Denis Novak DVM MRCVS
EERVC Chairman

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*Advancing the veterinary profession
in Eastern Europe*

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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.

Anesthesiology

Paulo Steagall (Canada)
DVM, Msc, PhD, DACVAA
(Anesthesiology)

Dr. Paulo Steagall is a Professor of Veterinary Anesthesiology and Pain Management at the City University of Hong Kong and the Université de Montréal. He is a board-certified specialist by the American College of Veterinary Anesthesia and Analgesia.

He is the head of a clinical research laboratory dedicated to improving pain management and animal welfare with cutting-edge research in pain assessment with emphasis on cats including the Feline Grimace Scale (www.felinegrimacescale.com). He has published over 130 scientific articles on pain management and the book "Feline Anesthesia and Pain Management" while lecturing internationally.

SUCCESSFUL INJECTABLE ANAESTHESIA IN CLINICAL PRACTICE

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Injectable anesthesia is commonly used in small animal practice and particularly during high-volume spay-neuter programs. These programs are becoming more popular as a mandatory component to decrease overpopulation and euthanasia of stray dogs and cats. Balanced anesthesia and multimodal analgesia should be combined to provide pain relief, muscle relaxation, unconsciousness and immobility. Protocols will vary with geographic location, equipment availability, facilities and familiarity of personnel with anesthetic drugs. The most ideal protocol should be effective, reversible, economically viable, provide pain relief, avoid adverse-effects, be species-specific, and have a small injection volume. Hypothermia should be prevented with the avoidance of conductive heat loss, excessive hair removal or the use of excessive alcohol scrubbing solutions and limiting body cavity exposure, among other strategies. Ideally, there should be a source of ventilation and oxygenation. Monitoring can be performed by trained observers and "hands-on" monitoring. Standard kits and drug charts are used for the anesthetic/analgesic protocols and for emergencies.

Lately, opioid-free injectable anesthesia has become a topic of interest as these drugs as well as inhalant anesthetics are not always available and used in cats undergoing spay-neuter. The lack of drug availability makes anesthesia and analgesia suboptimal, especially because opioids are the cornerstone of acute pain management in veterinary medicine. Limited availability of opioids makes pain management challenging leading to unnecessary animal suffering. It results in poor welfare for animals and compassion fatigue for veterinary health care professionals. This lecture will summarize the best practices for successful injectable anaesthesia protocols in dogs and cats highlighting the discussions on the use of opioid-free techniques.

CAESAREAN SECTION:
THE PUPPY, THE KITTEN, AND ANAESTHETIC PROTOCOLS

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This lecture will provide an overview of anesthetic and analgesic practices including protocols used for C-sections. Cesarean section is not as common a procedure in cats as it is in dogs and general considerations and anesthetic management of these cases are largely extrapolated from the canine literature in cats. The lecture will focus on different aspects and considerations related to the procedure and its effects on the puppy/kitten, 'mothers' as well as body systems. A quick reminder on drug effects on puppies and kittens is fundamental to understand the basic principles of anesthesia and how preparation and surgery time are important. In brief, anesthetic drugs cross the placenta and will affect fetal physiology and health of the newborns. Pregnancy-induced changes in maternal physiology such as slow gastric emptying, increased cardiac output and oxygen demand should be considered. The lecture will also discuss the controversial use of opioids during C-section and the concerns of respiratory depression in the newborns. Video-based material like the intraperitoneal and incisional anesthesia will be presented as local anesthetic techniques used as alternatives to epidural anesthesia before C-section. The use of a check-list for C-section is recommended. In general, preoxygenation is recommended followed by induction with propofol or alfaxalone, and maintenance with volatile anesthetics. These protocols have minimal effects on the newborns. Finally, we will review strategies for neonatal resuscitation and outcomes using a modified Apgar scores.

BECOMING THE CAT WHISPERER IN PAIN ASSESSMENT

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Pain assessment is the first step for optimal pain management. In fact, inability to adequately assess pain is one of the main reasons why pain is undertreated in cats, negatively impacting feline health and welfare. In clinical practice, pain assessment is based on observations of behaviors including facial expressions, body posture, level of activity, and interaction with the environment and observer. For a systematic approach to pain assessment, validated pain scoring instruments (i.e., pain scales) should be used. This ensures that veterinarians and nurses are looking at the same things when evaluating pain in animals and that pain scores are comparable among different individuals and over time. In addition, scores can guide clinical decision on the administration of analgesic (i.e., a cut-off score indicates that cats reaching those values are painful enough that analgesic administration is recommended, known as rescue analgesia). Acute (adaptive) and chronic (maladaptive) pain involve different mechanisms and occur in different circumstances although episodes of acute pain can occur in cats with chronic pain (i.e. acute on chronic). Examples of acute pain include postoperative pain, trauma, pancreatitis, urinary or gastrointestinal obstruction. Examples of chronic pain include osteoarthritis, cancer, periodontal disease, or skin, ocular or ear conditions. Different pain scales should be used for assessment of acute and chronic pain in cats. This lecture will present pain-related behaviors and the available tools for assessment of acute and chronic pain in cats during everyday practice.

TOP TEN TIPS IN SMALL ANIMAL ANAESTHESIA AND PAIN MANAGEMENT

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This lecture will give an overview of current practical techniques and drug protocols for small anesthesia and pain management that are readily applicable in clinical practice. This will involve a dynamic and interactive approach using video-based teaching with several resources presented to the audience. This may involve the use of intraperitoneal and incisional anesthesia, intratesticular block, gabapentin, opioid-free anesthetic protocols, supraglottic airway devices, monoclonal antibodies and novel methods for pain assessment in feline osteoarthritis.

UNIQUE CHALLENGES DURING FELINE ANAESTHESIA

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The cat is unique; and so, it is its analgesic and anesthetic management. From handling and pre-anesthetic assessment to their specific anesthetic and analgesic techniques including premedication, induction and maintenance of anesthesia, this lecture will provide a species-specific approach to anesthesia in cats.

The principles of feline-friendly practice include a safe and secure environment for the cat from transportation to handling in the clinical setting. It aims to minimize stress to these patients while working in a quiet area with separated areas to dogs and cats and using gentle handling. The cat "boarding" should include appropriate cages with elevated surfaces and enclosure with environmental enrichment. The wellbeing of the cat is a priority during consultation. Fearful cats should be handled gently by trained personnel to decrease stress and avoid escalating to "clinical disasters" for the cat.

This lecture will also provide an overview of factors influencing anesthetic-death related mortality. This includes extreme body weight and age, endotracheal intubation, absence of anesthetic monitoring, ASA III, IV and emergencies and fluid therapy. The principles of anesthetic management include protocols that are tailored to the individual. These protocols consider the patient's co-existing disease, drug, equipment and monitoring availability and familiarity of the veterinary care team with specific techniques. The induction of anesthesia and the use of injectable and inhalant protocols will be presented in detail.

Airway management provides a secure airway, allows appropriate oxygenation and ventilation of the patient. The potential issue of endotracheal intubation and the use of supraglottic airway devices will be presented. Practical and clinical tips will be introduced for successful intubation in cats. Additionally, fluid therapy is critical in cats to prevent and treat dehydration and electrolyte imbalances. At the same time, fluid overload can also be a problem. Techniques to administer accurate volumes of fluids must be used in feline practice to avoid complications related to fluid overload.

Finally, particularities of anatomy, physiology and pharmacology related to pain management can induce changes in the pharmacokinetics and pharmacodynamics of analgesics in cats especially to those with co-existing diseases; dosage regimens should be tailored to the patient to avoid drug overdose related to changes in metabolism and excretion. Reversible agents are preferred for analgesia and therapy should be based on continuous pain assessment. These issues will be discussed using an evidence-based approach and the speaker's clinical practice.

MONOCLONAL ANTIBODIES FOR THE TREATMENT OF OSTEOARTHRITIS: WHAT ARE THEY?

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Osteoarthritis is one of the most important causes of chronic pain in small animals. Nowadays, there is a major emphasis on the prevention of OA as environmental and lifestyle changes may reduce the incidence of this condition. However, the prevalence of chronic painful conditions in small animals will ultimately increase as the life expectancy of dogs and cats is also increasing.

Osteoarthritis is considered a degenerative and inflammatory disease of synovial joints that involves functional/structural cartilage changes, but also subchondral bone, synovium, meniscus and ligaments. The pathophysiology of OA is rather complex and can involve low-grade inflammation due to aging, sedentary life style, metabolic diseases and biomechanical factors. Ultimately, joint degradation leads to pain, muscle deterioration, reduced mobility and activity, poor quality of life and changes in sleep pattern. Changes in neuroplasticity may lead to peripheral and central sensitization.

Nonsteroidal anti-inflammatory drugs have been historically used for the primary treatment of canine and feline osteoarthritis along with environmental changes, weight loss and nutritional programs. These drugs are known for their efficacy and safety profile. However, these drugs may produce some adverse effects particularly when dosage regimens or contraindications are not respected.

Nerve growth factor (NGF) is a cytokine that has been identified as a potential target in the treatment of chronic pain as it is strongly involved into signaling pathways and structural changes in the development of osteoarthritis. The NGF binds to TrKA receptor leading to reduced nociceptive threshold and excitatory neurotransmission in the afferent nerve fibers. The ultimate consequence is that "inflammation will produce more inflammation". NGF is now recognized as a facilitator and perpetuator of chronic pain.

This lecture will discuss the advent of the monoclonal antibodies that are species-specific and developed for targeting and neutralizing NGF associated with osteoarthritic pain. A summary of the current literature will be discussed with a focus on evidence-based medicine and treatment regimens. Treatment of OA should target inflammation, NGF but also improve positive emotions and healthy life style combined with non-pharmacological therapy.

Cardiology

Laurent Locquet (Belgium)

Diplomate ECVIM-CA (Cardiology), GPCert(VC) MRCVS DVM
(Cardiology)

Laurent graduated in 2015 from Ghent University, Belgium and worked in general practice for one year both abroad in South-Africa as well as in Belgium, primarily with cats, dogs and wildlife, before starting a rotating Internship in a busy referral centre in the UK. During his Internship, Laurent obtained his certificate in Veterinary Cardiology. After completing his Internship, Laurent completed a Residency in Veterinary Cardiology at the University of Ghent before joining a busy referral practice in the Greater London Area for one year before joining Dick White Referrals in 2022.

Laurent enjoys all aspects of veterinary Cardiology though he has a particular interest in procedures involving cardiopulmonary bypass, minimally invasive interventions and wildlife cardiology.

CARDIAC EMERGENCIES IN CATS AND DOGS: RECOGNIZING, DIAGNOSING, AND MANAGING CRITICAL CASES (PART I AND II)

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Cardiac emergencies in cats and dogs represent a significant challenge for veterinary professionals. This presentation aims to provide a comprehensive overview of cardiac emergencies, focusing on the critical aspects of recognition, diagnosis, and management.

Understanding the pathophysiology of cardiac emergencies, including conditions such as congestive heart failure, arrhythmias, pericardial effusion, and feline arterial thrombo-embolism, is crucial for timely intervention. The presentation will delve into the key clinical signs and diagnostic tools, including electrocardiography, echocardiography, and biomarkers, to aid in accurate diagnosis.

Effective management of cardiac emergencies involves a multidisciplinary approach, encompassing medical therapy, supportive care, and in some cases, emergency interventions like pericardiocentesis. The presentation will highlight the latest advancements in treatment options and the importance of tailored strategies for individual patients.

Furthermore, this session will emphasize the critical role of client communication and education in managing cardiac emergencies, ensuring that pet owners are equipped to provide necessary at-home care and follow-up.

Ultimately, this presentation seeks to empower veterinary professionals with the knowledge and skills required to confidently address cardiac emergencies in cats and dogs, improving the overall prognosis and quality of life for these patients.

ECGS: TOO FAST? TOO SLOW? TOO SCARY?

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Electrocardiography (ECG) is a fundamental tool in veterinary cardiology, aiding in the assessment of cardiac health in cats and dogs. This presentation will provide a comprehensive exploration of ECG interpretation, focusing on key rhythms, diagnostic insights, and clinical applications.

The session will start with an overview of the basics of ECG, offering a refresher on lead placement, waveforms, and intervals. Attendees will gain a solid foundation in ECG interpretation, essential for accurate diagnosis and treatment.

Diving deeper into the subject, we will explore the common cardiac rhythms encountered in cats and dogs, from normal sinus rhythms to arrhythmias, including atrial fibrillation, ventricular tachycardia, and different types of atrioventricular blocks. Attendees will learn to recognize and differentiate these rhythms, enabling prompt and precise diagnosis.

This presentation will also emphasize the clinical relevance of ECG in assessing cardiac diseases such as hypertrophic cardiomyopathy, dilated cardiomyopathy, and valvular disorders.

Incorporating advancements in technology, we will discuss the utility of 24-hour Holter monitoring in capturing intermittent arrhythmias and unraveling complex cardiac issues. Furthermore, its value in evaluating patients with syncope or exercise intolerance will be highlighted.

To conclude, this session will help veterinary professionals with practical knowledge and skills to confidently interpret ECGs in cats and dogs. By mastering ECG interpretation, attendees will enhance their ability to diagnose cardiac conditions, provide targeted treatment, and ultimately improve the cardiac care of their patients.

THE DIAGNOSIS AND TREATMENT OF CONGENITAL CARDIAC DEFECTS IN CATS AND DOGS

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Congenital defects in cats and dogs pose unique challenges in veterinary medicine, demanding a thorough understanding of the intricate cardiac anatomy and specialized care required for these special patients. This presentation will provide a comprehensive exploration of the diagnosis and treatment of congenital heart defects in cats and dogs.

The first part will start by discussing the diversity of congenital heart defects that can affect cats and dogs, focussing on the most prevalent ones and emphasizing the importance of early detection. Attendees will gain insights into the critical role of breed predispositions and hereditary factors in the development of these defects.

Different diagnostic modalities essential for accurate assessment will be discussed, focussing on echocardiography and touching upon cardiac catheterization and advanced imaging techniques. Case studies will illustrate how these tools can be employed to precisely identify and classify congenital heart defects, enabling tailored treatment strategies.

The presentation will then discuss treatment options, highlighting the advancements in surgical interventions, such as patent ductus arteriosus (PDA) ligation and pulmonic stenosis (PS). Attendees will also learn about emerging minimally invasive techniques and their potential benefits in mitigating the surgical impact on young patients.

Medical management of congenital heart defects, including the use of medications to improve cardiac function and alleviate symptoms, will be discussed. Furthermore, attendees will gain an understanding of the importance of post-diagnostic counseling and long-term follow-up to ensure the best possible quality of life for affected animals.

In conclusion, this presentation will provide veterinary professionals with comprehensive knowledge and practical insights into the diagnosis and treatment of congenital heart defects in cats and dogs.

MYXOMATOUS MITRAL VALVE DISEASE IN DOGS: THE PRESENT AND THE FUTURE

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Myxomatous mitral valve disease (MMVD) is a the most commonly acquired cardiac disease in dogs, primarily in smaller breeds. This presentation will provide a comprehensive overview of the diagnostic methodologies, treatment approaches, and possible directions for future research and therapies.

The first part will elaborate on the fundamental pathophysiology of MMVD, highlighting the gradual degradation of the mitral valve and its consequential effects on cardiac function. Additionally, we will investigate breed predispositions, genetic factors, and potential biomarkers linked to this condition.

The second part will cover the diagnosis, including the application of echocardiography and cardiac biomarkers to improve early detection and risk assessment. Furthermore, we will explore the expanding role of advanced imaging methods in providing more detailed insights into MMVD progression.

Current treatment strategies for MMVD, including medical treatment to alleviate symptoms and slow disease progression and possible surgical interventions will discussed thereafter. Attendees will also be introduced to emerging therapeutic options and techniques.

Also, the presentation will underscore the pivotal importance of client education and communication in effectively managing MMVD, ensuring that pet owners are well-informed about the disease and its long-term care requirements.

In conclusion, this session aims to equip veterinary professionals with a comprehensive perspective on MMVD in dogs, covering current knowledge and future opportunities.

FELINE CARDIOLOGY: INSIGHTS INTO DIAGNOSIS, MANAGEMENT, AND ADVANCES (PART I AND II)

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Feline cardiology presents an intriguing and evolving field within veterinary medicine, often offering significant challenges for practitioners. This presentation aims to provide a comprehensive overview of cardiology in domestic cats, emphasizing essential aspects of diagnosis, management, and recent progress.

During the first part, different aspects of the physiology and pathology will be covered, highlighting their relevance in the divergent types of cardiomyopathies and arrhythmias in cats. A deep understanding of these is crucial for precise diagnosis and effective treatment.

In the second part, diagnostic methods in feline cardiology will be discussed, including echocardiography, 24-hour Holter monitoring, and the utility of cardiac biomarkers. Attendees will gain insights into interpreting feline electrocardiograms (ECGs) and the role of diagnostic imaging in identifying cardiac diseases.

Current therapeutic approaches for feline cardiac conditions, e.g. hypertrophic cardiomyopathy, will be explored comprehensively, including the use of medications, dietary management, and lifestyle modifications. Additionally, emerging treatment options and their potential influence on feline cardiac care will be discussed.

Also, this presentation will underscore the significance of client education and effective communication, ensuring that cat owners are well-informed about cardiac diseases, their management, and the importance of follow-up care.

In conclusion, this session will provide practitioners with a thorough understanding of cardiology in domestic cats and will be therefore better equipped to provide top-notch care for their feline cardiac patients.

BASIC DOG AND CAT CARDIOLOGY - FOCUS ON ECHOCARDIOGRAPHY: A PRACTITIONER SUMMARY

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Cardiac health is a cornerstone of well-being for cats and dogs. This presentation will provide a fundamental exploration of basic cardiology in cats and dogs, with a spotlight on basic though essential echocardiography principles. The echocardiographic findings of both a normal heart and the most common heart diseases, including myxomatous mitral valve disease, dilated cardiomyopathy, hypertrophic cardiomyopathy, and prevalent congenital diseases, will be discussed.

This presentation will start with an overview of the basics of echocardiography, offering insights into image acquisition, key measurements, and the interpretation of cardiac structures. Attendees will gain a solid foundation in echocardiography, essential for accurate diagnosis and monitoring of cardiac health. By understanding the "norm," attendees will be better equipped to identify deviations indicative of cardiac disease.

The presentation will then discuss the most prevalent cardiac conditions encountered in veterinary practice, such as myxomatous mitral valve disease, dilated cardiomyopathy, hypertrophic cardiomyopathy, and congenital defects. Case studies and real-life examples will illustrate how echocardiography can aid in diagnosing and managing these conditions, ultimately improving patient care.

Moreover, the session will emphasize the importance of early detection and intervention, as well as the role of client education.

In conclusion, this presentation aims to equip veterinary professionals with fundamental knowledge and practical skills in basic cardiology and echocardiography for cats and dogs. By mastering these principles, attendees will enhance their ability to provide timely and accurate cardiac assessments, leading to improved outcomes and the continued well-being of their patients.

Clinical Pathology

Charalampos Attipa (United Kingdom)
DVM, MVetMed, MRes, MRCVS, Diplomate ACVP
(Clinical Pathology)

Charalampos qualified as a veterinary surgeon in 2010 from the Aristotle University of Thessaloniki Greece, with 1st class honors, having also completed a research internship at Cambridge University UK. Following 3 years in small animal general practice and completing an internship at Bristol University, Charalampos moved to the Royal Veterinary College for a residency in Veterinary Clinical Pathology and a master's in veterinary medicine.

After becoming a Diplomate of the American College of Veterinary Pathologists and an RCVS recognised specialist in Veterinary Clinical Pathology, Charalampos was awarded a Wellcome Trust Fellowship at Liverpool School of Tropical Medicine to study the role of neutrophils in pediatric cerebral malaria in Malawi. Since 2023 he has been a Senior Lecturer in Veterinary Clinical Pathology at the Royal (Dick) School of Veterinary Studies, Edinburgh University. Charalampos has published in leading scientific journals and his professional interests include hematopathology, cytology and infectious disease.

IN-HOUSE BLOOD SMEAR: HOW TO MAKE THE MOST OF IT?

Dr Charalampos Attipa DVM, MRes, MVetMED, PhD, DipACVP, MRCVS
RVCS & American Recognised Specialist in Veterinary Clinical Pathology
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When carrying out a complete blood count (CBC), preparation and evaluation of a blood smear should always be performed alongside. A blood film review will help confirm numerical data provided by the analyser and perform a differential cell count. It will also help identify morphological features that instruments cannot assess, such as left shift (increased immature neutrophils), toxic neutrophils, reactive lymphocytes, atypical white blood cells (WBC), abnormally shaped red blood cells (RBC)-poikilocytes and platelet clumps.

Although we often rely on external laboratories, blood smear examination can also be performed in house. This will allow vets to rapidly gain information regarding the health of the animal with minimal cost and in some occasions reach a final diagnosis.

A quality blood smear is the key

The biggest problem when reviewing in-house blood smears is often the bad quality of the preparations. In order to ensure a good quality blood smear:

- Collect blood with atraumatic venepuncture and place instantly in EDTA blood tube. Filled the tube as per manufacturer's instructions and mix gently by rotating the tube.
- Blood smears should be prepared immediately after collection. Within a few hours of collection storage artefacts will affect the cells.
  https://www.youtube.com/watch?v=nbRUiWl2Qrs&t=4s
- Allow the blood smear to fully air-dry.
- Hand dipping using well-maintained Romanowsky-type stains (e.g. Diff-Quik). Ideally have a second set of rapid stains for the "dirty" slides such as ear/skin cytology and aspiration of fatty lumps.

A good quality microscope with the proper adjustments and basic maintenance is needed and should be a part of every vet practise. Currently there is a plethora of companies manufacturing affordable microscopes that should be at a minimum equipped with four objectives (4x, 10x, 40x and 100x oil immersion) and a 10x eyepiece.

Once your blood smear is air-dried ensure you systematically follow the same steps every time when reviewing the smears. This will help for not missing any findings, will increase the confidence and speed in reviewing in-house blood ears, which can be done in few minutes.

Before starting to review your smear ensure that the condenser is raised to the top and the iris diaphragm opened. Always follow this 5 steps:

1. Evaluation of the feathered edge (10x lens)
2. Identification of the monolayer (40x lens)
3. Platelet evaluation (100x lens)
4. RBCs evaluation (100x lens)
5. WBC evaluation (100x lens)

1 Evaluation of the feathered edge

Initially scan the whole smear at low power using 10x lens or 20x lens (100 or 200 magnification). Aim to recognize the three areas of a blood smear: feathered edge, monolayer and body. Check the entire feathered edge on a 10x lens for platelet clumps, large abnormal cells (e.g. neoplastic cells) and parasites (e.g. microfilaria). If in any doubt, use the 100x oil lens to have a more detailed examination.

Identifying platelet clumps is the priority when examining the feather edge especially if there was thrombocytopenia on the CBC. Platelet clumps artifactually decrease platelet numbers and can

cause pseudo-thrombocytopenia. Thus, a low platelet count on the CBC has to be always be confirmed with a blood smear examination. Platelet clumps are typically an artefact of slow blood collection causing clotting, and cats in cats we often see pseudo-thrombocytopenia.

2 Identification of the monolayer

The second step of the blood smear examination is performed using the 40x lens. It is important to highlight that if the quality of the smear is poor, then often the monolayer is absent hindering further evaluation.

The monolayer is the area between the feather edge and the main body of the smear. In this area roughly half of the RBCs adhere to each other whilst the other half do not. The main body of the blood smear is deeper and is identified as the area in which almost all the RBCs adhere between them and it should not be evaluated as often morphologically artefacts are present on the main body. Once the monolayer area has been identified systemically evaluate the platelets, RBCs and WBCs using the 100x oil immersion lens. Ensure you stay within this part of the blood smear (Allison and Meinkoth, 2007).

3 Platelet evaluation

The platelets are fragments of anuclear cytoplasm. The main focus should be a manual platelet count that following this steps:
   a) In the monolayer, count the number of platelets in at least 10 fields using the 100x oil immersion lens.
   b) Calculate the average number.
   c) Multiply the average platelet number by 20 = estimated platelet count (x 10^9/L).
   d) Around 200-700 x 10^9/L is normally expected.

Remember that the manual platelet count will be falsely decreased if platelet clumps are present. A minimum of 8 to 10 platelets per high power fields should be seen in order to be interpreted as adequate (Day et al., 2000).

A free online atlas from Cornell University for blood cell morphology can be found at:
https://eclinpath.com/hematology/morphologic-features/

4 RBCs (erythrocyte) evaluation

The RBCs are non-nucleated, round biconcave shaped, have a uniform size and carry a central pallor in dogs. Note that in feline RBCs there are 3 main differences we normally do not see in the canine RBCs i) feline RBC have very limited central pallor, ii) slight anisocytosis (variation in the size of the RBC) is normally expected and iiI) rouleaux formation (red cells arranged in stacks, 'like coins') is often seen in feline smears and should not be associated with agglutination (Harvey, 2012).

Below are the most important changes we should always try to identify if present on the monolayer:
• *Polychromatophils*: Immature RBCs that stain slightly basophilic and are larger than normal. Low numbers of polychromatophils can be seen in blood smear from healthy animals. These cells are the best tool to judge regeneration on an in-house blood smear. Marked polychromasia is suggestive of a regenerative response. Anaemias caused by haemolysis and blood loss tend to exhibit marked regeneration, following an initial period of 3 to 5 days that the bone marrow needs to respond.
• *Nucleated RBCs*: Commonly seen in high numbers due to regenerative response of the bone marrow to anaemia. Other causes include bone marrow injury, infiltrative marrow disease, FeLV associated erythroid neoplasia and splenic dysfunction.
• *Howell-Jolly bodies*: Remnants of the nucleus that appear a dark blue round inclusion. Low numbers can be present in healthy cats. Increased numbers can be seen in regenerative anaemia, splenic dysfunction and erythroid dysplasia.
• *Basophilic stippling*: aggregation of ribosomes appearing as small basophilic granules. It can be seen in regenerative anaemia, mainly within polychromatophils. When not associated with severe anaemia, it may indicate lead toxicity.

• *Heinz bodies*: Appear as paler or of the same colour, small round structures inside or protruding from the RBCs. These structures are a result of oxidative damage that denatured haemoglobin and are more often seen in cats than dogs. If they are present in high numbers (more than 20%) then oxidative damage is present (toxins, drugs). Small Heinz bodies are normally present in low numbers without causing anaemia. Cats with hyperthyroidism lymphoma or diabetes mellitus (especially with ketoacidosis) can have increased numbers of Heinz bodies without anaemia (still the lifespan of RBCs is reduced).

• *Poikilocytosis*: Variation in the morphology of the erythrocytes. Low numbers of poikilocytes can be seen in healthy animals or may not be of diagnostic relevance in some ill animals. If found, these should be interpreted in view of other haematological findings, other laboratory findings and clinical signs. Amongst the most significant are:

Echinocytes: Have numerous small projections, which are evenly spaced. These are mostly artefactual (crenation) but can be caused by electrolyte imbalances and renal disease. **Very frequently seen**.

Acanthocytes: Have few large projections unevenly distributed. Often a result of liver disease, such as hepatic lipidosis (due to changes in the lipid content of cell membrane) or fragmentation injury (e.g. disseminating intravascular coagulation(DIC)).

Eccentrocytes: Appear condensed on one side and clear on the other, with the edge of the membrane barely visible; they are a result of oxidative injury on the cell membrane of the RBC.

Keratocytes: Have a single or two projections and give a "bite-shape" appearance. Low numbers can be seen in cats without a clinical significance. When they are present in high numbers or with other poikilocytes they can indicate fragmentation injury or liver disease.

Agglutination: Grape shaped aggregates of RBCs. They suggest immune-mediated haemolytic anaemia. It is important not to confuse agglutination with rouleaux formation which is often see in healthy cats.

Hypochromasia: Erythrocytes that appear pale with central pallor due to lower haemoglobin concentration. When seen with microcytosis (smaller RBCs), iron deficiency should be strongly suspected.

Spherocytes: RBCs that have the shape of a sphere rather than the normal discoid shape. Thus they are smaller and denser on the blood smear. Moderate to high numbers of spherocytes are diagnostic of immune-mediated haemolytic anaemia (IMHA). They are only recognised in dogs

Ghost cells: Appear as pale-staining RBCs with minimal haemoglobin and a faint cell membrane. Can be formed during intravascular haemolysis or in vitro.

5 White blood cells (WBC) evaluation

The WBC found in dogs and cats includes the granulocytes (neutrophils, eosinophils and basophils) lymphocytes and monocytes. Neutrophils are the most numerous WB of dogs and cats.

Neutrophils: Normal neutrophils have a well-segmented nucleus. They have a clear or very pale eosinophilic cytoplasm on most commonly used rapid stains. With some stains, small and very pale eosinophilic cytoplasmic granules may be seen.

Left Shift: The presence of immature neutrophils in circulation in numbers exceeding the established reference interval for that species. This is triggered by increased demand, such as in severe inflammatory conditions. Band neutrophils are the most commonly seen (with an unsegmented nucleus with two parallel bands or "S" shaped).

*Toxic change*s: Morphologic abnormalities caused by an accelerated maturation in the bone marrow secondary to increased demand. Toxic changes are commonly seen with a left shift, as the stimulus is the same (strong inflammatory stimulations such as bacterial infection, immune-mediated disease or neoplasia), however these can be seen individually. The main toxic changes include: Cytoplasmic basophilia, Döhle bodies (pale blue aggregates in the cytoplasm), cytoplasmic foaminess and toxic granulation. Note that healthy cats have low numbers of small Döhle bodies, so these alone do not indicate toxic change (Stockham and Scott, 2013).

Eosinophils: These are larger than neutrophils. Their nucleus is less segmented than that of neutrophils and has a dense chromatin pattern. Their cytoplasm contains small rod-shaped pink-orange granules.

Basophils: These are a rare finding in healthy animals. They are similar or larger in size to eosinophils. Their cytoplasm stains gray to pale purple/blue and contains pale purple/blue granules.

Lymphocytes: Most of the lymphocytes that circulate in healthy animals are small (mature) lymphocytes. They have a round nucleus and a small amount of pale blue cytoplasm. Normal lymphocytes need to be differentiated from nucleated red blood cells, reactive lymphocytes and neoplastic cells. Reactive lymphocytes usually have deeper blue cytoplasm and their nuclear to cytoplasmic ratio is often smaller than in normal lymphocytes; these are associated with antigenic stimulation (e.g. following a vaccination, young animals or chronic inflammation).

Monocytes: These are larger than neutrophils and can be fairly variable in size and appearance. Their nucleus varies in shape and is often. Their cytoplasm is moderate to abundant, usually stains blue-grey and often contains a few variably sized vacuoles

Neoplastic cells: These will be typically indicating an acute leukaemia typically of lymphoid or myeloid origin. They are large cells (typically larger than a monocyte or neutrophil) with a large nucleus often bigger than a RBC. The nucleus can have an abnormal morphology and the cytoplasm is deeply basophilic.

Blood smears are a useful and inexpensive diagnostic tool. With practice and methodical approach you can review them in house for rapid assessment of blood cells.

References
https://eclinpath.com/hematology/morphologic-features/

ALLISON, R. W. & MEINKOTH, J. H. 2007. Hematology without the numbers: in-clinic blood film evaluation. *Vet Clin North Am Small Anim Pract,* 37**,** 245-66, vi.
DAY, M. J., MACKIN, A. & LITTLEWOOD, J. D. 2000. *BSAVA Manual of Canine and Feline Haematology and Transfusion Medicine*, British Small Animal Veterinary Association.
HARVEY, J. W. 2012. *Veterinary Hematology: A Diagnostic Guide and Color Atlas,* St. Louis Missouri, USA, Elsevier Saunders.
STOCKHAM, S. L. & SCOTT, M. A. 2013. *Fundamentals of veterinary clinical pathology*, John Wiley & Sons.

IN-HOUSE CYTOLOGY OF LUMPS AND BUMPS: JUST DO IT!

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Introduction

Cytology is the examination of cells in smears and fluids. It requires minimal equipment, it is not invasive, is fast and most vets can learn to how to make an accurate diagnosis in a range of conditions easily. Still in many occasions it will only act as a screening test and histopathology or other axillary tests will be needed for a final diagnosis.

The smears are the key!

Fine needle aspirates biopsies (FNABs)

Suitable for cutaneous masses, internal masses and organs, lymph nodes etc. Avoids superficial contamination and allows collection of samples from deep within the lesion/tissue. There is the risk of coming out of small lesions or missing them altogether.

- ➢ Non-suction technique: insert the needle into the lesion, redirect in different directions (centre and edges), and take out the needle.
- ➢ Small needle 22-24 G, even insulin needle in cats

  Non-suction techniques cause less cell damage and haemorrhage so are ideal for delicate tissues (e.g. lymph node aspirates) but cellularity may be less than with the suction technique.

  Use this technique initially!! If not enough material is collected then use the suction technique.

- ➢ Suction technique: insert the needle of the syringe in the lesion, apply suction, redirect the needle, release suction, take out the needle.

- ➢ To prepare the smear: detach the needle (if needed), fill the syringe with air, reattach the needle, position the needle near the edge of the slide, and squirt out the material onto the slide. Repeat if necessary.
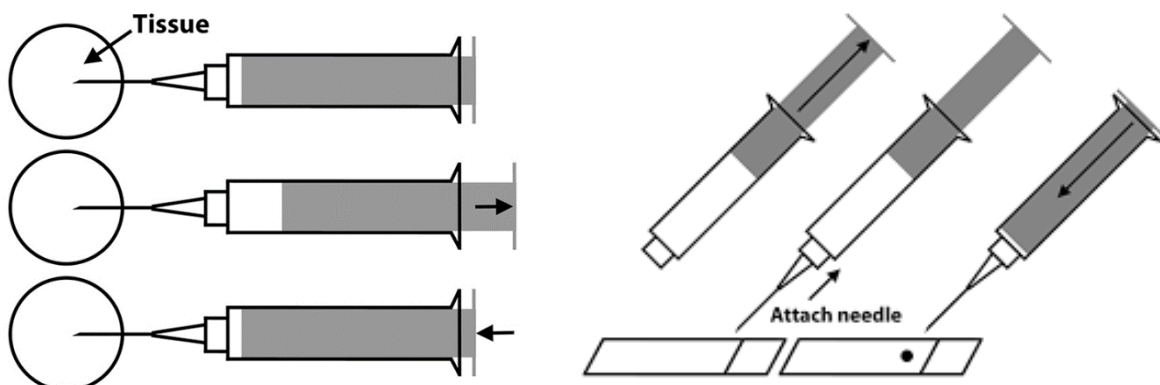
Figure 1: Schematic representation of FNAB and of how to place the aspirated material onto a glass slide

The material needs to be smeared out properly, **immediately** after being placed on the slide or it will dry as droplets, often too thick to be evaluated.

Squash preparation
The sample is placed on one side of the slide and the spreading slide placed on top to form a cross; then gently slide the spreading slide towards one end of the sample slide.
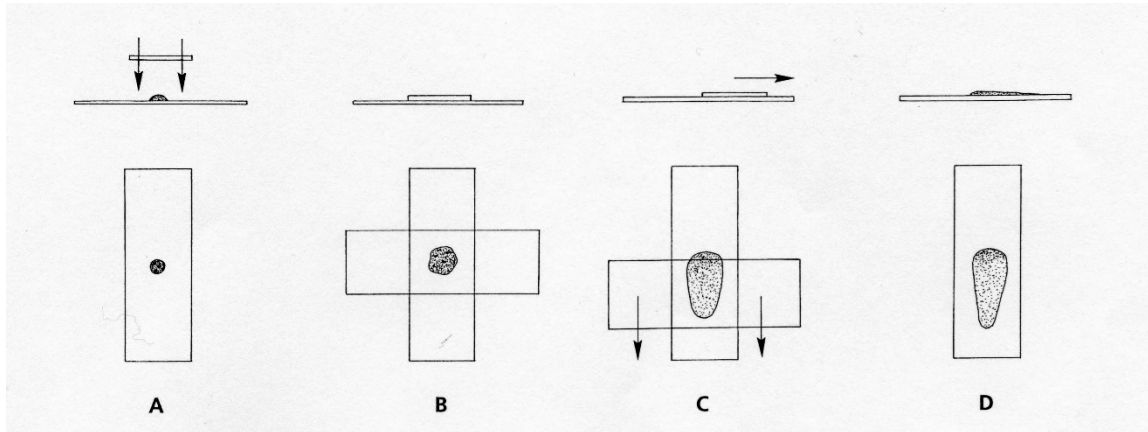
Figure 2: smearing of a cytological preparation using the squash technique

Swabs
Suitable for tissues which are not readily reached e.g. vagina, fistulous tracts.
Use cotton swab moistened in 0.9% NaCl to collect the sample. Then **roll** the swab down middle of the glass slide (do not slide across).

Touch imprints (aka "impression smears")
Suitable for rapid diagnosis of some external lesions and excised tissues, which may subsequently be examined by histopathology.
They yield fewer cells than scrapings, and there is a risk of only detecting surface inflammation/blood or contaminants.
For excised tissues, make a fresh cut surface, blot on absorbent paper to remove excess blood and then **gently** make multiple impressions on a slide (straight down onto slide and straight up again; do not smear across the slide). The remaining tissue should be undamaged and can then be placed in buffered formalin for histological sections to be made.

Always remember that **1 sample equals ZERO sample**!! Thus ensure you collect multiple samples

Do not forget labelling!!

Slide labelling
Lack of, or incomplete labelling of slides causes confusion with the potential for misdiagnosis and serious consequences. Glass slides with a frosted end must be used and the patient identity and source of the material written clearly in pencil on the same side as the material is on. **Don't use pens of any kind** as even "permanent" ink comes off during staining. The details of what has been sampled and clinical details should also be written on the submission form.

Stains for cytology
Many stains for cytology are available but it is best to stick to simple stains for general work. The main stains used in practice are:

- Diff-Quik® or Rapi-Diff® - general cytology and haematology (part of the Romanowsky stains). They do not stain some granules in cells well, especially mast cell granules.

Laboratories use their own staining, so sending un-stained slide is best.

Ideally have **TWO SET OF STAINS**. One for "dirty" slides (e.g. fatty slides, ear samples) and one for "clean" slides (e.g. blood smears and FNABs).

EVALUATING CYTOLOGY SMEARS

Be methodical and always follow the same steps when evaluating your smears.

General assessment of cytology slides
1. Scan your slight with x10 lens
   ➢ Cellularity
   ➢ Arrangement – clusters, sheets or individual
   ➢ Background – mucus, blood / Large organisms – larvae, fungi

2. Focus on an area with x40 lens
   ➢ Shapes
   ➢ Variability
   ➢ Degree of cellularity

3. Land on an area with x100 immersion oil lens

Evaluate cells populations and all the details following this decision tree (DICN)
   ➢ Diagnostic ?
   ➢ Inflammatory ?
   ➢ Cell type ?
   ➢ Malignant ?

Making a diagnosis/ Decision tree

1. Diagnostic sample ?

No
- Poor sampling technique
- Non-exfoliating mass

Yes

2. Is it inflammatory ?

Yes
- Type of inflammation ?
- Cause ?

No

3. What type of cells I have ?

What type of round cell ?
- Epithelial ?
- Mesenchymal ?
- Round ?

4. Is it neoplasia ?
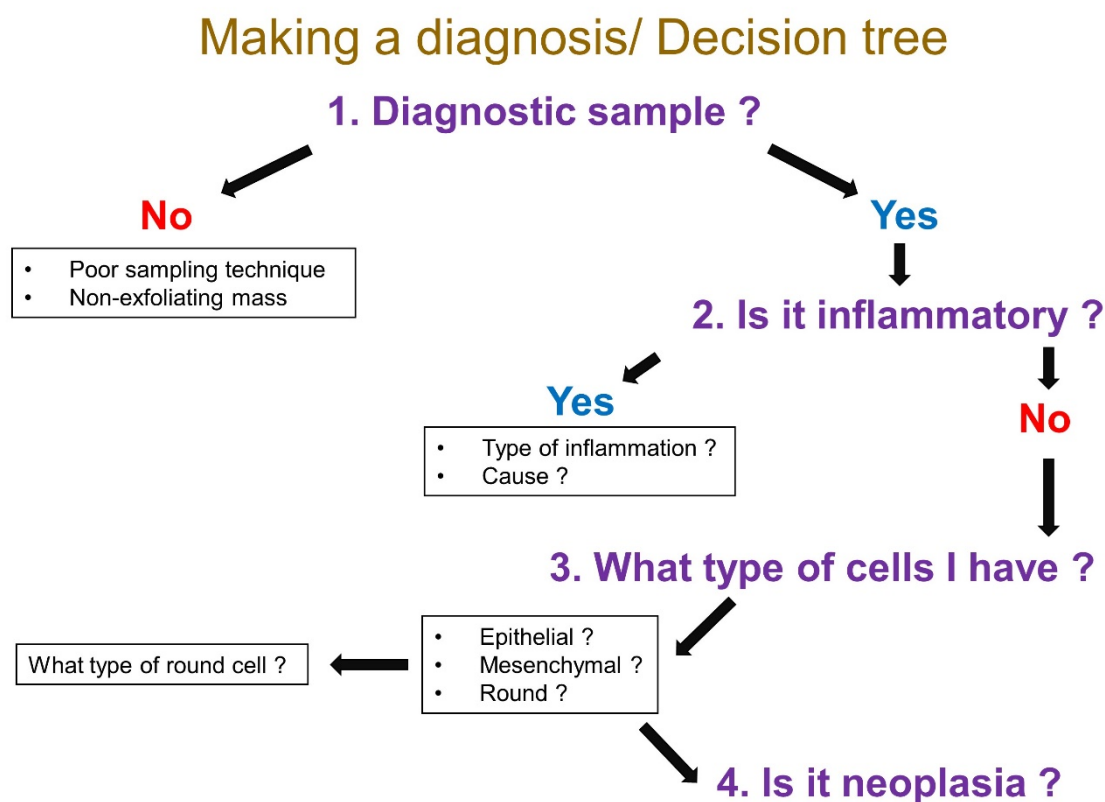
Question 1: Is it diagnostic?
If truly non-diagnostic
- ➢ Re-aspiration with negative pressure (FNABs)
- ➢ Use a bigger size needle/ultra-sounded guided
- ➢ Ensure no ultrasound gel/blood/formalin contamination and be gently when smearing
- ➢ Perform histopathology

If sample is diagnostic, then we got to question number 2 →

Question 2: Is it inflammatory?
Predominance of inflammatory cells
- Neutrophils→ Neutrophilic inflammation can be associated with bacteria (especially if neutrophils appear degenerate and their nucleus appears puffy and smudged), autoimmune disorders, and acute inflammation.

- Eosinophils→ Eosinophilic inflammation can be associated with hypersensitivity, parasites, and neoplastic conditions such as MCT

- Macrophages→ Macrophages (with or without neutrophils) are generally associated with foreign bodies, fungal, protozoal infections.

- Lymphocytes/plasma cells→ Lymphocytes and plasma cells, together with macrophages, can be associated with a more chronic inflammation, viral infections and other

- Mixed inflammation

If truly inflammatory
- ➢ Classified the type on inflammation
- ➢ Try to identified the cause if inflammation in conjunction with clinical history
- ➢ Remember you need bacterial cultures to rule out an infection
- ➢ **If multiple inflammatory populations with atypical cells then best for the slide to be reviewed by a board-certified clinical pathologist**

If sample is diagnostic but non-inflammatory, then we got to question number 3 →

Question 3: What type of cells I have?
Cell types
Cell types can be divided into **three main categories**, so when evaluating slides, decide which category(ies) is present first then decide what the cells are:

- **Epithelial -** e.g. squamous cells, basal cells, hepatocytes, glandular and duct lining cells.
    Typically exfoliate in **good** numbers
    Often found in **sheets, clusters**
    Large, oval to angular cells
    Cell-to-cell junctions
    Nuclei round, centrally located
    Cytoplasm **often abundant**

- **Mesenchymal** – mainly connective tissue cells e.g. fibroblasts, osteoblasts.
    Typically exfoliate in low numbers
    Often found in individually
    Medium, spindle to fusiform to stellate
    Indistinct/wispy cell borders
    Oval nucleus
    With extracellular matrix

- **Round cell**: lymphocytes, histiocytes, plasma cells, mast cells
    Typically exfoliate in good numbers
    Often found in discrete arrangement

Small to medium, round to oval cells
Clear cell borders
Round nucleus
Cytology more useful than histology often

If you have diagnosed one of the round cells types
Identified which on the round cells you have
You have reached a diagnosis!! No need for the 4th question

If its epithelial or mesenchymal then need to ask question number 4 →

In some occasions you might not be able to tell the origin of your cells. In that case just move on to question number 4 →

Question 4: Is it neoplasia?
Neoplasia – Benign or malignant neoplastic cells. Benign neoplasia may resemble the normal cells of that type, or appear mildly pleomorphic. For appearance of malignant cells, see below.

N.B. More than one process may be present at the same time e.g. an inflamed tumour or a cystic tumour.

Abnormal cell morphology

Important cytological concepts:

- **Hyperplasia** – May look normal or have mild anisocytosis, slightly variable nucleus to cytoplasm (N:C) ratio and/or increased cytoplasmic basophilia.
- **Dysplasia** – Results from asynchronous maturation of different parts of the cell e.g. immature nucleus in mature cytoplasm. Can occur with chronic inflammation/irritation. Mild to moderate anisocytosis, variation in nuclear size (anisokaryosis), increased N:C ratio, occasionally coarse chromatin. **Be careful in diagnosing neoplasia where there is significant inflammation** as some of the changes are similar in dysplasia and neoplasia.
- **Neoplasia** – Benign or malignant tumours (see below).
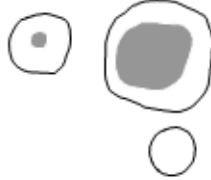
Neoplasia
Cytological criteria of malignancy
Certain "criteria of malignancy" are used in cytology to try to decide whether malignant neoplasia is present. If they are absent it is more likely the lesion is benign, but some tumours e.g. endocrine tumours tend to look benign even when they are malignant. Conversely, some e.g. cutaneous histiocytoma sometimes look malignant even although they are benign. The following are some general rules for identifying criteria of malignancy.
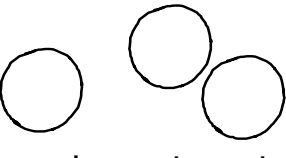
Criteria of malignancy
(General / whole cell)

Criteria	Description	Schematic representation
Pleomorphism	**Variable size, shape and nucleus:cytoplasm ratio in cells of the same type (exception: lymphoid tissue)**	
Anisocytosis Macrocytosis	**Marked variation in cell size, some cells > 1.5 times larger than normal**	
Hypercellularity	**Increased cell exfoliation (decreased cell adherence)**	
Disordered alignment of the cells in clusters		6

(Nucleus 1)

Criteria	Description	Schematic representation
Anisokaryosis	**Marked variation in nuclear size especially nuclei of multinucleated cells**	
Macrokaryosis	**Increased nuclear size especially nuclei with diameter > 10 μm**	
Increased nucleus: cytoplasm (N:C) ratio	**≥1:2 (normal, nonlymphoid tissue: 1:3 to 1:8)**	
Multinucleation	**Multiple nucleation in a cell, especially important if nuclei vary in size (exception: osteoclasts, megakaryocytes)**	

(Nucleus 2)

Criteria	Description	Schematic representation
Increased mitotic figures	**Mitosis is rare in normal tissue**	
Abnormal mitosis	**Atypical mitotic figures, single chromosomes, division in three parts, incorrect alignment of chromosomes**	normal abnormal
Atypical chromatin pattern	**Cord-like, coarse, clumps, fragments, nuclear wall hyperchromasia, variations in chromatin content**	
Nuclear moulding	**Deformation of nuclei by other nuclei within the same cell or adjacent cells**	8

Artefacts

It is important to be able to recognise artefacts in smears so they are not misinterpreted. These include nuclear streaking due to too much pressure when making the smear, haemorrhage during sample collection (the presence of platelets suggests this whereas the presence of erythrophagocytosis suggests the haemorrhage was present before sample collection), and ultrasound and lubricant gel (bright pink granular material).(Stockham and Scott, 2013, Rose E. Raskin and Meyer, 2015, Cowell et al., 2007)

Common lesions

Skin tag's / keratin lesions

- ➤ Vast category of mostly benign skin masses that on cytology look similar
- ➤ Keratin cysts, epitheliomas, hair tumors etc
- ➤ White material on FNB that looks like pus
- ➤ Keratin material and cholesterol crystals
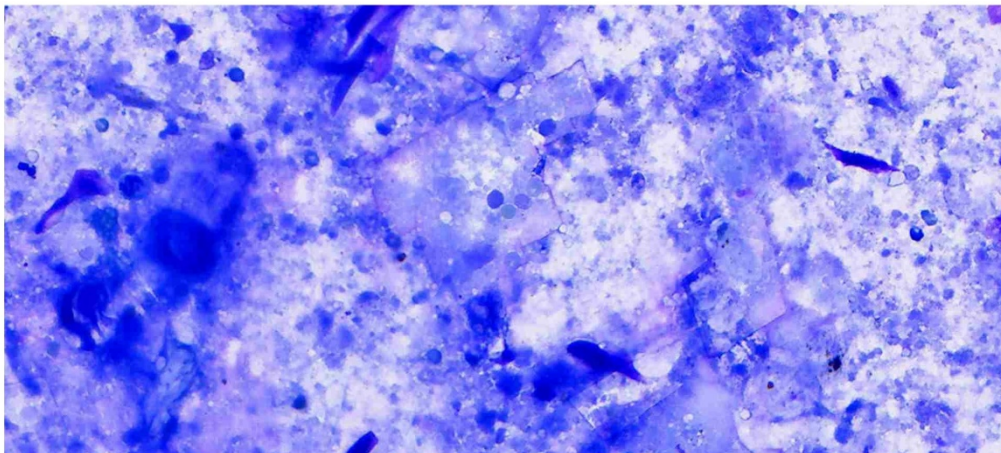
3. Common lesions

Lipoma
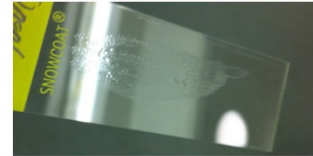
➢ Most common subcutaneous mass in companion animals
➢ The slides do not dry out
➢ Looks exactly like adipose tissue
➢ Most of the time you get no cell only fat droplets
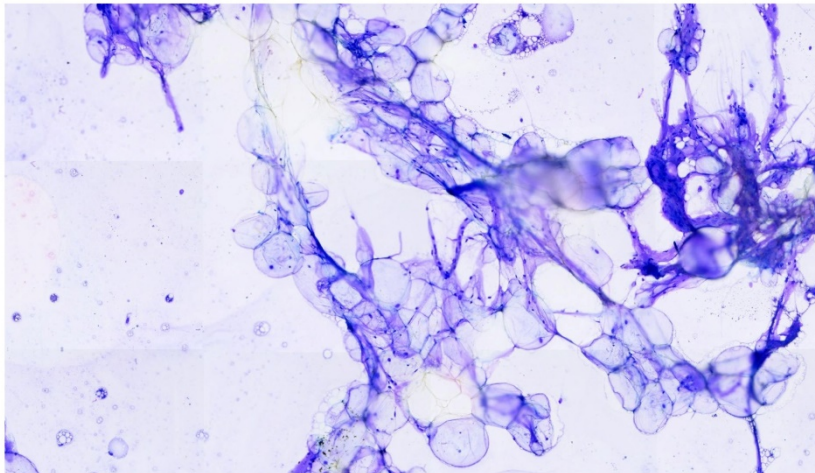
3. Common lesions

Mast cell tumour (MCT)

➢ Most common cutaneous tumor in dogs, also seen in cats
➢ Most cases surgery is curative but always histopathology for grading and margins
➢ Classic well granulated magenta stained round cells.
➢ Often eosinophils with collagen and fibroplasia
➢ Diff-Quick may not stain the granules (re-stain)
➢ Cytology can indicate a high grade MCT
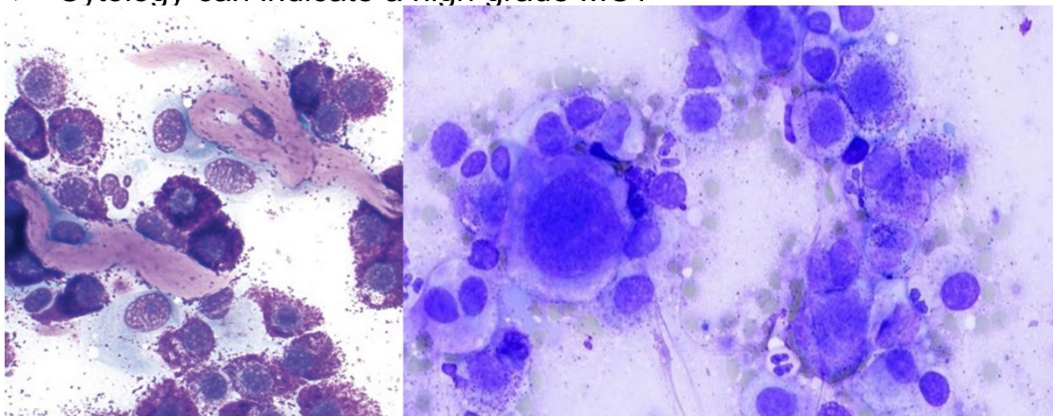
3. Common lesions

Histiocytoma

➢ Most common tumor in young dogs, often in the head and limbs

➢ "Typical round cells, with watery-blue cytoplasm and often basophilic background

➢ Small lymphocytes can be seen when the histiocytoma is regressing
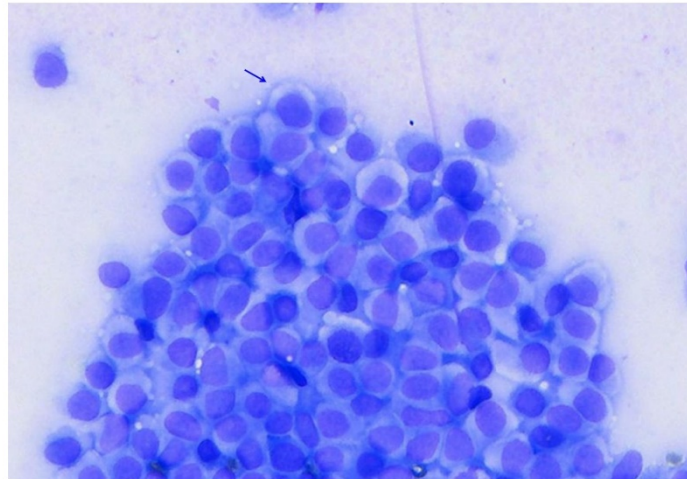
3. Common lesions

Transmissible Venereal Tumour (TVT)

➢ Nodular to multilobulated, erythematous, ulcerated surface, often at the external genitalia

➢ Large, round cells that have a moderate volume of pale blue cytoplasm with many clear **vacuoles**.

➢ **Reticulated/ropey chromatin**

➢ Prominent, mostly single, **basophilic nucleoli**

➢ **Mitotic** figures are common
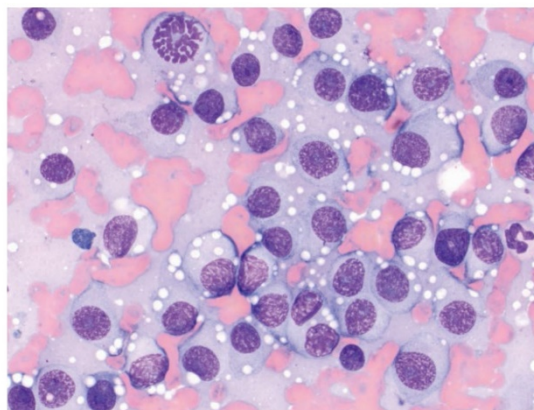
3. Common lesions

LYMPHOMA

➢ Typically, multicentric affecting the LNs

➢ Uniform population of medium or large lymphocytes that are >50% of the lymphoid population

➢ Classic 1st opinion lymphoma all lymph nodes enlarge and >90% of the lymphocytes are large

➢ **Most lymphomas as diagnosed on Cytology. PARR** (PCR for Antigen Receptor Rearrangements) can be done on the slides for immunophenotyping.

References
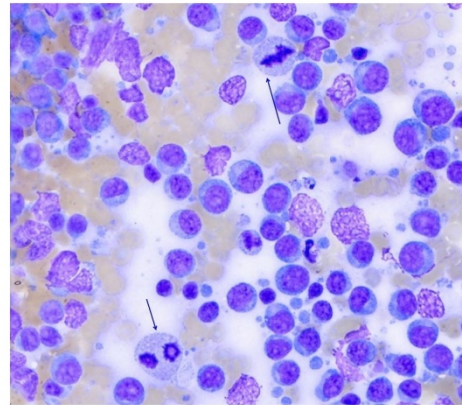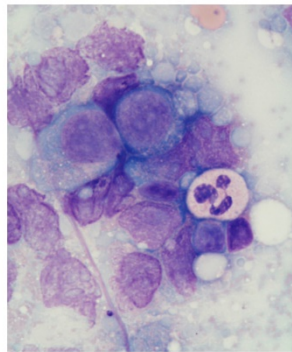
https://eclinpath.com/hematology/morphologic-features/

COWELL, R. L., TYLER, R. D., MEINKOTH, J. H. & DENICOLA, D. B. 2007. *Diagnostic cytology and hematology of the dog and cat-E-book*, Elsevier Health Sciences.

ROSE E. RASKIN & MEYER, D. J. 2015. *Canine and Feline Cytology,* St. Louis, MO, Saunders Elsevier.

STOCKHAM, S. L. & SCOTT, M. A. 2013. *Fundamentals of veterinary clinical pathology*, John Wiley & Sons.

LIVER ENZYMES IN DOGS AND CATS: DO THEY REALLY MEAN ANYTHING?

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Introduction

The main serum liver enzymes that we routinely check in dogs and cats are alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and gamma-glutamyltransferase (GGT).

ALT and AST are cytosolic enzymes meaning they are located inside a hepatocyte and are used as markers of **hepatocellular damage**. ALT is present in the cytoplasm of the hepatocytes and AST in present mainly in the mitochondria of hepatocytes. Thus, ALT and AST should be considered as hepatocellular "leakage" enzymes.

ALP and GGT are non-cytosolic enzymes, located on hepatocytes lining the bile canaliculi surface outside hepatocytes and are **markers of cholestasis**. When there is cholestasis (intra- or extrahepatic) this causes increased surface tension in the canaliculi and bile ductules which upregulates and increases the production of these two surface enzymes; "induction enzymes".

Liver enzymes can be elevated due to a primary liver disease or secondary by other diseases or processes outside the liver, such as endocrinopathies (e.g. Cushing's disease, diabetes, hyperthyroidism), pancreatitis or intestinal disease (Table 1).

Additionally many medications (e.g. steroids or phenobarbital), can also cause elevations in liver enzymes activity. This means that whilst liver enzymes are sensitive markers for hepatobiliary disease, they are not very specific.

Decreased liver enzymes concentrations do not have significant clinical importance.

Most importantly liver enzymes are not markers of liver function!

Liver can still be functioning in full capacity despite having severe damage.

Table 1 Selective causes of increased liver enzyme activity

	ALT/AST	ALP/GGT
Hypoxia	Congestion, anaemia, sepsis, thrombosis	Less frequently and mild elevation compared to ALT/AST
Inflammatory	Acute or chronic hepatitis, cholangitis, cholecystitis	Acute or chronic hepatitis, cholangitis, cholecystitis
Infectious	Leptospirosis, bacterial, FIP, toxoplasmosis	Less frequently and mild elevation compared to ALT/AST
Endocrine	Feline hepatic lipidosis, diabetes mellitus, feline hyperthyroidism, canine hypothyroidism, hyperadrenocorticism	Feline hepatic lipidosis, diabetes mellitus, feline hyperthyroidism, canine hypothyroidism, hyperadrenocorticism
Neoplasia	Lymphoma, hepatocellular carcinoma, metastatic	Bile duct carcinoma, lymphoma, metastatic
Medications	Azathioprine, tetracyclines, phenobarbital	Corticosteroids (dogs), phenobarbital
Toxins	Zinc, aflatoxin, muschroom, heavy metals	Less frequently and more elevation compared to ALT/AST
Other	Steroid hepatopathy, pancreatitis, enteritis, benign nodular hyperplasia	Extrahepatic bile duct obstruction (gallbladder, mucocele, choledocholithiasis, neoplasia), benign nodular hyperplasia, growth (young dogs), vacuolar hepatopathy, osteoblastic activity

ALT (alanine aminotransferase)

This enzyme is found in the cytoplasm of hepatocytes and in a smaller degree in myocytes and even erythrocytes. ALT leaks in the bloodstream when the cell membrane is damaged (e.g. necrosis) or has increased permeability (e.g. regeneration). As a results **ALT is a sensitive marker of hepatocellular injury and is more specific than AST**.

Yet, other conditions such as very severe muscle damage or haemolysis can increase the activity of ALT.

ALT has a half-life of approximately 60 hours in dogs. Which means when we monitor this enzyme in dog, we anticipate meaningful changes after 3-days. Note that if ALT is increase over weeks then this indicates of chronic hepatopathy.

On the other hand feline ALT has a very short half-life of approximately 3.5 hours, thus even a very small increase in cats it is significant, especially in conditions such as feline hyperthyroidism that can affect the liver.

AST (aspartate aminotransferase)

This enzyme is located primarily in the mitochondrial as well as in the cytoplasm of the hepatocytes and other cells. Similar to ALT, damage of cell membrane will cause leak of cytoplasmic AST. However, for the leak of mitochondrial AST it is required severe and permanent damage of the liver.

AST is increased in parallel with ALT, but is less specific than ALT, since muscle injury (skeletal and cardiac) and haemolysis can increase AST. If creatine kinase (CK) is also elevated with AST, whilst ALT is not increased, then this is indicative of muscle damage.

The half-life of AST is approximately 24-hours in dogs and 1.5 hours in cats. This shorter half-life compared with ALT means that AST activity decreases and returns to normal quicker than ALT in patients with acute liver injury.

ALP (Alkaline phosphatase)

ALP is non-cytosolic enzyme found on the surface of hepatocytes lining the bile canaliculi. It is released into the circulation during intra- or extrahepatic cholestasis. Whilst it is a very sensitive marker for cholestasis in dogs, it is not specific due to the multiple extra-biliary source of this enzyme.

Other extra-biliary causes (isoenzymes) of elevated ALP activity includes
- Bone remodelling due to growth, fracture, inflammation or neoplasia: Young growing animals (especially giant breeds) have an ALP activity mildly increased. A mild increase of bone ALP can be seen in patients with osteomyelitis, bone reforming following a fracture or in an osteosarcoma that is considered negative prognostic marker.
- Glucocorticoids, both endogenous and exogenous: Dogs with hyper-adrenocorticism and those receiving glucocorticoids can be expected to have increased ALP activity due to the glucocorticoid-induced isoenzyme.

Due to various isoenzymes ALP has there is lack of tissue specificity which means ALP can be hard to interpret. Note that routinely biochemistry analysers cannot differentiated the different isoenzymes. Still high activities of ALP have been reported with cholestasis, steroid hepatopathy, chronic hepatitis, and hepatic necrosis.

The half-life of ALP is approximately 70-hours in dogs and feline ALP only 6-hours. It is important to highlight that cats do not have a glucocorticoid-induced isoenzymes. And in conjunction with the shorter half-life, the increased feline ALP activity is more specific for biliary diseases than in dogs and should always be investigated.

GGT (gamma-glutamyltransferase)

This enzyme similarly to ALP is non-cytosolic, found on the surface of hepatocytes lining the bile canaliculi as well as periportal hepatocytes. It is a cholestatic marker for both intrahepatic (e.g. feline hepatic lipidosis) or extrahepatic (e.g., bile duct obstruction).

In comparison with ALP in dogs, GGT is more specific (meaning when increased most likely there is cholestasis) but has a lower sensitivity (meaning is not always elevated when cholestasis is present). In cats GGT is considered more sensitive marker for hepatobiliary disease than ALP. Note that feline hepatic lipidosis is an exemption as GGT is generally only mildly elevated. Whilst data are still lacking, GGT is considered to have a similar half-life as ALP.

Interpreting liver enzyme elevations

The degree of the increase in the previous enzyme activities is the key on the way we interpret them. As a rule of thumb we considered the elevation in activity:

- **Mild: 2-3x fold**
- **Moderate: 5-8x fold**
- **Severe: >10x fold**

Yet, there are exemptions that we need to remember.
End-stage chronic hepatopathy and portosystemic shunts do not cause notable increase of liver enzymes. During the resolving/regenerative phase of a liver insult, the liver enzymes are often elevated and should not be used as an indication of ongoing disease.

When evaluating liver enzymes, it is important to determine if this is a primary hepatocellular damage or cholestasis. If ALT and AST are more increased than ALP and GGT then this indicates a more

significant hepatocellular damage. If ALP and GGT are more increased than ALT and AST then this indicates a more significant cholestasis (intrahepatic or extrahepatic). Establishing which is the primary pattern is may help narrow the differential diagnosis. Yet, there are liver diseases that can display a mixed pattern (e.g. phenobarbital hepatopathy or cholangitis).

In an **asymptomatic patient** with mild increased liver enzymes and no likely explanation we have two options; either begin a diagnostic evaluation of the patient (e.g. ultrasound and functional assays such as bile acids) or if there are financial restrictions re-evaluate the liver enzymes is 6–8 weeks. If there are still elevated liver enzymes further investigation will be needed.

The most common cause for elevated liver enzymes are the secondary/reactive hepatopathies resulting from a plethora of primary non-hepatic conditions (Stockham and Scott, 2013, Ettinger et al., 2016, Dirksen et al., 2017, Twedt, 2009).

Conclusions

Liver enzymes is a fairly cheap, fast and easy to perform diagnostic test that can guide us towards hepatobiliary disease and further narrow down the list of differential diagnosis (hepatocellular damage, cholestasis, or both). However on their own they do not provide a specific diagnosis nor aetiology.

Thus additional test are needed to further investigate hepatobiliary disease including liver function tests (e.g. serum albumin, cholesterol, blood urea nitrogen, glucose, bilirubin, bile acids, ammonia), advance imaging, infectious diseases testing, cytology and histopathology. The previous should always be interpreted in conjunction with the history, clinical signs and physical examination.

References

https://eclinpath.com/chemistry/liver/

DIRKSEN, K., BURGENER, I., ROTHUIZEN, J., VAN DEN INGH, T., PENNING, L., SPEE, B. & FIETEN, H. 2017. Sensitivity and specificity of plasma ALT, ALP, and bile acids for hepatitis in labrador retrievers. *Journal of veterinary internal medicine,* 31**,** 1017-1027.

ETTINGER, S. J., FELDMAN, E. C. & CÔTÉ, E. 2016. *Textbook of Veterinary Internal Medicine-Inkling E-Book*, Elsevier health sciences.

STOCKHAM, S. L. & SCOTT, M. A. 2013. *Fundamentals of veterinary clinical pathology*, John Wiley & Sons.

TWEDT, D. 2009. Abnormal liver enzymes: a pratical clinical approach.

Diagnosis of canine and feline leishmaniosis

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Introduction

Leishmaniosis is a vector-borne zoonotic disease that in companion animals of Europe is mainly caused by the protozoan parasite *Leishmania infantum*. Dogs are the main reservoir for *L. infantum* that is transmitted by sand flies of the *Phlebotomus* species. In endemic areas the sero-prevalence in dogs may approach up to 90% but the majority of infected dogs do not develop any clinical signs or snow a mild disease. Leishmaniosis is a chronic disease with a long incubation period – it can be 3 months to 7 years after infection that clinical signs develop. Generally in canine leishmaniosis (CanL) when cell mediated immune response fails to control the infection and in conjunction with marked humoral response then clinical disease progress. Feline leishmaniosis (FeL) is less studied and understood compared to CanL, still the past two decades extensive prevalence studies have been performed showing a sero-prevalence of 11% and an overall PCR positivity of 10%.

Clinical signs
For both species they are non-specific.

- **CanL**: In dogs are extremely variable. Some of the most common ones includes skin lesions (scaling, alopecia, ulceration), exfoliative dermatitis often on the head, lymphadenomegaly, ocular signs (e.g. blepharitis, uveitis, conjunctivitis, keratoconjunctivitis), splenomegaly, pale mucous membranes, polyarthropathy, kidney disease and associated signs (polyuria & polydipsia) onychogriphosis (abnormal nails), weight loss & poor body condition and fever.

- **FeL**: In cats we do see some similar clinical signs as with dogs, but fewer have been reported. The most common ones includes lymphadenomegaly, weight loss, anorexia, ulcerative or nodular dermatitis, ocular (e.g. blepharitis) and stomatitis

Haematology and biochemistry findings
For both species they are non-specific.

- **CanL**: Common non-regenerative anaemia. Occasionally thrombocytopenia or neutropenia if the bone marrow has been affected. Hyperproteinaemia due to hyperglobulinaemia and hypoalbuminaemia is also a very common finding. Azotaemia and mild elevated liver enzymes can also be seen.
- **FeL**: Similarly with the dogs, the cats with FeL can have non-regenerative anaemia, rarely pancytopenia, hyperproteinaemia due to hyperglobulinaemia and hypoalbuminaemia as well as azotaemia.

CYTOLOGY
Is considered an **important diagnostic tool for both CanL and FeL.** We can confirm diagnosis with a minimally invasive procedure, by finding *Leishmania* organisms on stained smears from fine needle aspirates or impression smears.

- **CanL and FeL**: For both cats and dogs, we can find *Leishmania* amastigotes in parasitophorous vacuoles of infected macrophages in lymph nodes, skin lesion, bone marrow, joints or ocular lesions. The parasites can also be present extracellularly (often the cells lyse during the preparation) in low to high numbers. Additionally we see lymphoid hyperplasia and plasma cell expansion in the lymph nodes infected with *L. infantum*.

  It does require some basic training and familiarity with microscopy/cytology. A negative results does not rule out clinical disease, since often the parasites cannot be found easily.

SEROLOGY
Is considered an **important diagnostic tool for CanL**

- **CanL**: The detection of *Leishmania*-specific serum IgG antibodies in the serum of dogs using quantitative techniques is very useful in the diagnosis of *Leishmania* infection. However, serology indicates exposure to *Leishmania*, and should be considered alongside clinical signs and additional clinicopathological testing.

  Seroconversion takes typically 5-6 months and in high levels of antibodies are consistent with clinical disease. A negative result does not rule out clinical disease as rarely some dogs do not seroconvert.

  Antibodies are typically detected by either ELISA or immunofluorescence (IFAT) and both are regarded as being good tests although some subjectivity occurs in the interpretation of IFAT titres.

  Serial monitoring should be performed **using the same assay at the same laboratory**. Results from different laboratories are not comparable.

- **FeL**: Whilst antibody detection has been extensively used in cats for research (IFAT, ELISA, DAT) it is less widely available for diagnostic purposes. A cut off
  IFAT at 1:80 dilution (similar to that used in dogs) has been established and almost all cats affected by clinical FeL have detectable antibody level. Yet discrepancies do occur and diagnosis should be made using serology alone.

Polymerase chain reaction (PCR)
Can be used as an additional test for diagnosing CanL

- **CanL**: Sensitive and specific test. With Real-time (quantitative) PCR we can also quantify the *Leishmania* DNA in the sample. Common samples that can be used includes bone marrow, lymph nodes, skin aspirates, spleen aspirates and whole blood. Due to its high sensitivity the PCR can be positive in dogs that just infected and not have CanL. Thus serology should be performed in this asymptomatic dogs and monitor their clinical development. A negative test does not rules out leishmaniosis.

- **FeL**: PCR has been used mainly for prevalence studies in whole blood. Currently there are limited data regarding the clinical usefulness of PCR in FeL.

(Attipa et al., 2017a, Attipa et al., 2017b, Baneth et al., 2008, Pennisi et al., 2013, Pennisi et al., 2015, Solano-Gallego et al., 2011, Pennisi and Persichetti, 2018).

References

ATTIPA, C., NEOFYTOU, K., YIAPANIS, C., MARTÍNEZ-ORELLANA, P., BANETH, G., NACHUM-BIALA, Y., BROOKS-BROWNLIE, H., SOLANO-GALLEGO, L. & TASKER, S. 2017a. Follow-up monitoring in a cat with leishmaniosis and coinfections with *Hepatozoon felis* and '*Candidatus* Mycoplasma haemominutum'. *Journal of Feline Medicine and Surgery Open Reports,* 3**,** 2055116917740454.

ATTIPA, C., PAPASOULIOTIS, K., SOLANO-GALLEGO, L., BANETH, G., NACHUM-BIALA, Y., SARVANI, E., KNOWLES, T. G., MENGI, S., MORRIS, D., HELPS, C. & TASKER, S. 2017b. Prevalence study and risk factor analysis of selected bacterial, protozoal and viral, including vector-borne, pathogens in cats from Cyprus. *Parasites & Vectors,* 10**,** 130.

BANETH, G., KOUTINAS, A. F., SOLANO-GALLEGO, L., BOURDEAU, P. & FERRER, L. 2008. Canine leishmaniosis - new concepts and insights on an expanding zoonosis: part one. *Trends Parasitol,* 24**,** 324-30.

PENNISI, M. G., CARDOSO, L., BANETH, G., BOURDEAU, P., KOUTINAS, A., MIRO, G., OLIVA, G. & SOLANO-GALLEGO, L. 2015. LeishVet update and recommendations on feline leishmaniosis. *Parasit Vectors,* 8**,** 302.

PENNISI, M. G., HARTMANN, K., LLORET, A., ADDIE, D., BELAK, S., BOUCRAUT-BARALON, C., EGBERINK, H., FRYMUS, T., GRUFFYDD-JONES, T., HOSIE, M. J., LUTZ, H., MARSILIO, F., MOSTL, K., RADFORD, A. D., THIRY, E., TRUYEN, U. & HORZINEK, M. C. 2013. Leishmaniosis in cats: ABCD guidelines on prevention and management. *J Feline Med Surg,* 15**,** 638-42.

PENNISI, M. G. & PERSICHETTI, M. F. 2018. Feline leishmaniosis: Is the cat a small dog? *Vet Parasitol,* 251**,** 131-137.

SOLANO-GALLEGO, L., MIRO, G., KOUTINAS, A., CARDOSO, L., PENNISI, M. G., FERRER, L., BOURDEAU, P., OLIVA, G., BANETH, G. & THE LEISHVET, G. 2011. LeishVet guidelines for the practical management of canine leishmaniosis. *Parasit Vectors,* 4**,** 86.

FIP diagnosis in the era of outbreaks and anti-viral treatments

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Introduction

Feline infectious peritonitis (FIP) is a historically fatal disease caused by mutations of the ubiquitous RNA feline corona virus (FCoV). FCoV transmission is faecal-oral via litter trays and fomites as it is a primary enteric virus causing only occasionally mild enteritis.

From the FCoV-infected cats a small proportion develops FIP. The current theory is that internal mutations of FCoV (that appears unique for every cat) cause the infection of monocytes that drives the pathogenesis of FIP via vasculitis. The most common clinical presentation includes effusions (commonly abdominal and/or pleural, and rarely pericardial), anorexia, fever, and weight loss. The effusive form is often referred as "wet" form. Also, a so called "dry" form is reported that includes abdominal lymphadenopathy and granulomas formations without effusions. Lastly a neurological form, as well are ocular presentations can occur.

Until recently, there were few treatments for FIP, which causes significant illness and mortality in cats globally. Following the COVID-19 outbreak, a plethora of antiviral drugs against SARS-CoV-2 have been licensed with some being also effective in FIP. The most widely used treatment so far is the antiviral oral GS-441524 and its prodrug injectable remdesivir. These drugs have become available via legal sources in some countries.

Outbreaks of FIP have previously been documented in the UK, USA and Taiwan, but were usually small in scale, and restricted to individual catteries and rehoming centres. Recently an outbreak of FIP has been reported in Cyprus have affected at least 8000 cats in the first six months of 2023. The Cyprus outbreak has become widespread in different districts of the island very quickly. This is extremely alarming and suggests that a highly virulent strain of FCoV is present in Cyprus that may potentially be transmitted by mechanical vectors or directly between cats.

Below we will be discussing different diagnostic tools we have available and how we can used them to reach a diagnosis. Sampling the effusion for cytology, biochemistry and FCoV reverse transcription (RT)-PCR are the most useful diagnostic step for FIP when the "wet" form is present. When no effusion is present fine-needle aspiration biopsy (FNABs) from the organs or CSF collection followed by cytology and FCoV RT-PCR are the most meaningful diagnostic steps. The golden standard in diagnosis is considered having the compatible histopathological changes in the affected tissues with positive intra-cellular FCoV antigen immunostaining.

- **Signalment**: FIP can occur in cats of all ages but is more common in young cats (especially <2 years). Pedigree cats as well as males are at a slightly higher risk. Multi-cat households or cats with recent stressing events (e.g. adoption, being in a shelter) are these that commonly develop FIP.

- **History**: The most commonly reported are weight loss, swollen abdomen, persistent fever and the cat coming from a multi-cat household.

- **Clinical examination**: High fever (typically <40°C), a body score <5/9 as well as icterus/jaundice are three common signs in all forms of FIP. In the effusive forms we commonly find ascites, organomegaly (e.g. kidneys, lymph nodes, masses on the intestines). If there is also a pleural effusion then during auscultation we might have absence or dullness of heart sounds, absence of lung sounds and tachypnoea or dyspnoea. If there is a neurological form of FIP then cats often present ataxia, seizures and behaviour changes amongst others. Lastly if ocular examination can reveal changes in iris colour, anisocoria as well as hyphaema amongst other.

- **Haematology**: A non-specific mild neutrophilia with lymphopaenia are frequently seen in cats with FIP as well as a mild non-regenerative anaemia. Recently it has been highlighted that immune-mediated haemolysis can be present during FIP.

- **Serum biochemistry**: Hyperbilirubinaemia, hyperglobulinaemia with or without hyperproteinaemia are the most common findings in routine biochemistry. Evaluating the serum albumin to globulin (A:G) ratio can increase or suspicion index for FIP.

  > Historically a serum
  > A:G ratio < 0.4 → FIP likely; although recent studies shown this is not useful.
  > **A:G ratio > 0.6 → FIP unlikely; still useful in ruling out FIP.**

- **Serology**: The measurement of anti-FCoV antibody titres is commonly over-interpreted. Such tests are performed on serum using enzyme-linked ELISA, indirect immunofluorescence antibody tests or in-house rapid immunomigration tests.

  There is **NO "FIP antibody test"** all that can be measured is antibody against FCoV. Thus a positive FCoV antibody test only indicates previous infection with FCoV and has developed antibodies. Avoid using this test as a diagnostic tool for FIP.
  A negative serum-FCoV antibody results cannot rule out FIP, as cats with confirmed FIP can be FCoV antibody-negative (e.g. hyper-acute FIP or failure to seroconvert).

- **Protein electrophoresis and acute phase proteins**: An increase in a-globulins (acute phase response) and a polyclonal gammopathy (broad-based increase in g-globulins) on protein electrophoresis has historically been used to support the diagnosis of FIP. Still, in the recent years two acute phase proteins Alpha1-acid glycoprotein (AGP) and serum amyloid A (SAA) has shown promising results especially in monitoring FIP patients.
    - **AGP**: When markedly elevated (>3.0 g/L) could support a diagnosis of FIP in cats with a low pre-test probability and also is useful in the non-effusive FIP cases. **Most importantly AGP measurement can be used to monitor treatment response and identify when the cat has been likely cured or only entered remission**. However, as with every acute phase proteins it is not specific for FIP (can be increased in other diseases) and is only available in only small number of countries.
    - **SSA**: Is markedly elevated especially in the effusive FIP cases. Not specific for FIP.

- **Cytology and biochemistry on effusions**: Macroscopically they have a very yellow colour and often are very sticky and thick fluids. FIP effusions are rich in proteins (>35 g/L) and depending on the cell count can be categorised as protein rich (modified) transudates or exudate. On cytology often a neutrophilic or mixed inflammatory response (non-degenerative

neutrophils, macrophages and lymphocytes) is present on a thick eosinophilic background with protein crescents.

The A:G ratio can also be used in the effusions and:
        A:G ratio < 0.4 → FIP likely
        A:G ratio > 0.8 → FIP unlikely

Rivalta's test has been historically used, but is important to highlight that that is not an FIP test, and septic peritonitis, lymphoma and other types of effusions can be positive with this test. The Rivalta's test can be used only for exclusion of FIP when is negative (negative predictive value of 93%).

- **PCR test**: The FCoV RT-PCR assay can be performed in effusions, tissue (including cells obtained by FNABs), CSF or aqueous humour.

  Quantitative RT-PCR assays should be used ideally as the reported the FCoV load (amount) present in the analysed sample. **A positive PCR with high FCoV load on a cat with sings consistent with FIP provide adequate evidence to start treatment**.
  Importantly a negative result cannot rule out a diagnosis of FIP since the viral load could have been low, or there were PCR inhibitors in the sample. Recent studies have shown that RT-PCR on blood can also be useful.

- **Immunostaining for FCoV antigen**: Immunohistochemistry (IHC) on biopsies or immunocytochemistry (ICC) with the detection of intra-cellular FCoV and compatible pathological changes is considered the golden standard for FIP diagnosis. Biopsy samples of affected organs (e.g., liver, LN, spleen, kidney) can be collected and used for immunostaining. In effusions, FNABs (e.g., of mesenteric lymph nodes), CSF and aqueous humour samples can be collected for cytology and immunostaining afterwards. It is important to contact the diagnostic laboratory prior sample collection and submission of the samples. Histopathology on its own whilst it increases the suspicion index it is not diagnostic for FIP. A negative immunostaining does not rule out FIP (Ettinger et al., 2016, Tasker et al., 2023, Addie et al., 2009, Addie and Jarrett, 1992, Pesteanu-Somogyi et al., 2006, Benetka et al., 2004, Pedersen et al., 1981, Malbon et al., 2020, Attipa et al., 2023, Tasker, 2018).

References

ADDIE, D., BELAK, S., BOUCRAUT-BARALON, C., EGBERINK, H., FRYMUS, T., GRUFFYDD-JONES, T., HARTMANN, K., HOSIE, M. J., LLORET, A., LUTZ, H., MARSILIO, F., PENNISI, M. G., RADFORD, A. D., THIRY, E., TRUYEN, U. & HORZINEK, M. C. 2009. Feline infectious peritonitis. ABCD guidelines on prevention and management. *J Feline Med Surg,* 11.
ADDIE, D. D. & JARRETT, O. 1992. A study of naturally occurring feline coronavirus infections in kittens. *Vet Rec,* 130.
ATTIPA, C., GUNN-MOORE, D., MAZERI, S., EPAMINONDAS, D., LYRAKI, M., HARDAS, A., LOUKAIDOU, S. & GENTIL, M. 2023. Concerning feline infectious peritonitis outbreak in Cyprus. *Veterinary Record,* 192**,** 449-450.
BENETKA, V., KÜBBER-HEISS, A., KOLODZIEJEK, J., NOWOTNY, N., HOFMANN-PARISOT, M. & MÖSTL, K. 2004. Prevalence of feline coronavirus types I and II in cats with histopathologically verified feline infectious peritonitis. *Vet Microbiol,* 99**,** 31-42.
ETTINGER, S. J., FELDMAN, E. C. & CÔTÉ, E. 2016. *Textbook of Veterinary Internal Medicine-Inkling E-Book*, Elsevier health sciences.

MALBON, A. J., MICHALOPOULOU, E., MELI, M. L., BARKER, E. N., TASKER, S., BAPTISTE, K. & KIPAR, A. 2020. Colony Stimulating Factors in Early Feline Infectious Peritonitis Virus Infection of Monocytes and in End Stage Feline Infectious Peritonitis; A Combined In Vivo And In Vitro Approach. *Pathogens,* 9.

PEDERSEN, N. C., BOYLE, J. F., FLOYD, K., FUDGE, A. & BARKER, J. 1981. An enteric coronavirus infection of cats and its relationship to feline infectious peritonitis. *Am J Vet Res,* 42**,** 368-77.

PESTEANU-SOMOGYI, L. D., RADZAI, C. & PRESSLER, B. M. 2006. Prevalence of feline infectious peritonitis in specific cat breeds. *J Feline Med Surg,* 8**,** 1-5.

TASKER, S. 2018. Diagnosis of feline infectious peritonitis: Update on evidence supporting available tests. *J Feline Med Surg,* 20**,** 228-243.

TASKER, S., ADDIE, D. D., EGBERINK, H., HOFMANN-LEHMANN, R., HOSIE, M. J., TRUYEN, U., BELÁK, S., BOUCRAUT-BARALON, C., FRYMUS, T., LLORET, A., MARSILIO, F., PENNISI, M. G., THIRY, E., MÖSTL, K. & HARTMANN, K. 2023. Feline Infectious Peritonitis: European Advisory Board on Cat Diseases Guidelines. *Viruses,* 15.

Zoonotic infections: The most important risks companion vets face

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Introduction

We will be discussing the most important zoonotic infections that companion animals vets are in risk in Europe, and how we can decrease the risk for our veterinary community. Note that we will be discussing the zoonotic disease that do not require a vector for transmission to humans.

The most important ones are:

- Rabies
- Brucellosis
- Cat scratch fever/*Bartonella henselae*
- Leptospirosis
- Toxoplasmosis

Exposure to occupational health risk for zoonotic diseases is an inherent risk in veterinary medicine. Whilst it is not achievable to completely eliminate all the potential risks for zoonotic disease, we should focus in decreasing the risks. This can be archived with early recognition, diagnosis and appropriate management of such infections in companion animals.

It should be priority for every veterinaries to pay extra attention to personal hygiene when handling any animal. Most importantly **do not forget your rabies vaccination**! (Weese et al., 2002a, Weese et al., 2002b, Trevejo, 2000, Sebzda and Kauffman, 2023, Lin and Saccoccio, 2023).

References

LIN, S. & SACCOCCIO, F. M. 2023. Cat scratch disease: Pediatric case series for varying presentations of Bartonella henselae. *IDCases,* 33**,** e01875.

SEBZDA, M. K. & KAUFFMAN, L. K. 2023. Update on Brucella canis: Understanding the Past and Preparing for the Future. *Vet Clin North Am Small Anim Pract,* 53**,** 1047-1062.

TREVEJO, R. T. 2000. Rabies preexposure vaccination among veterinarians and at-risk staff. *J Am Vet Med Assoc,* 217**,** 1647-50.

WEESE, J. S., PEREGRINE, A. S. & ARMSTRONG, J. 2002a. Occupational health and safety in small animal veterinary practice: Part I--nonparasitic zoonotic diseases. *Can Vet J,* 43**,** 631-6.

WEESE, J. S., PEREGRINE, A. S. & ARMSTRONG, J. 2002b. Occupational health and safety in small animal veterinary practice: Part II--Parasitic zoonotic diseases. *Can Vet J,* 43**,** 799-802.

https://www.cdc.gov/media/releases/2019/s0506-zoonotic-diseases-shared.html

https://www.gov.uk/government/publications/list-of-zoonotic-diseases/list-of-zoonotic-diseases

https://www.ecdc.europa.eu/en/zoonoses

Azotemic or non-azotemic: An update on recent diagnostic approaches for kidney disease

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Introduction

Azotemia is defined as the increased concentrations of urea (UN) and/or creatinine. Urea is formed in the liver following metabolism of excess NH4+. Creatine phosphate is energy molecule for muscle contraction. When is utilised in the muscle creatinine is formed. Both urea and creatinine enter the blood and are mainly secreted via the urinary system.

Creatinine concentration can be elevated due to azotemia (pre, renal, post) but also when there is physiologic increased muscle mass (e.g. greyhounds). Similarly it can be decreased when the animals has decreased muscle mass.

Typically urea and creatinine increase in parallel if glomerular filtration rate (GFR) decrease. **Creatinine is constantly produced, freely filtered, not reabsorbed**. Urea has a more variable production, is reabsorbed in tubules and also can be excreted in GIT. Thus creatinine is a better indicator of GFR than UREA.

Uraemia is reflects the clinical signs due renal disease (e.g. vomiting, diarrhoea, coma, convulsions, uremic breath).

Azotemia has 3 classifications

A. Prerenal azotemia:
   a. Causes:
      i. ↓ renal plasma flow: **hypovolemia** (dehydration, shock), shock, ↓ cardiac output
      ii. ↑ urea or creatinine production: ↑ **muscle mass**, GI haemorrhage, high UN or creatinine intake, protein catabolism
   b. ↓ renal plasma flow → ↓ GFR → ↓ clearance of urea and creatinine
   c. If severe and persistent ↓ renal plasma flow > renal hypoxia > acute kidney injury

B. Renal azotemia: Loss of **65-75% nephrons** → ↓ GFR → ↓ excretion urea, creatinine
   a. Causes: **Often never identified**
      i. Inflammatory: glomerulonephritis, pyelonephritis, tubular-interstitial nephritis
      ii. Amyloidosis
      iii. Toxic: hypercalcemia, ethyleneglycol, hgb/myoglobin, gentamycin, NSAIDs, lilies, grapes
      iv. Renal ischemia or hypoxia: prolonged poor perfusion,
      v. congenital hypoplasia/aplasia, polycystic kidneys
      vi. hydronephrosis
      vii. neoplasia (renal or metastatic)

C. <u>Postrenal azotemia</u>: problem is distal to the nephron
   a. Causes:
      i. **Urinary tract obstruction**: uroliths, plugs, compression (tumor, prostate)
      ii. **Leakage** from urinary tract: trauma, neoplasia, prolonged obstruction

<u>Differentiating the different types of azotemia</u>

Clinical examination and urine specific gravity are the keys!
- <u>Prenal</u>: USG > 1.030 (canine), >1.040 (cats). If the USG is below these values + no evidence of ↑ urea production → renal or extrarenal

- <u>Renal</u>: USG: 1.007-1.013 (isosthenuria) → impaired tubulointerstitial function. >1.013 but inappropriately low then considered
   a. Glomerular function impaired > tubulointerstitial function (often in cats and in acute renal disease)
   b. High urine [protein], [glucose] → false elevation of USG

- **<u>UN:Creatinine ratio</u>**
A. **↑ UN more than ↑ creatinine usually prerenal**
   a. UN:Creatinine highest w/ prerenal azotemia, ↑ urea production, or ↓ muscle mass
   b. Small animals: prerenal ratio ≈50, renal and postrenal ratio ≈ 30
B. ↑ Creatinine more than ↑ urea usually renal or postrenal
   a. Azotemia more severe in renal and post-renal
   b. Or concurrent cause for ↓ urea production

<u>Update on novel renal biomarker</u>
The past 10 years we have seen an explosion of new renal markers and in the near future more and more will becoming available. Below we are presenting some of the most promising ones, or currently being used.

<u>Cystatin C</u>
This small protein is constantly produced by cells and freely filtered, reabsorbed and catabolized by renal tubules without re-entering bloodstream or being excreted in urine. Cystatin C is used as a marker for GFR mainly in **chronic renal disease of dogs**. Serum cystatin C is generally considered superior to creatinine as a marker of GFR in dogs but not in cats. Has not be evaluated in acute kidney disease.

<u>SDMA</u>

Symmetric dimethylarginine (SDMA) is an endogenous metabolite of intranuclear methylation of L-arginine, and is excreted by the kidneys.

SDMA was considered a sensitive and early marker (more sensitive than serum creatinine) of declining GFR in dogs and cats. However recent studies showed that SDMA might not be a better marker of GFR than serum creatinine measurement as it less specific.

<u>Iohexol Assay</u>
This is the **golden standard** assay for measurement of GFR and can be performed even in 1st opinion practises. It is expensive and does requires a rather long protocol but is currently available in Europe (RVC, UK <u>https://www.rvc.ac.uk/pathology-and-diagnostic-</u>

[laboratories/therapeutic-drug-monitoring#:~:text=Serum%20iohexol%20concentration%20is%20measured,to%20calculate%20clearance%20of%20iohexol](laboratories/therapeutic-drug-monitoring).). The main thing required is to accurately inject the dose of iohexol (OmnipaqueTM 300) intravenously at a dose of 1 ml/kg and then to take 3 blood samples at 2, 3, and 4 hours following injection.

The patient needs to be fasted for 12 hours prior to the test but should have free access to water throughout. The calculation of the patient's GFR, and an interpretation of whether or not it is normal, will then be returned by the laboratory.

The results can help identify early renal dysfunction in a dog or cat. It may also be useful as a screening tool for older cats or for some dog breeds known to be at risk of nephropathies. (Ettinger et al., 2016, Stockham and Scott, 2013, Ghys et al., 2016, Hokamp and Nabity, 2016, Prieto et al., 2020, Kopke et al., 2018).

References

https://eclinpath.com/chemistry/kidney/

ETTINGER, S. J., FELDMAN, E. C. & CÔTÉ, E. 2016. *Textbook of Veterinary Internal Medicine-Inkling E-Book*, Elsevier health sciences.

GHYS, L. F., PAEPE, D., LEFEBVRE, H. P., REYNOLDS, B. S., CROUBELS, S., MEYER, E., DELANGHE, J. R. & DAMINET, S. 2016. Evaluation of Cystatin C for the Detection of Chronic Kidney Disease in Cats. *J Vet Intern Med,* 30**,** 1074-82.

HOKAMP, J. A. & NABITY, M. B. 2016. Renal biomarkers in domestic species. *Vet Clin Pathol,* 45**,** 28-56.

KOPKE, M. A., BURCHELL, R. K., RUAUX, C. G., BURTON, S. E., LOPEZ-VILLALOBOS, N. & GAL, A. 2018. Variability of Symmetric Dimethylarginine in Apparently Healthy Dogs. *J Vet Intern Med,* 32**,** 736-742.

PRIETO, J. M., CARNEY, P. C., MILLER, M. L., RISHNIW, M., RANDOLPH, J. F., FARACE, G., BILBROUGH, G., YERRAMILLI, M. & PETERSON, M. E. 2020. Biologic variation of symmetric dimethylarginine and creatinine in clinically healthy cats. *Vet Clin Pathol,* 49**,** 401-406.

STOCKHAM, S. L. & SCOTT, M. A. 2013. *Fundamentals of veterinary clinical pathology*, John Wiley & Sons.

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Dr Cedric Tutt graduated from the veterinary faculty in South Africa in 1992 and became an European Veterinary Specialist in Dentistry in 2007. He is registered as a Veterinary Dental Specialist in Europe, UK, Hong Kong and South Africa; offering advanced dentistry and oral surgical options for a wide range of animals, including: cats, dogs, horses, many wild cat species, small and large non-human primates and marine and terrestrial mammals. His list of species treated exceeds 67.

Dr Tutt's services include root canal therapy, dental restoration, extractions, orthodontics, prosthodontics and treatment of some oral cancers in addition to the repair of oral trauma cases and some congenital abnormalities.

The European Veterinary Specialist in Dentistry in South Africa, Dr Tutt offers veterinary dentistry and orofacial surgery services in Cape Town, Hong Kong, Singapore and Malaysia.

Dr Tutt also provides post-graduate training in veterinary dentistry and oral surgery to veterinarians, veterinary nurses and veterinary technicians. He authored the text: Small Animal Dentistry – a manual of techniques (which was translated into Simplified Chinse) and was Senior co-editor of the BSAVA Manual of Canine and Feline Dentistry 3rd Edition.

Cedric has published (as author or co-author) 27 articles in Peer Reviewed CPD journals and 8 articles in scientific Peer Reviewed journals.

FELINE AND CANINE APPLIED
ANATOMY OF THE HEAD

CEDRIC TUTT

DIPLOMATE EVDC

SKULL

- Essential framework

  - Accommodates the masticatory muscles
  - Oral mucosa
  - Teeth
  - Tongue – with associated muscles, taste buds, papilla
  - Salivary glands, ducts and puncta
  - Lymph structures
  - Nares / nasal passages / olfactory system
  - Eyes, ears, lips and skin

Skulls of the same species differ in size and shape

Some are dictated by breed standards

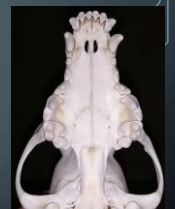CAT AND DOGS JAWS ARE ANISOGNATHIC

Mandibles narrower than maxillae

Dental arches are uneven
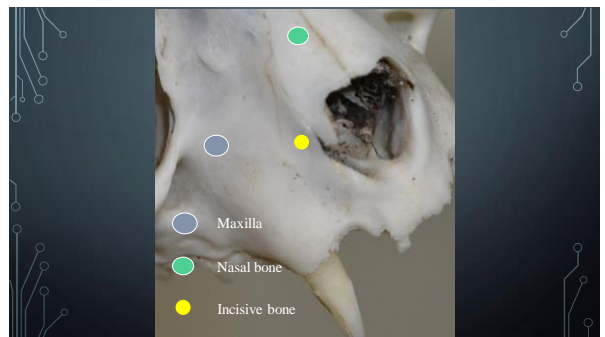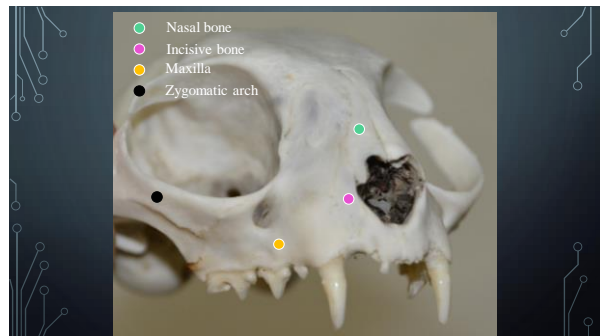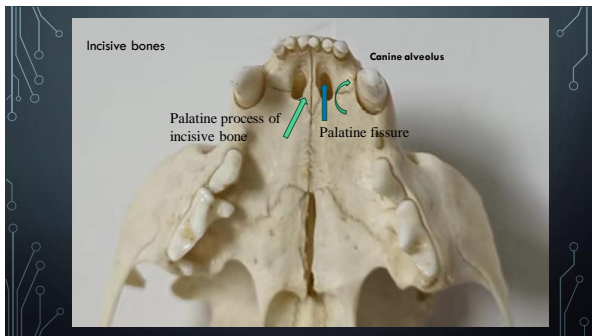Mandibles narrower and
Maxillae wider

SKULL

- Essential framework

  - Bony skeleton, including:

    - Maxilla
    - Mandibles
    - Hyoid bones

SKULL

- Maxilla - upper jaws
  - Incisive bones
    - House incisors
    - Forms medial wall of canine alveolus
    - Form rostral part of palatine fissures
  - Maxillary bone – house canine, premolars and molars
  - Palatine process of maxilla forms hard palate shelf rostrally between premolars
  - Palatine bone (horizontal part) forms hard palate shelf caudally between the molars

INCISIVE BONE

Nasal process of the incisive bone

Palatal canine alveolar wall
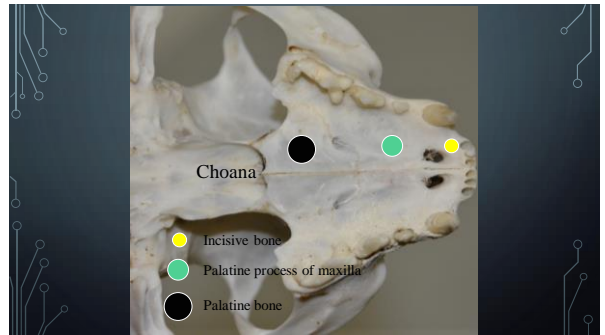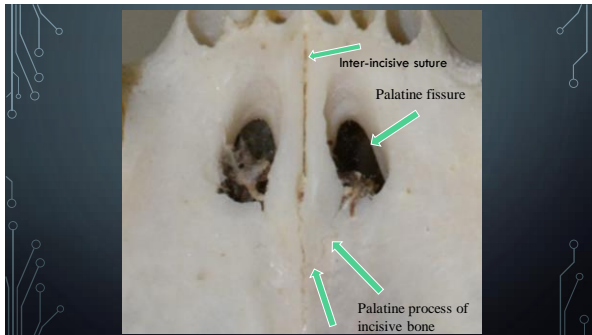
Palatine process of the incisive bone

SKULL

- Maxilla - u

  - Caudal m   oid bone
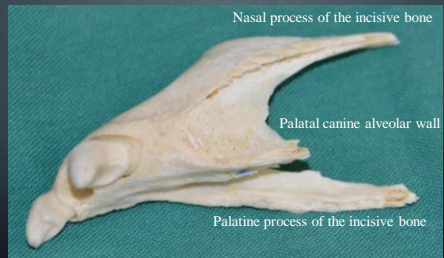   form the

Palatine fissure

Inter-incisive foramen

Inter-incisive suture
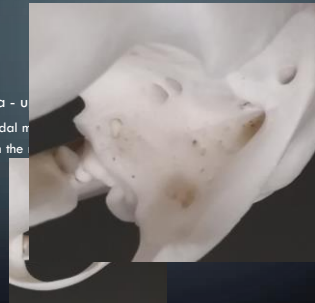
SKULL

- Maxilla - upper jaws

  - Hamulus of pterygoid bone

Cat hamulus

Dog hamulus
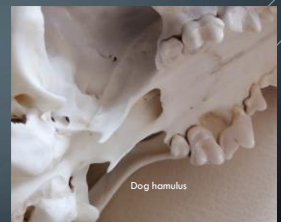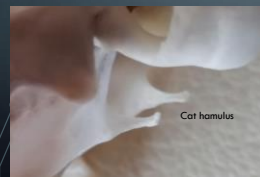
Part / projection of the pterygoid bones
Tendon of tensor veli palatini

JAWS

- Symphyseal union is a synchondrosis
- Temporomandibular joints
  - Mandibular condylar process
  - Mandibular fossa, Retroarticular process, temporal bone

HAMULUS

Hard palate

Soft palate

Coronoid process

TMJ

Condyle

Ramus

Mandibular fossa

RAP
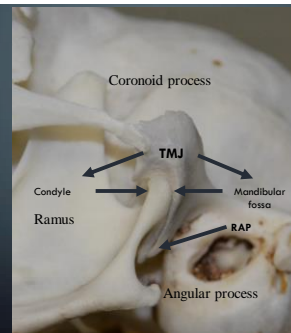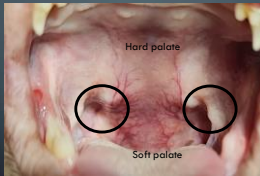
Angular process

SKULL

- Mandibles
  - Three joints associated with jaws
    - TMJs caudally
    - Condylar process and mandibular fossa
      - Hinge function
      - Little lateral movement
    - Symphysis rostrally
    - Synchondrosis
      - Allows minimal sliding for carnassial alignment

Carnassial alignment

Coronoid process

Condylar process

Ramus

Angular process

Mandibular foramen

Mandibular body
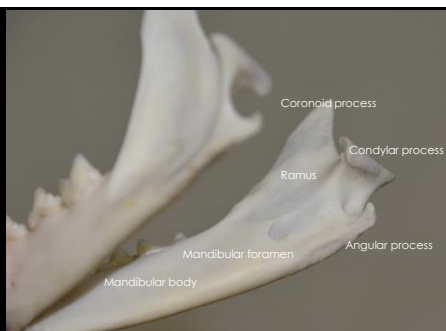
Symphyseal shift enables alignment of the carnassials

MAXILLARY FORAMINA

Infra-orbital foramen

OTHER FORAMINA

Palatine fissure

Major Palatine foramen

Minor Palatine foramen
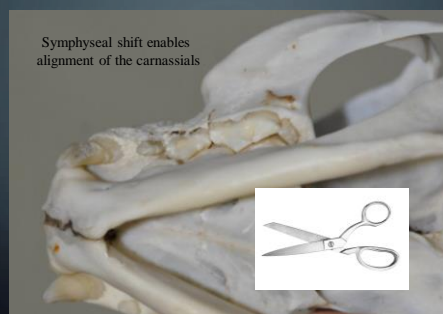
MAXILLARY FORAMINA
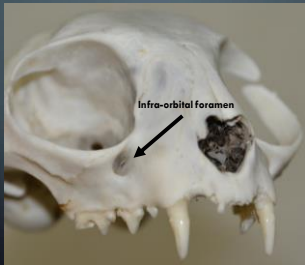
Maxillary foramen

OTHER FORAMINA

MAXILLARY FORAMINA

Infra-orbital canal

3

!!!!!

Mandibles

Ramus

Body

Body houses the premolars and molar in the cat

MANDIBULAR FORAMINA

Middle and caudal mental foramina may coalesce into one

MANDIBULAR FORAMINA

Mandibular foramen

Middle and caudal mental foramina fused

Middle and caudal mental foramina

Rostral mental foramina – I2

MANDIBULAR FORAMINA

Mental foramina

Caudal
Middle
Rostral

Rostral
Middle
Caudal

SKULL

- Mandibles
  - Body – horizontal and dentate – incisors, canines, premolars and molars
  - Ramus – vertical and edentate
    - Coronoid process – well developed in carnivores
    - Condylar process and neck
    - Angular process
    - Medial aspect – mandibular foramen
- Jaws develop alveoli in dentate parts
- No alveoli in edentate parts –
  - caudal to molars
  - where teeth are missing

MASTICATORY MUSCLE FORCES ON THE JAWS

- Muscles of mastication
  - Temporal
  - Masseter
  - Pterygoid
  - Digastric
  - Geniohyoid
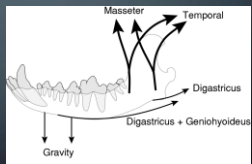
MASTICATORY APPARATUS

Species differences in coronoid process in relation to TMJ

Carnivores strong leverage for grasping prey and cutting into pieces

Herbivores strong grinding forces

MASTICATORY MUSCLE FORCES ON THE JAWS

- Jaw fractures
  - Stable vs unstable (favourable vs unfavourable)

Herbivore relatively small coronoid process

Cat – large coronoid process

Lion– large ramus / coronoid process Large muscle attachment
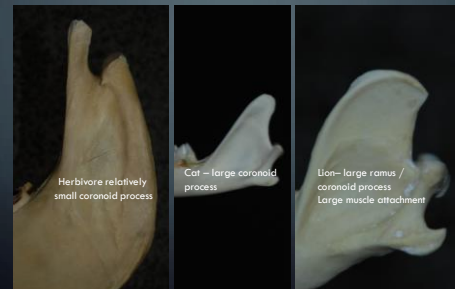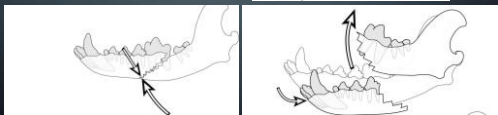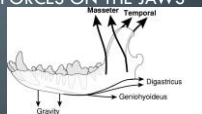
Jaw fractures

Teeth involvement
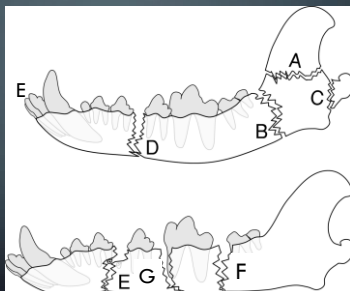
Giant Panda – robust ramus and zygoma

DOGS AND CATS

- Have large mouths that can open wide
- Long mobile tongue – longer in dogs than cats
- Generally – large lips

Brachycephalic
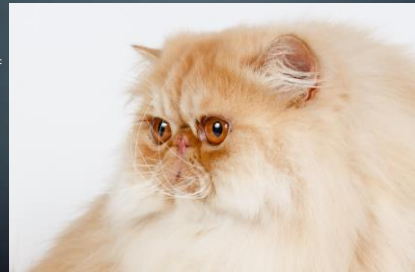
Ursula vd Riet

HEAD SHAPES

- Brachycephalic
  - Short faced
- Mesocephalic
  - Face and skull proportional
- Dolichocephalic
  - Long faced

Brachycephalic
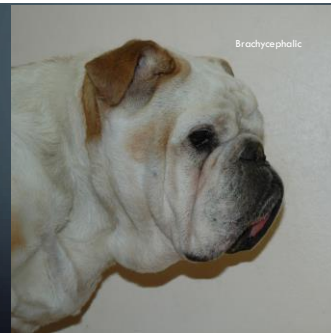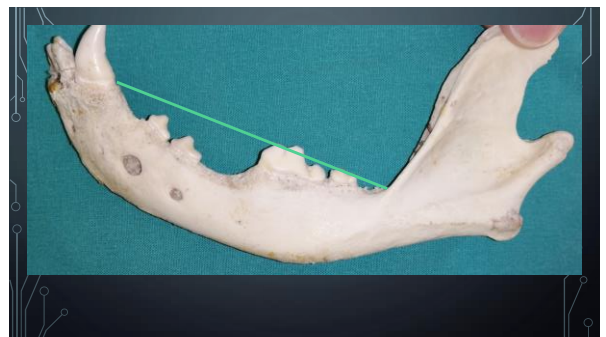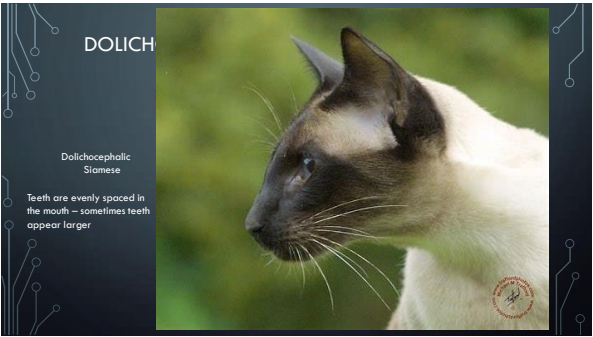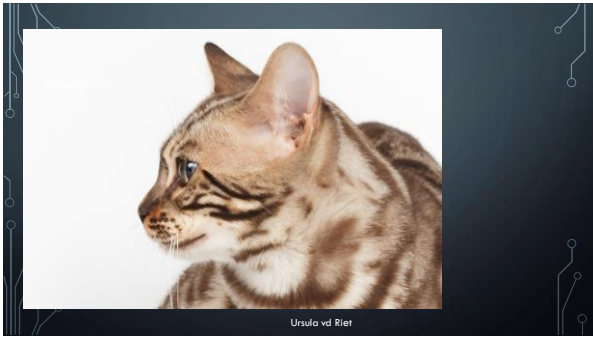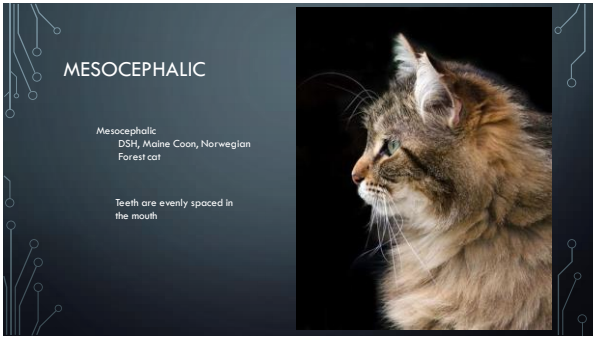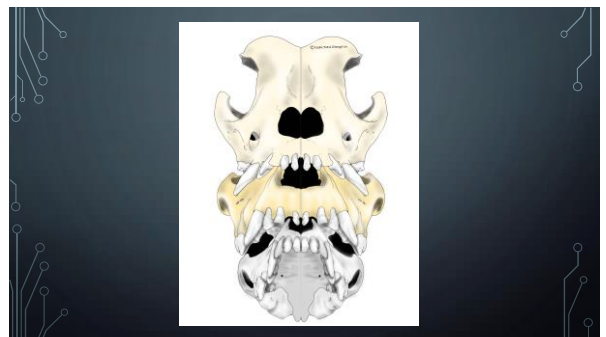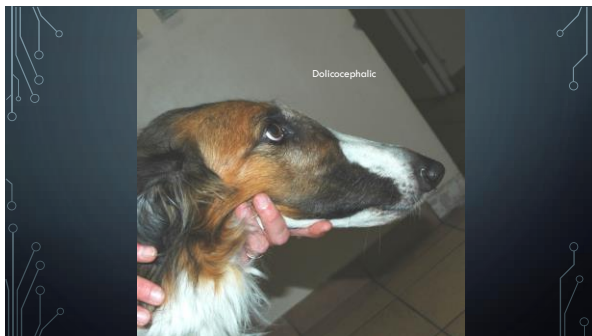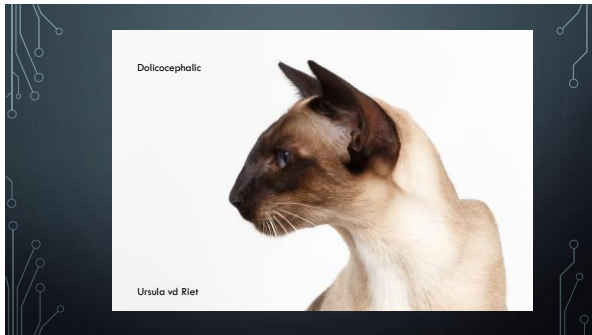
Teeth are crowded especially in the maxilla sometimes incisors are crowded too

Brachycephalic
Persian / Exotic

Mesocephalic
Mesaticephalic

MESOCEPHALIC

Mesocephalic
DSH, Maine Coon, Norwegian
Forest cat

Teeth are evenly spaced in
the mouth

Ursula vd Riet

DOLICH

Dolichocephalic
Siamese

Teeth are evenly spaced in
the mouth – sometimes teeth
appear larger

CANINE TOOTH ANGULATION
Brachycephalic
50°

CANINE TOOTH ANGULATION - MESOCEPHALIC
Rostro-caudal view
60°
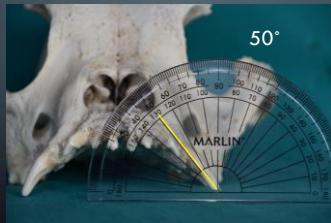
CANINE TOOTH ANGULATION
Mesocephalic
76°

CANINE TOOTH ANGULATION - BRACHYCEPHALIC
Rostro-caudal view
55°
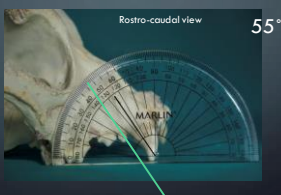
TEETH

- Gomphosis
  - Joint describing the fitting of teeth into the jaws – immovable joint

TEETH

- Two aspects to the "living" tooth
  - Pulp entering the tooth via the apical delta and accessory canals
  - Periodontium
    - Blood vessels and nerves in the periodontal ligaments and gingiva
    - Along with alveolar bone and cementum – secure the tooth in the bone
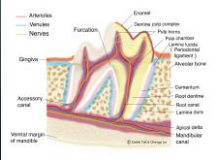
DENTITION IN DOGS AND CATS

- Secodont
  - Sharp cutting surfaces

- Bunodont - in dogs
  - Crushing teeth

- Neither dogs nor cats can grind food because of the canines

TEETH VIABILITY

- Keep the pulp and periodontium alive

- Pulp dead but periodontium alive – root canal therapy

- Pulp alive but periodontium destroyed – inevitably extraction

DENTAL FORMULA IN DOGS

- Dogs: 2   {I3 C1 P4 M2
                 {I3 C1 P4 M3   = 42

- Puppies: 2 {i3 c1 p3
                 {i3 c1 p3   = 28

DENTITION IN DOGS AND CATS

- Diphyodont
  - Deciduous teeth
  - Secondary teeth
- Heterodont
  - Incisors, canines, premolars and molars
- Brachydont
  - Proportionately shorter crowns and longer roots
- Anelodont
  - Limited eruption

DENTAL FORMULA IN CATS

Cats are strict carnivores:

Cats: 2x I3C1P3M1
                 I3C1P2M1   = 30
Kittens: 2x i3c1p3
                 i3c1p2   = 26
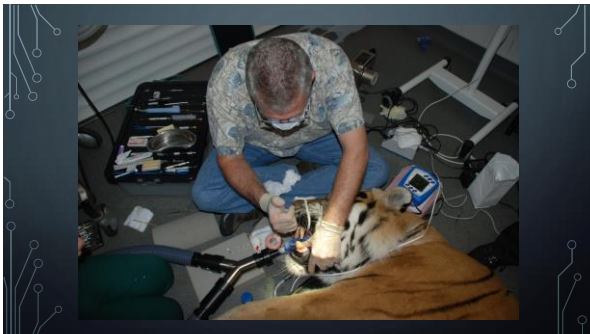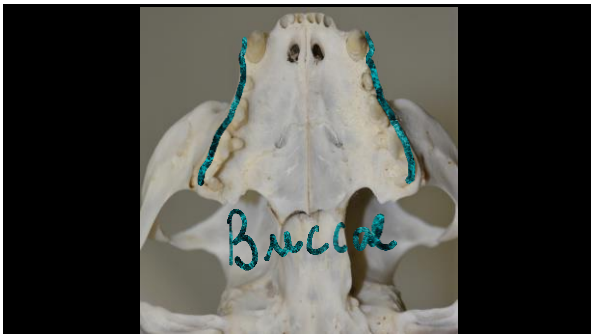
DENTITION

- Two rooted teeth
  - Maxillary
    - P2, P3, M1
      - P2 may be fused, appearing single
      - 10% of P3 have 3 roots
      - Many P3 distal root is almost double mesial root
      - Some M1 have fused roots, appearing single
  - Mandibular
    - P3, P4, M1

DENTITION

- Three rooted teeth
  - Maxillary P4
  - (10% of maxillary P3 in cats)

DENTITION

- Single rooted teeth
  - Incisors and canines

DENTITION

- Maxillary M1 in the cat
  - Is small and oriented at 90° to P4
    - Buccal and palatal roots
  - Is slightly palatal
  - Is rostro-caudally flattened

DENTITION

Incisors
Canine
Premolars
Molar

I 1-3
C
P2
P3
P4
M1
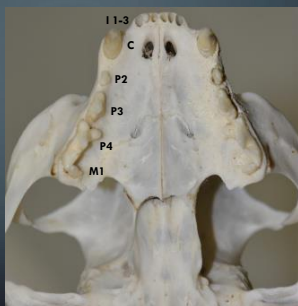
CANINE DEVELOPMENTAL GROOVES

MAXILLA

Tip of the molar 1 visible from the side view
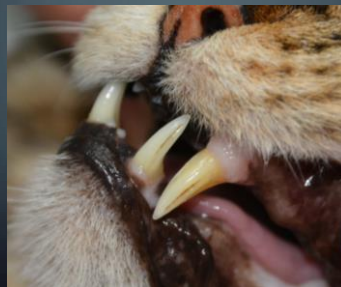
109 AT 90° AND PALATAL TO 108

NORMAL DENTAL ANATOMY

- Enamel
  - Ectoderm
  - 96% hydroxyapatite
- Dentine
  - Mesoderm
  - 70% hydroxyapatite

NORMAL DENTAL ANATOMY

- Dentine – pulp organ
  - Dentinal tubule
  - Odontoblastic process (Tomes fibre)
  - Peritubular dentine

  Intertubular dentine – bulk of dentine

CEJ

- Cemento-enamel-junction (CEJ)
  - Overlap

  - Abut

  - Gap
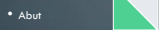
NORMAL DENTAL ANATOMY

- Dentine
  - Primary – root development
  - Secondary (develops after apexogenesis is complete) – organised and disorganised
  - Tertiary – disorganised 2°
    - Reparative
    - Few or no dentinal tubules
    - Stains easily

NORMAL DENTAL ANATOMY

- Hypercementosis
  - Bulbous roots
  - Secondary to periodontitis
  - Complicate extraction

NORMAL DENTAL ANATOMY

- Cementum
  - 45-50% hydroxyapatite
  - Vital (living – contains cementocytes) – has reparative capability
- Cemento-enamel-junction (CEJ)
  - Overlap
  - Abut
  - Gap

NORMAL DENTAL ANATOMY

- Pulp cavity
  - Pulp chamber, pulp horns and Root canal
  - Pulp - mesoderm

NORMAL DENTAL ANATOMY

- Pulp
  - Blood vessels
  - Nerves
  - Lymphatics
  - Fibroblasts
  - Collagen fibres
  - Reserve mesenchymal cells, connective tissue and odontoblasts

INCISOR MALOCCLUSION – NARROW MANDIBLE

NORMAL ORAL ANATOMY

- Periodontal ligament
  - Alveolar bone (cribriform plate / lamina dura)
  - Cementum
  - Sharpey's fibres

  Alveolar bone
  Cortical, cancellous, cribriform plate

NORMAL ORAL ANATOMY

- Free gingiva
- Gingival sulcus
- Attached gingiva (+periosteum)
- Mucogingival line
- Oral mucosa
- Mucocutaneous junction
- Skin

SALIVARY GLANDS

- Parotid
- Xygomatic
- Mandibular
- Monostomatic sublingual

SALIVARY GLANDS

- Sublingual polystomatic
- Buccal
- Pharyngeal

Colour Atlas of Veterinary Anatomy
The dog and cat. Done et al. Mosby
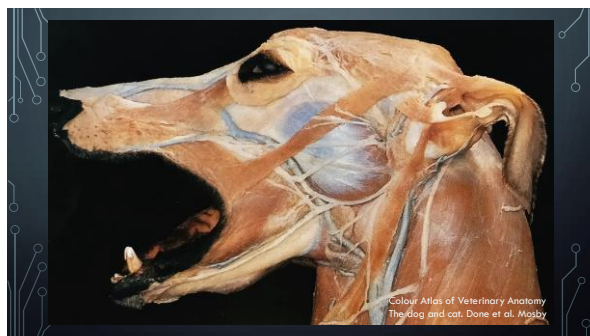
SALIVARY GLANDS

- Paired major salivary glands – long ducts secreting saliva away from the gland
  - Parotid
  - Mandibular
  - Sublingual mono-stomatic and poly-stomatic
  - Zygomatic – carnivores only

Colour Atlas of Veterinary Anatomy
The dog and cat. Done et al. Mosby
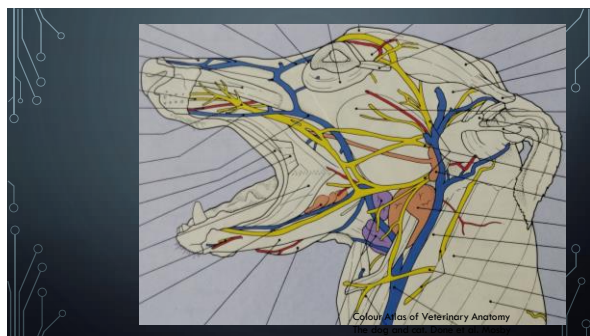
SALIVARY GLANDS

- Minor salivary glands
  - Sublingual poly-stomatic
  - Buccal
  - Lingual
  - Pharyngeal
  - Labial
  - Lingual Molar – poly-stomatic (cats only)

SALIVARY GLANDS

- Mono-stomatic
  - Parotid
  - Mandibular
  - Sublingual
- Poly-stomatic
  - Sublingual – 8-12 ducts
  - Zygomatic – up to 5 ducts in the dog

    - Anatomy of the Domestic Animals, Sisson and Grossman, 4th Ed Saunders

PAROTID GLAND

- The Parotid gland
  - Situated
    - Caudal to the ramus
    - Ventral to the external ear
  - Duct
    - Stensen's duct - Runs from rostral border of the gland, over the masseter to the parotid caruncle and punctum situated in the buccal mucosa at about the level of maxillary PM4
  - Saliva
    - Mucoserous – mainly but can contain some mucous too

MANDIBULAR GLAND

- The Mandibular gland
  - Situated
    - At the bifurcation of the jugular (maxillary and linguofacial veins)
    - At the angle of the mandible
  - Duct
    - Wharton's Duct - Runs sublingually to sublingual caruncle may have a shared punctum with sublingual monostomatic – or separate. Left and right on either side of the lingual frenulum
  - Saliva
    - Serous
    - Mucous
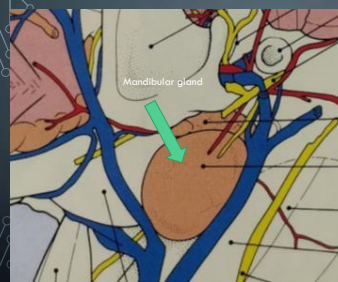
SUBLINGUAL MONO- AND POLY-STOMATIC GLAND

- The Sublingual mono- and poly-stomatic gland
  - Situated
    - Mono-stomatic part shares a capsule with the Mandibular gland
    - Poly-stomatic part is longer and narrower and runs medial to the mandible
  - Duct
    - Bartholin's Duct - Runs with or may be joined to that of the mandibular gland
    - Mono-stomatic part may have its own punctum or share with the mandibular gland
    - Poly-stomatic part – ducts empty directly into mouth or may join the mono-stomatic duct
  - Saliva
    - Mucoserous

ZYGOMATIC GLAND (ONLY IN CARNIVORES)

- The zygomatic gland
  - Situated
    - Caudal, and ventral to the zygomatic bone where it joins the zygomatic process of the maxillary bone
  - Duct
    - Ducts run from the gland to the oral / buccal mucosa
    - It has up to 5 puncta arranged in an arc in the buccal mucosa around maxillary molar 1
  - Saliva
    - Mucoserous

Mono-stomatic sublingual

Poly-stomatic sublingual

Colour Atlas of Veterinary Anatomy
The dog and cat. Done et al. Mosby

Colour Atlas of Veterinary Anatomy
The dog and cat. Done et al. Mosby

Parotid

Zygomatic

M1

PM4

M2

Buccal salivary gland puncta

Incisive papilla
with bilateral puncta
- Vomeronasal organ
- Auxiliary olfactory organ
  Palatal rugae

LYMPHNODES

- Mandibular - string

- Lateral retropharyngeal
- Medial retropharyngeal

- Superficial cervical (pre-scapular)

NORMAL PALATAL GINGIVA 204

2 Oral examination, charting and routine prophylaxis

Cedric Tutt
Diplomate EVDC

Oral Examination

- Soft and hard tissues
  - colour (P,M,G)
  - swelling, ulcers
  - lymphoid tissue – tonsils
  - abnormalities – cleft, degloving, fistulas, sinus tracts
  - fractures – teeth, bones
  - Lacerations / ulcers – lip, cheek, tongue

Clinical examination

- Examine and palpate the head
  - part of general clinical exam
- Symmetry
- Inflammation
  - swelling (face, eye, heat, pain)
- Discharge (or salivation)
- Lymph nodes
- Breathing – bilateral air flow

Oral Examination

- Under GA
  - jaw movement – lateral excursion
  - abnormally shaped / mobile teeth
  - lacerations / puncture wounds
  - missing teeth (not always!!)
  - extra teeth

Clinical examination

- Lift lip
  - gingivae and mucosae
  - occlusion
  - general appearance
- Open mouth
  - pain
  - cursory exam
  - occlusion

Charting the mouth

- Be systematic
- Periodontal probe
  - sulcus, pockets, gingival recession
  - gingival enlargement
- Explorer
  - subgingival calculus, enamel defects, resorptive lesions
- Examine – tooth, gingiva, bone

Hand instruments

- Veterinary dentistry can be performed using hand instruments alone
  - Teeth can be
    - Examined
    - Cleaned
    - Using hand instruments

Examining the mouth

Graduated periodontal probe   Dental explorer

Electro-mechanical and pneumatic equipment

- Gets the procedure done quicker
- More efficiently
- Safer for the animal

Know your probe graduations
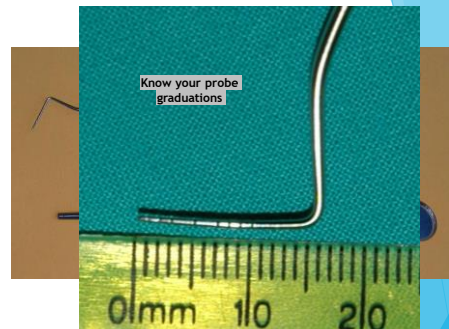
Hand instruments

- Examination
  - Periodontal probe - most important
  - Dental explorer
  - Dental mirror
  - Dental chart
  - Good light source
  - Anaesthetised patient

Hand instruments

Bent

Hand instruments

Edentulous
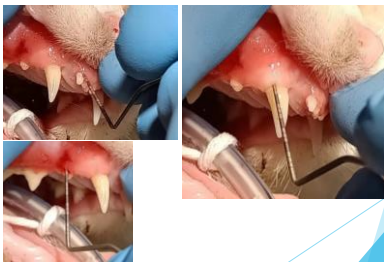
Periodontal probing

Furcation

F2

Deep pockets

Deep palatal pocket at 204

Periodontal probing
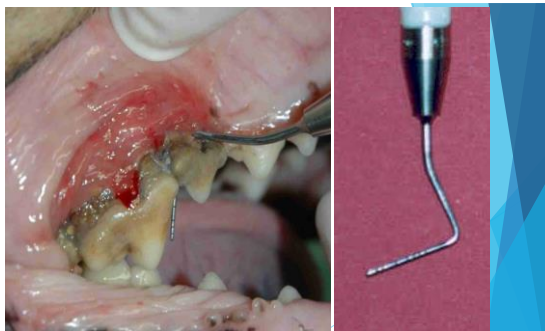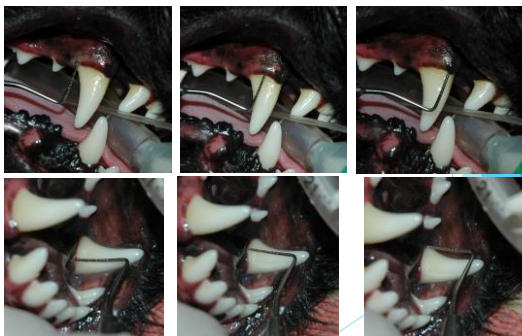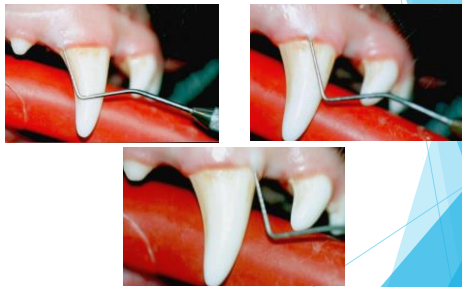
Explorer
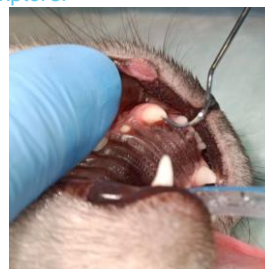
Tooth extrusion
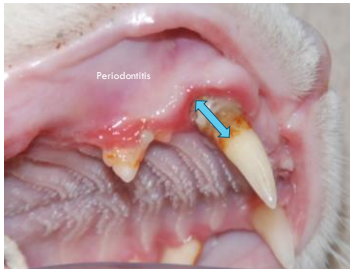
Extensive periodontal disease
Tooth extrusion
Pocketing
Mobility

Create a flap, extract,
suture closed

Periodontitis and stomatitis

After treatment

Complicated crown fractures

Periodontitis

Gingivitis 2
Recession
Furcation involvement
Pocketing
Extrusion of canine

Treated

Type 2 tooth resorption Stage 4c

TR2 4c

♀ SN root of 107

Canine extrusion

Treated

Post-op

Dental charts

FELINE

CCF

CCRF

Adult Feline Dental Record
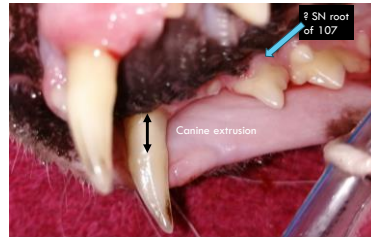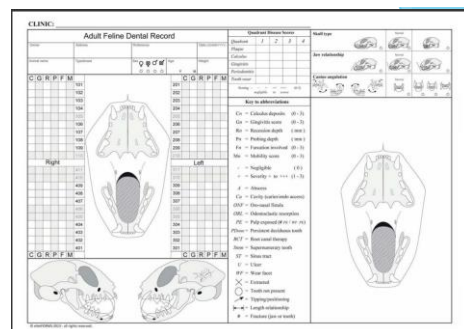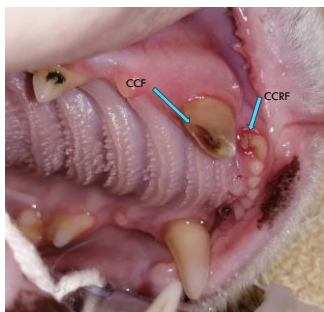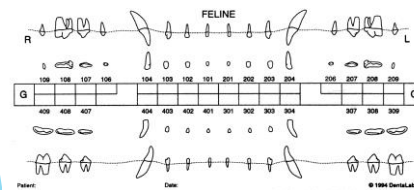
Key to abbreviations

Cn	= Calculus deposits	(0 - 3)
Gn	= Gingivitis score	(0 - 3)
Rn	= Recession depth	(mm)
Pn	= Probing depth	(mm)
Fn	= Furcation involved	(0 - 3)
Mn	= Mobility score	(0 - 3)
-	= Negligible	(0)
+	= Severity + to +++	(1 - 3)

A	= Abscess	
Ca	= Cavity (caries/endo access)	
ONF	= Oro-nasal fistula	
TR	= Tooth resorption	
PE	= Pulp exposed (# PE / WF PE)	
PDmm	= Persistent deciduous tooth	
RCT	= Root canal therapy	
Snn	= Supernumerary tooth	
ST	= Sinus tract	
U	= Ulcer	
WF	= Wear facet	
✕	= Extracted	
◯	= Tooth not present	
➚	= Tipping/positioning	
↔	= Length relationship	
#	= Fracture (jaw or tooth)	

Calculus cracking forceps
Calculus dislodging forceps

Calculus removing forceps
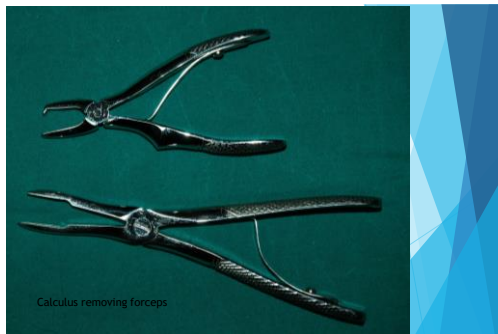
Electromechanical scalers

- Use the modified pencil grip
- Stabilize the instrument with one or two fingers on the patient
- Ensure sufficient cooling water flow
- Use as much of the tip as possible
- Move on to the next tooth

Piezoelectric scaler

Use the side / edge
of the scaler
Not the point!

Electromechanical scalers

Piezoelectric

Magnetostrictive
Metal stack   Ferrite rod

Mechanical energy is
converted to heat energy.

Don't spend more than
6 seconds on a tooth
at one time

Scale the upper surfaces
of both arches
Buccal / palatal
Buccal / lingual

Ensure the mouth is
lower than the pharynx
for drainage.
Place an instrument in the
cheek at the commissure
to aid drainage.

Be aware of soft tissues
when scaling.

Scaler will damage
soft tissue on contact

Use a subgingival tip
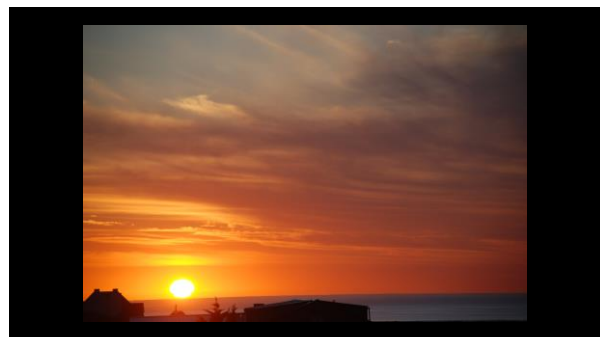
Polishing

- Aim of polishing is to remove remaining plaque
- Rotating polishers will generate more heat
- Reciprocating polishers generate less heat
- Medium paste rather than coarse
- Friction causes heat and will damage pulp – restrict polishing time per tooth

Polishing

Different coloured prophy cups have different texture

Rotating   Rotating   Rotating   Reciprocating
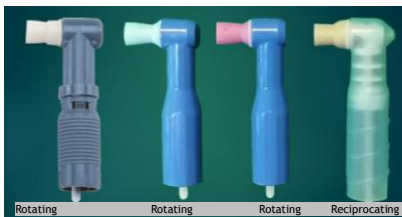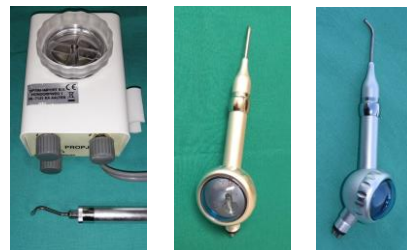
"Air polishing"

Air polishers use particles – need to protect the soft tissues

Periodontal therapy

- Prophy cup
- Prophy paste
- Rinse
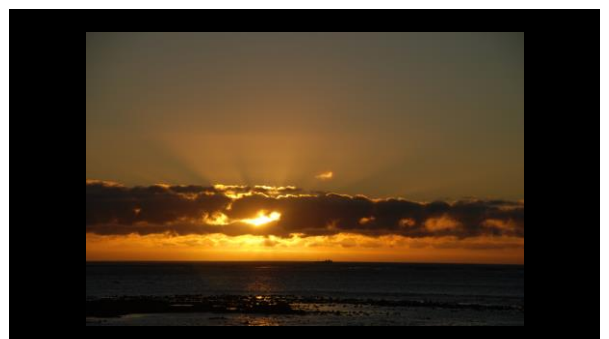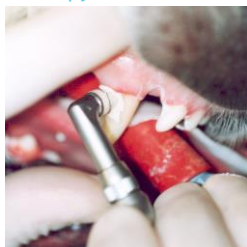
Uncommon clinical findings

Supernumerary maxillary P4

Persistent 604

Note jugal width

Supernumerary mandibular P4

Supernumerary teeth

Major palatine artery trauma

History of intermittent severe haemorrhage.

At the clinic no injuries found.

Eventually these lesions seen.

Allergy treated, grooming stopped, palate healed. No further bleeding.

Malocclusion – what to do?

308 partial gemmination
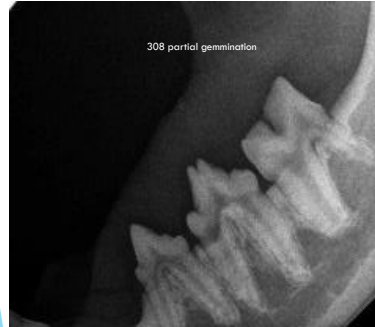
Malocclusion

Examine closely – investigate inflamed areas

308 partial gemmination

Periodontitis

History of intermittent inability to close the jaws

Left maxillary carnassial mobile

Interfering with occlusion

Marked attachment loss

Self-evacuation

Tooth dislodged during examination
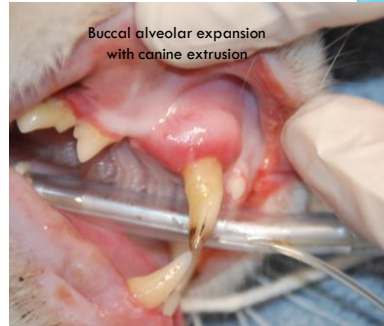
Buccal alveolar expansion with canine extrusion

Buccal alveolar expansion
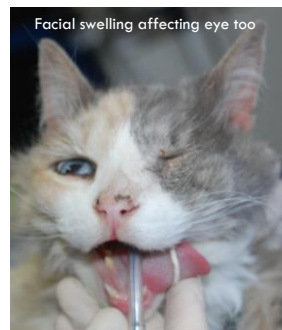
Facial swelling affecting eye too

Bilateral Buccal alveolar expansion

Facial swelling affecting eye too

Canine # CCF

Extraction the only option

This will heal

Take a closer look

Traumatic ulcerative alveolar mucositis

Sinus tract through the alveolus

Attrition

History of grinding teeth
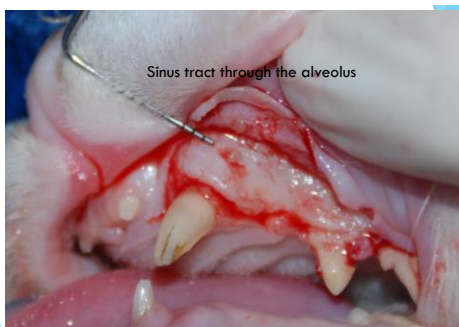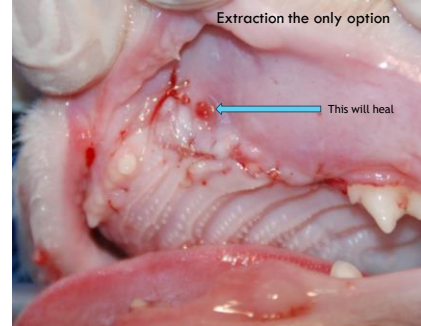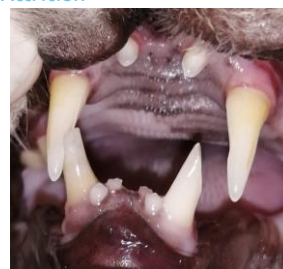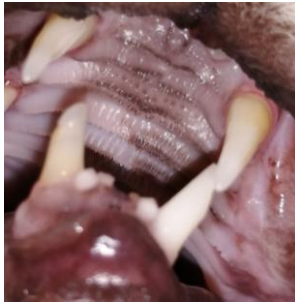
Canine-canine contact
Attrition

Oral Antiseptics and Antibiotic use

- Chlorhexidine gluconate oral rinse
  - Applied prior to S&P procedure
  - As effective in reducing bacterial aerosol
  - As 5 days of clindamycin therapy

Imperforate Soft palate
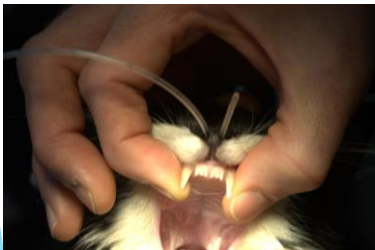
Antibiotic choice

- Previous culture (literature)
- Clinical presentation (bacterial)
  - Amoxycillin-clavulanic acid (20mg/kg BID)
  - Cephalosporins (10-30mg/kg BID)
    - 14 day long-acting formulation
  - Clindamycin (11mg/kg OID)
  - Metronidazole (plus Spiramycin) (20mg/kg BID)
  - Doxycycline 10mg /kg OID
- Culture if no response!

Oral Antiseptics and Antibiotic use

- Bacteraemia
- Systemic illness / infection
- Maxillofacial surgery
- Cardiac
- CGS

Antibiotic choice

- Clindamycin
  - good penetration into oral tissues
  - good penetration into bone
  - effective in presence of pus
- Refrigerate for cats

Quiz

Quiz

Caudal left maxilla
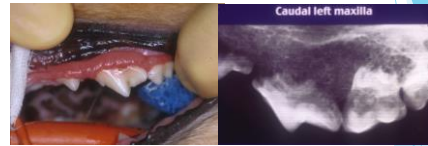
Quiz

Quiz

Quiz

Quiz
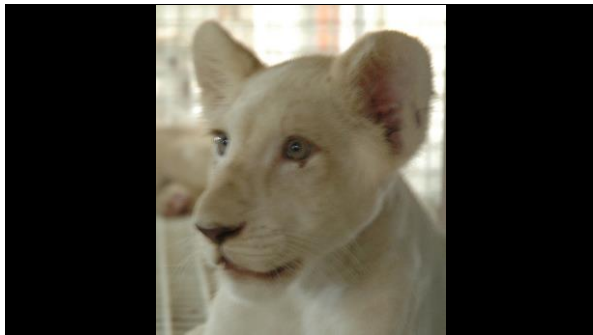
3 Dental radiography and other diagnostic imaging modalities

Cedric Tutt
Diplomate EVDC

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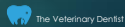
Definitions

- Radiology
  - The art, science and skill of interpreting a radiograph
    - Know normal anatomy
    - Know variations of the normal
  - **Pattern recognition**

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#noxrays-nodentistry

DR-DIGIREX SENSOR

Size 1 : 40*24mm
Size 2 : 41*31mm

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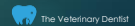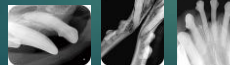
Definitions

- Radiography
  - The art of obtaining a radiograph
    - Precise
    - Accurate
      - Lacking elongation or foreshortening
    - Lacking superimposition
    - Good quality
      - Exposure, brightness, contrast, etc
    - Diagnostic

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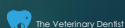
CR-EXL PSP SCANNER

Scan up to Size #5
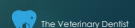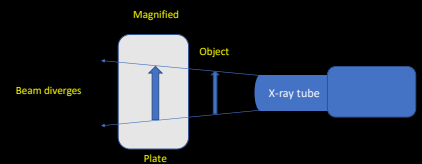
The Veterinary Dentist
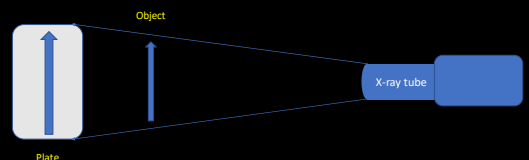
Beam/plate mal-alignment

X-ray tube
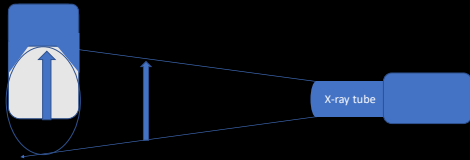
Beam angulation

- Vertical angulation

    - This is to provide an image the same size as the tooth

    - Too high a position → foreshortening

    - Too low a position → elongation

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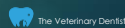
Radiographic technique

- What is the aim:

    - To view what is hidden below the gingiva
    - To obtain an image which represents the tooth under review
    - To limit elongation and fore-shortening
    - Eliminate artefacts
        - Calculus
        - Plate effects
            - Scratches
            - Blood
    - Appropriately enhanced using a computer

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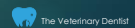
Beam angulation

- Horizontal angulation

    - This is to eliminate superimposition of structures on the tooth

    - SLOB rule
        - Separation of roots
        - Separation of normal structures

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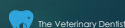
Veterinary Dental Radiography

The parallel Technique
The bisecting technique

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Dental Radiographic Techniques

- Parallel technique
  - Plate placed parallel to the tooth
  - Limited by mandibular symphysis and palate

- Bisecting angle technique
  - Plate placed close to tooth
  - Can be used to image most teeth

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Parallel technique

#0

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Dental Radiographic Techniques

- Parallel technique
  - The film, transducer or plate is positioned parallel to the tooth
    - The plate must protrude beyond the ventral margin of the mandible
    - The edge of the plate must be parallel to the crowns and project slightly beyond them - difficult to achieve in large breed dogs
  - The x-ray beam is directed perpendicular to the tooth and plate
    - The resultant image:
      - Is slightly enlarged (x-ray beam diverges on leaving the cone)
      - Is a good representation of the tooth
      - Has at least 3mm of plate beyond the ventral mandibular margin and all aspects of the tooth

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Incident Beam Technique

- Incident beam technique
  - Plate is placed as close to the tooth as possible
  - The angle formed by the tooth and the plate (outside the oral cavity) is bisected
  - The x-ray beam is directed along this line
    - The resultant image:
      - Is slightly enlarged (x-ray beam diverges on leaving the cone)
      - Is a good representation of the tooth
      - Has at least 3mm of plate surrounding all aspects of the tooth
  - Can be used to image most teeth

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Cat mandibular cheek teeth
Use parallel technique

Plate parallel to teeth
Size #0 or #1

X-ray beam
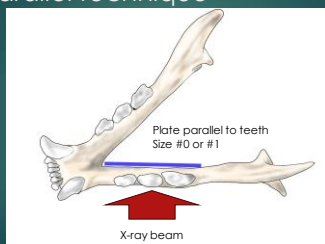
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Incident Beam Technique

- To illustrate the incident beam technique, let us use the sun and shadows cast by objects within it's rays.

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Mid morning

Tree
Shadow cast
Rising sun

Bisecting the angle

Noon
Shadow cast

This gives the same result as bisecting technique
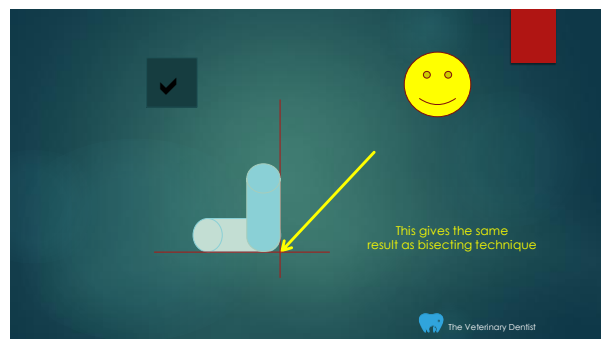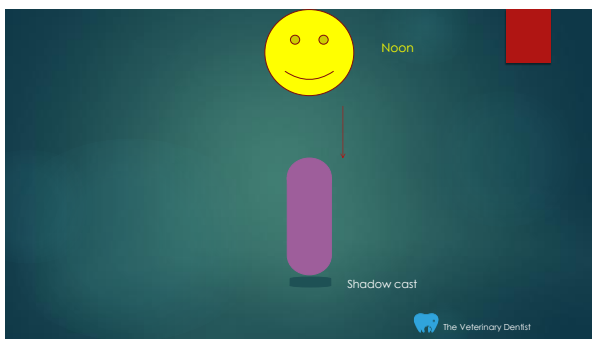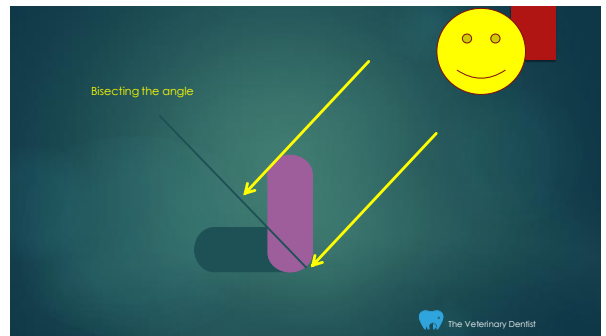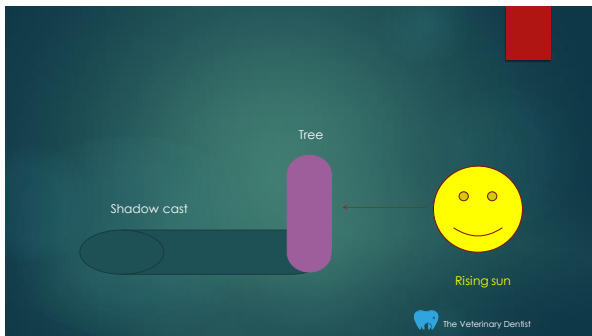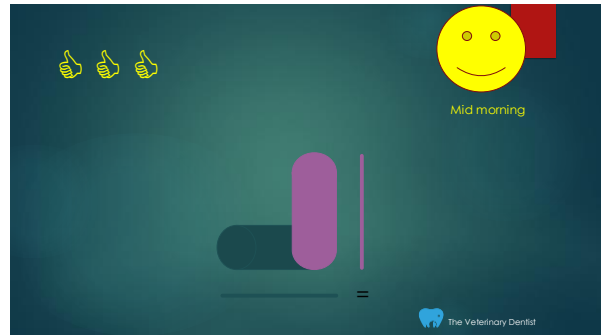
Incident Beam Technique
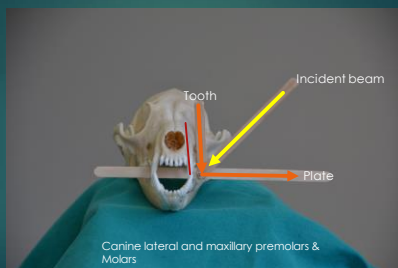
Incident Beam Technique

Dog Mandibular incisors rostro-caudal view
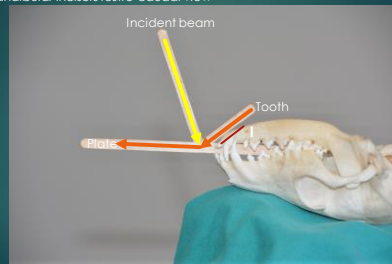
Cat maxillary P4
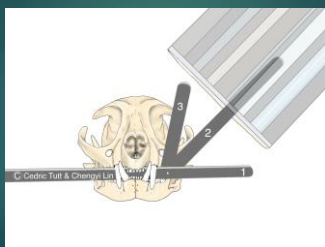
Cat mandibular incisors

Incident Beam Technique
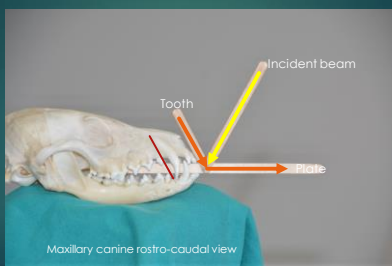
Cat mandibular canine - lateral

Right mandible

Left mandible

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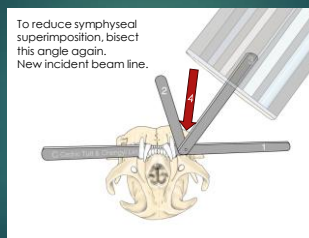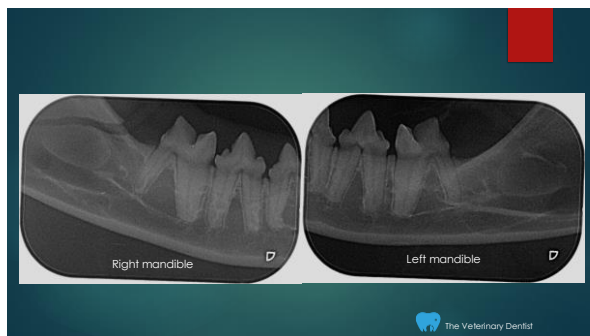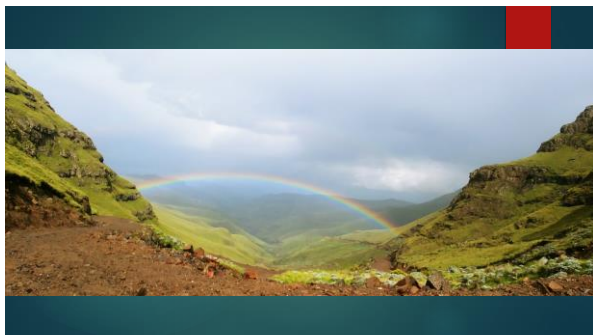
Buccal mounting

▶ By convention:

   ▶ Maxillary teeth crowns down; roots up

   ▶ Mandibular teeth crowns up; roots down

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CANINE DENTAL RADIOGRAPHIC SET: 2017-05-12
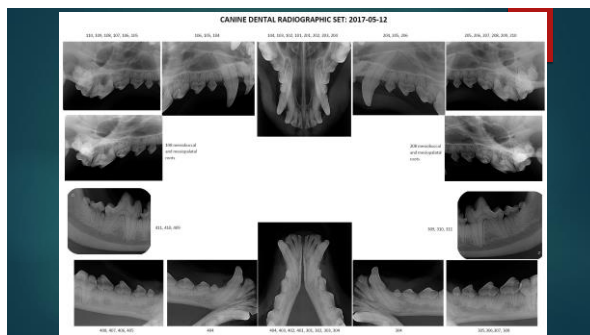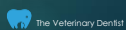
Buccal mounting

▶ By convention:

   ▶ Right is to left

   ▶ Left is to right

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FELINE DENTAL RADIOGRAPHIC SET: 2017-06-02
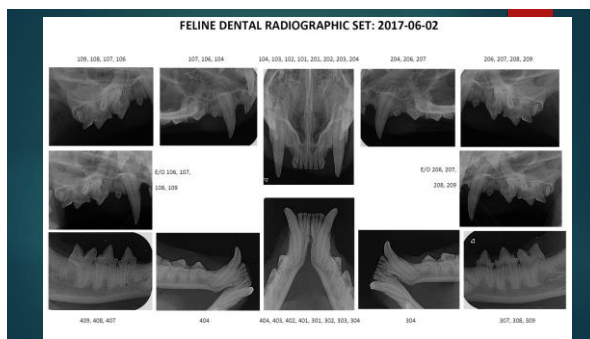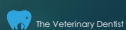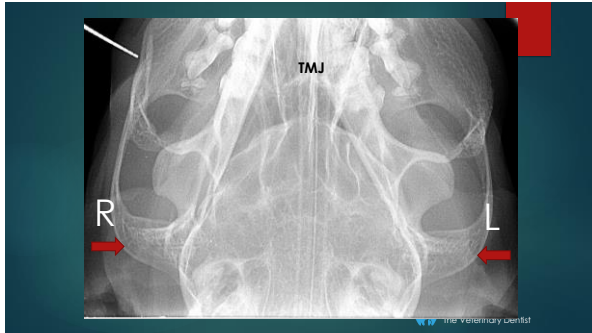
Veterinary dental radiology

- Look for:

  - Acquired
    - Fractures
    - Widening of the periodontal ligament space
    - Disruption of lamina dura
    - Periapical pathology
    - Peri-radicular pathology

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Veterinary dental radiology

- Develop your own routine

  - Soft tissue
  - Bone
  - Teeth

- Darkened viewing area

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Veterinary dental radiology

- Look for:

  - Acquired
    - Pulp chamber
    - Pulp horns
    - Root canal

    - Have roots developed normally

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Veterinary dental radiology

- Look for:

  - Developmental normality / abnormality
    - Normal number of teeth
    - Normal shape
    - Normal number of roots

  - Normal adjacent structures
    - Foramen
    - Canal

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Veterinary dental radiology

- Look for:

  - Acquired
    - Thickness of dentine
    - Thickness of enamel

    - Bone destruction
    - Bone proliferation

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Normal anatomy
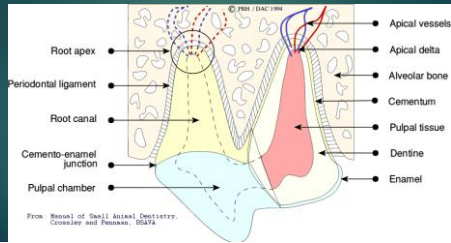
SLOB Rule
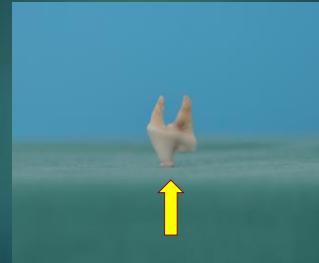
Veterinary Dental Radiography

▶ Lamina dura
  ▶ visible due to being seen *en face*

$$(ab + cd) < ef$$
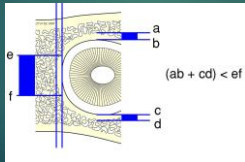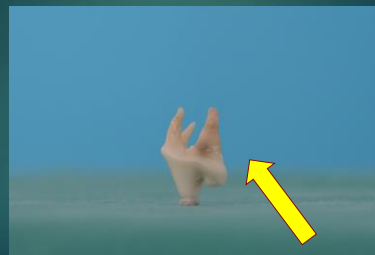
SLOB rule

Same-Lingual-Opposite-Buccal (SLOB) Rule

▶ When the beam is lateral/lateral the roots are superimposed

▶ When the beam is moved caudally the part that moves caudally is on the lingual side

▶ When the beam is moved caudally the part that moves rostrally is on the buccal side

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SLOB Rule
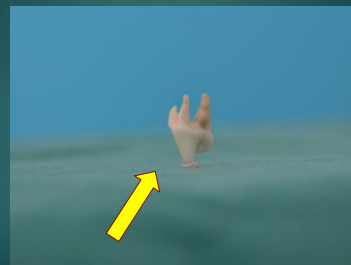
Removing superimposition

#2
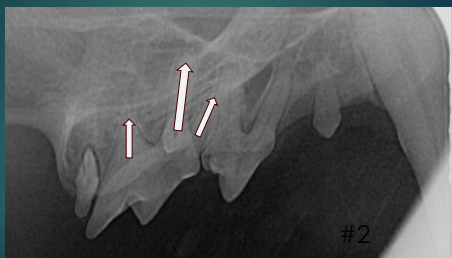
Radiology

- Make it easy

  - Buccal / labial mounting
  - Magnification
  - Brightness and gamma settings
  - Subdued lighting
  - If it's not good quality – take another

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Right mandible

Left mandible

Right mandible – lateral
Canine view
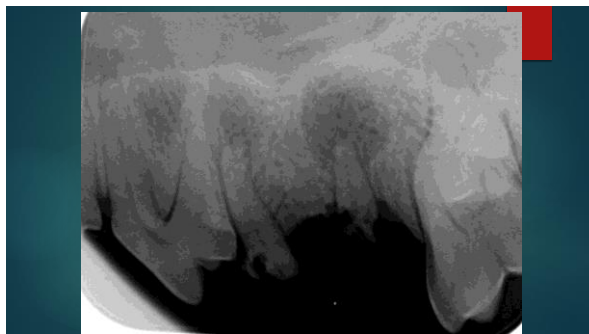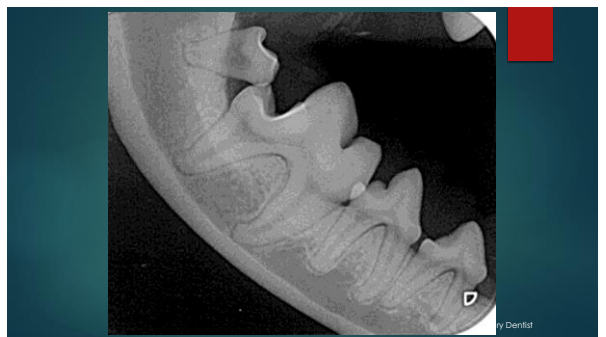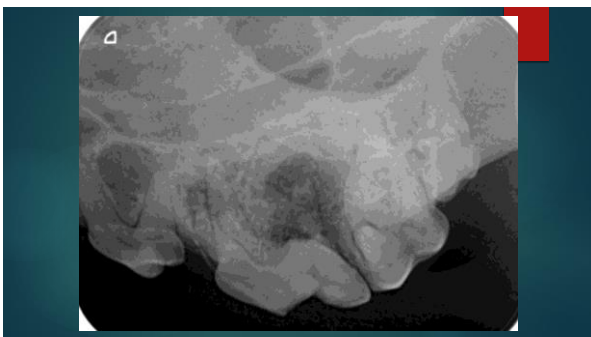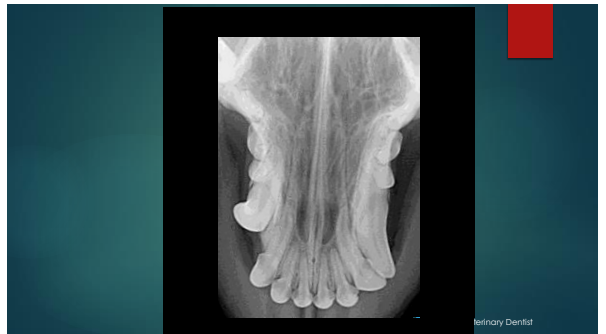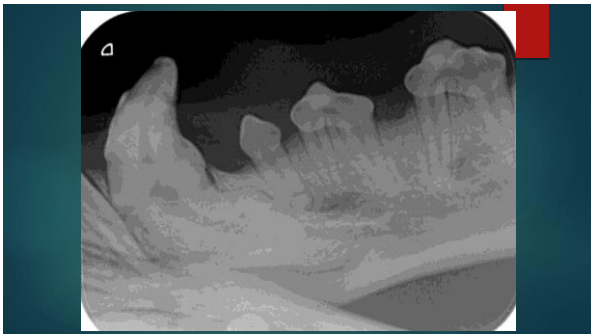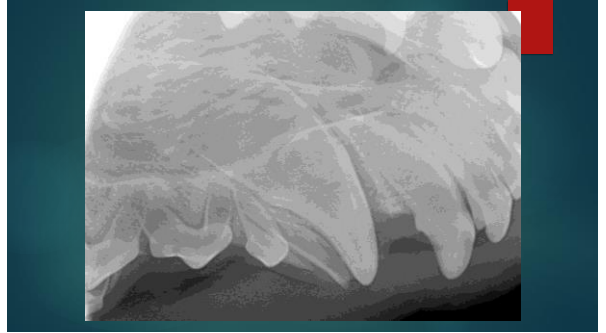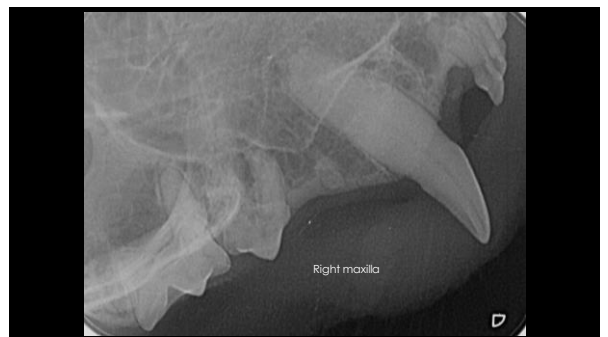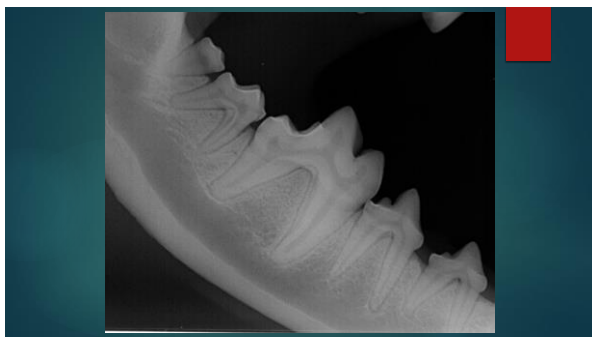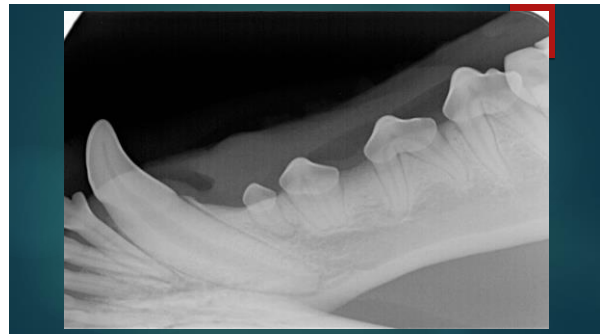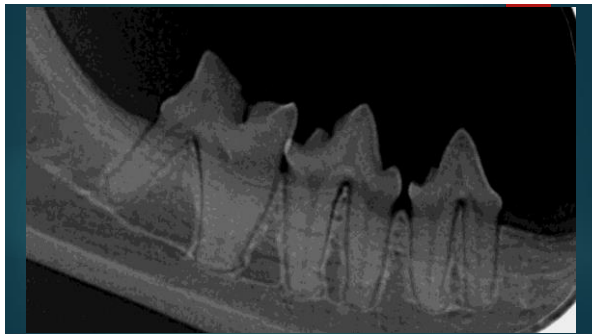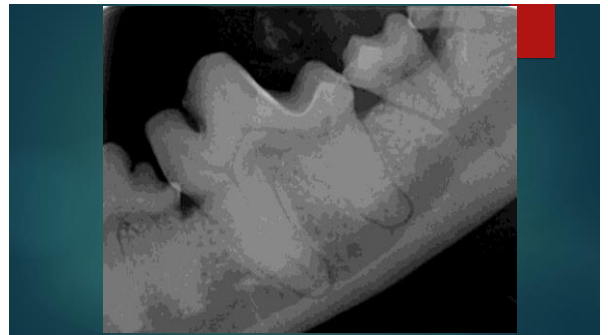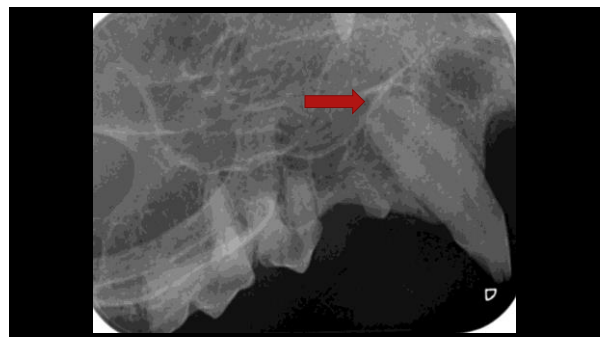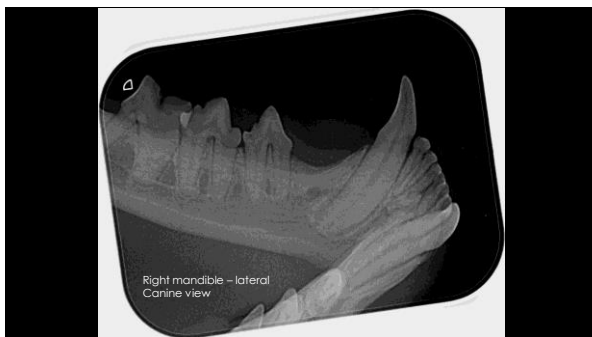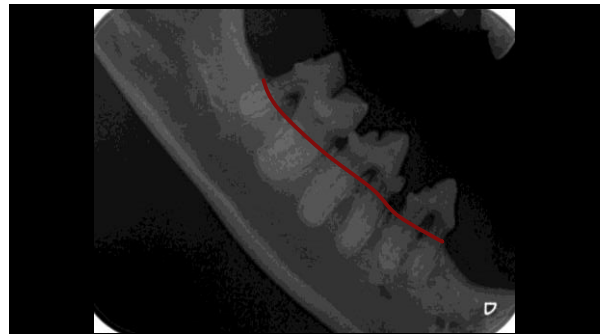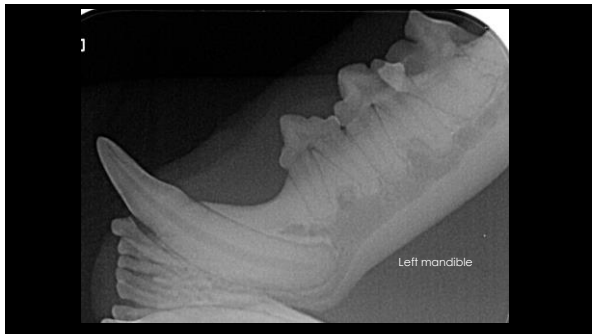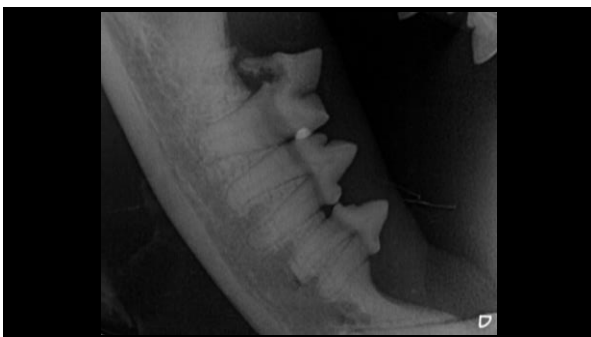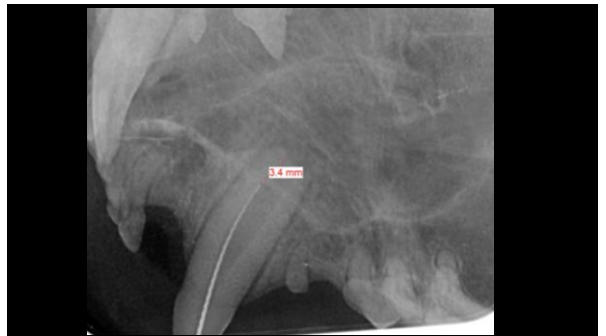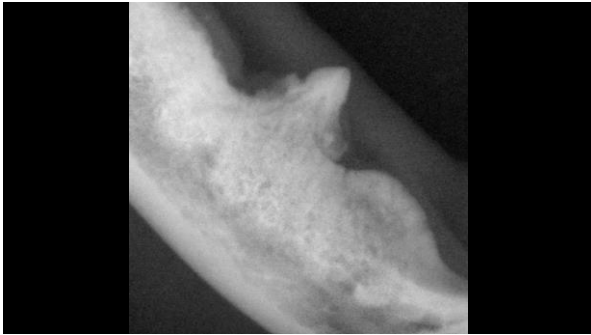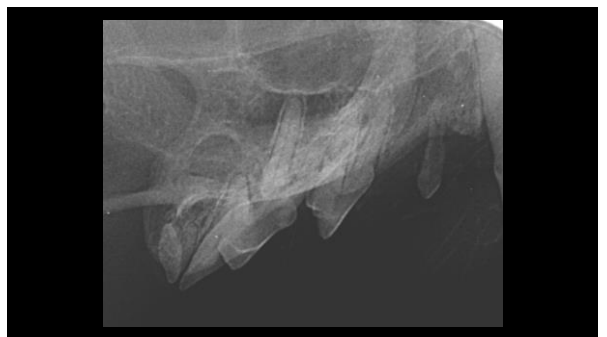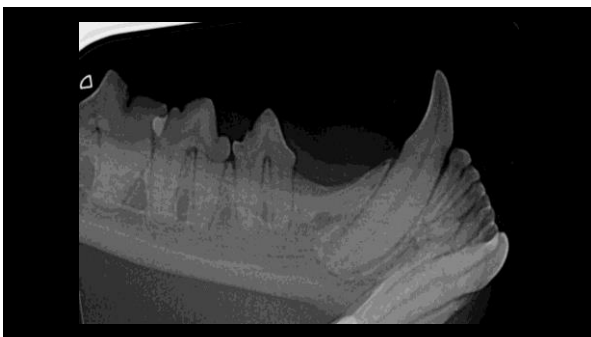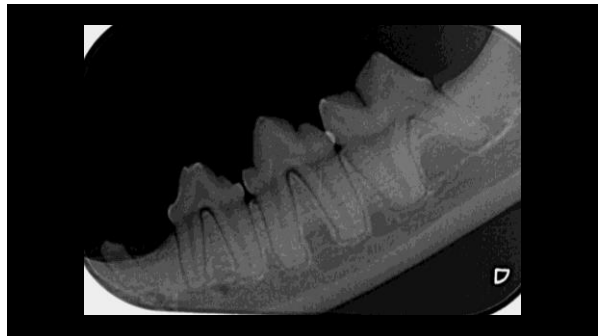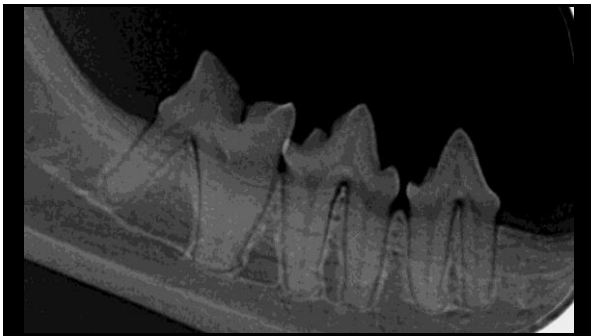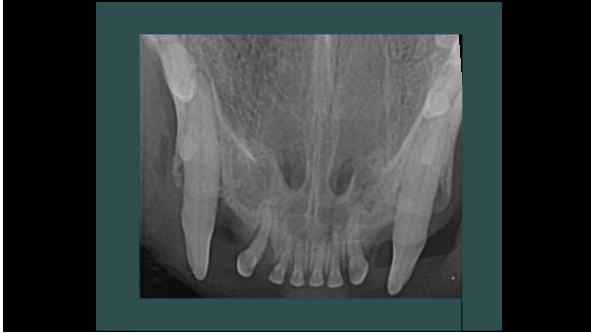
MULTIMODAL ANALGESIA AND
LOCAL/REGIONAL ANAESTHESIA IN CANINE
AND FELINE DENTISTRY AND ORAL SURGERY

Cedric Tutt
Diplomate EVDC

REGIONAL ANAESTHESIA

- Pre-emptive regional anaesthesia
  - Prevents sensation of pain
  - Prevents central wind-up – release of bradykinins
  - Reduces post-operative analgesic requirements

- **Habit** of use vs **technique**, prevents regular usage
  - Needs to be part of the anaesthesia / surgery protocol
  - Essential where systemic analgesics are not available

INTRODUCTION

- Aim
  - Lower anaesthesia requirements
  - Pain prevention – sensation "blocking"
  - Pain-free recovery
  - Reduced post-operative analgesia requirements

- Duration
  - Drug dependant
  - Overlap of effect required

REGIONAL ANAESTHESIA

- Local anaesthetic drugs

  - At physiological pH a larger proportion of local anaesthetic is in the charged cationic form [BH]$^+$
  - Uncharged form [B] crosses biological membranes to the site of action (therefore needed in this form near the site of action)
  - Cationic form [BH]$^+$ has Sodium channel blocking effect
    - Preventing depolarization and pain sensation transmission

MULTIMODAL / BALANCED ANALGESIA

- Pre-emptive
- Delivered / administered prior to inflicting pain
  - Opioid
  - NSAID
  - Ketamine
  - Gabapentin
  - Alpha-2 agonists

- Ensure duration of action overlaps
  - e.g. Fentanyl patch must be applied in adequate time
- Remember agonist/antagonist activity of Opioids
  - Buprenorphine after Morphine
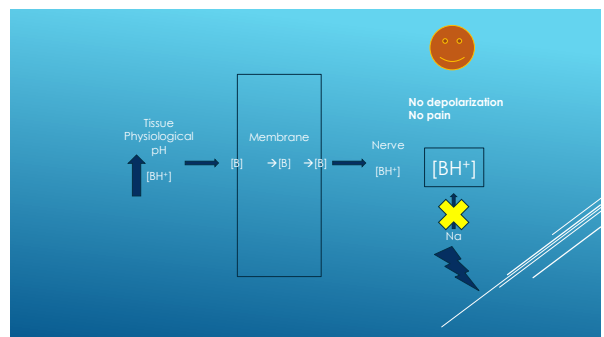
LOCAL ANAESTHETIC

- Dissociation formula

$$[BH^+] = [B] \times 10^{pKa-pH}$$

$$[\text{"Active"}] = [\text{"transport form"}] \times 10^{pKa-pH}$$

- Therefore:
  - If tissue pH = 7 and pKa = 8 then:
  - $[BH^+] = [B] \times 10^{8-7}$
  - $[BH^+] = [B] \times 10$

  - If tissue pH = 6 and pKa = 8 then:
  - $[BH^+] = [B] \times 100$

LOCAL ANAESTHETIC

- Therefore

  During inflammation, because pH is low

  → need 100[B] for 1[BH⁺]

  Need a much higher volume of transport form to produce one volume of active form

  Therefore a much greater volume of local required and may exceed toxic volume without reaching anaesthesia levels

---

REGIONAL ANAESTHESIA

- Sensory innervation of the teeth and oral structures
  - Trigeminal nerve (CN V)
    - (Ophthalmic)
    - Maxillary – superior alveolar nerve
    - Mandibular – inferior alveolar nerve
      - Buccal – dorsal and ventral branches
      - Lingual

Local Anaesthesia drugs

Local anaesthetic	Dosage (mg/kg)	Onset of activity	Duration of activity (min)
Lidocaine	2-5 (3-4.5)	Short	60-120
Mepivacaine	2 (4.5-5)	Intermediate	90-180
Bupivacaine	2 (2-2.5)	Intermediate	180-240
Ropivacaine	2 (2-3)	Intermediate	180-240

REGIONAL ANAESTHESIA

- Superficial mental block
  - Middle mental foramen

  - Effect
    - Ipsilateral mandibular lip, oral mucous membranes, chin

Middle mental foramen
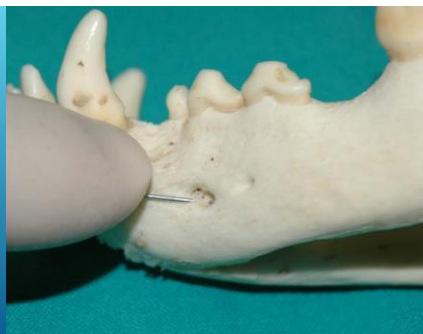
REGIONAL ANAESTHESIA

- Mandibular / inferior alveolar block
  - Mandibular foramen
  - Per os or per cutaneous
  - Digital isolation orally
  - **Beware of lingual nerve**
  - Effect
    - Ipsilateral mandibular lip, oral mucous membranes, chin and cheek and teeth
    - *NOT caudal buccal gingiva*

REGIONAL ANAESTHESIA

- Deep mental block ???
  - Middle mental foramen
    - Place needle in canal via foramen
    - Place needle beneath lip frenulum – from rostral
  - Effect
    - Ipsilateral mandibular lip, oral mucous membranes and chin; premolar 3??, canine and incisors
    - Difficult to perform
    - Neuropraxia ??

Anatomic landmarks inferior alveolar block

Molar 1 and angular process

M1

AP

Intra-oral needle approach

M1   AP

Percutaneous needle approach

SUPERIOR ALVEOLAR BLOCK

▸ In the cat

Orbit

<3mm

Maxillary foramen — Infraorbital foramen

DO NOT exit IO canal

REG

Displace globe caudally using forceps

Direct needle caudal to zygoma onto pterygoid fossa

Zygomatic process of the Maxillary bone

MAJOR PALATINE BLOCK IN THE CAT

Major palatine foramen

SPHE

Pterygopalatine foramen

Maxillary foramen

Dorsal branch – cd buccal

CNV Buccal branch of mandibular branch

Ventral branch – cd buccal

REGIONAL ANAESTHESIA

▸ Major oral surgery
  ▸ Repeat local block at end of surgery ??

▸ Possible complications
  ▸ IV administration
  ▸ Pulp necrosis due to vasoconstriction
  ▸ Self trauma

REGIONAL ANAESTHESIA

▸ Buccal branch of mandibular nerve (trigeminal)

  ▸ Divides into dorsal and ventral branches to supply buccal mucosa and buccal gingiva – maxilla and mandible

  ▸ Block site in buccal mucosa over ramus – line block

  ▸ Beyond the ramus buccal nerve divides
    ▸ Dorsal buccal branch
    ▸ Ventral buccal branch
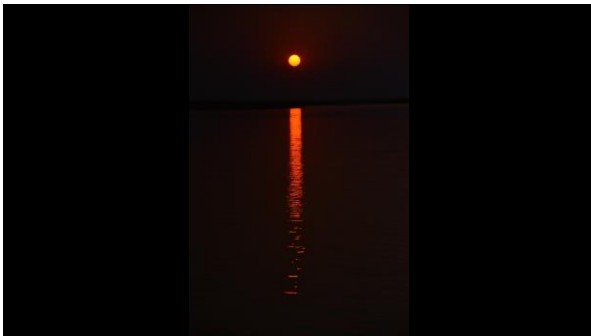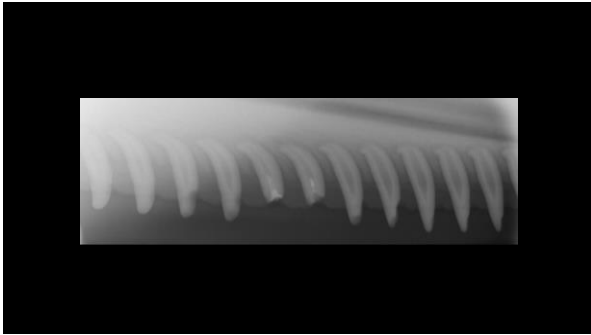
5 Closed extraction, open extraction and crown amputation techniques

Cedric Tutt
Diplomate EVDC

Surgical kit

- Scalpel handle – preferably round or hexagonal – easier to manoeuvre
- Periosteal elevator – range of sizes – small and medium
- Tissue forceps
  - Adsons disecting / Adson Brown
- Tissue scissors
  - Metzenbaum
  - Iris
  - (sharp-sharp)
- Suture scissors

FELINE VETERINARY DENTISTRY
EQUIPPING THE SURGERY AND THE SURGEON

Some equipment required is specific for cats

Take care!!

Luxator type

"beak gaps" – need a range

Too wide for cats

Root tip picks

Left Straight Right

Root tip extraction forceps
Need to be able to reach into the alveolus, open and grasp the root

Extraction forceps – for cats the beaks must be close together or meet when closed

When creating flaps, protect the soft tissues and bone.

Luxator too small

When creating flaps, protect the soft tissues and bone. Cut teeth before the flap is raised.

Luxator too large

Know the dimensions of instruments

Luxator – good fit

Luxator™ or elevator?

- Elevator – small sizes for cats
  - More robust
  - 45° on convex side
  - Sharpened on convex
  - Greater rotational forces
  - Sharp tips engage root

Techniques - Luxation

- Aim
  - Extraction doing no harm
  - Choose an instrument with the same size/shape as the tooth being elevated

  - Sever the periodontal ligament
  - Compress the alveolar bone surrounding the tooth
  - Fatigue the ligament circumferentially around the root

Luxator® or elevator?

- Luxator®
  - Sharp blade
  - Sharpened concave side
  - Sever soft tissue attachments
  - Compress alveolar bone
  - (May be used to deliver tooth)

Techniques - Elevation

- Aim

  - Deliver the tooth from the alveolus

  - Rotation forces
  - Between tooth fragments
  - Between alveolus and tooth

DO NOT

- Use a healthy tooth as a fulcrum during extraction of teeth

Technique – Extraction forceps

- Know the root shape prior to applying forceps – RADIOGRAPHY!

- Aim
  - Sever gingiva
  - Fatigue the ligaments – stretch beyond
  - Tear and rupture the ligaments
  - Deliver the tooth from the alveolus

Alveolotomy or not

- Single rooted teeth
  - For canines usually required
- Two rooted teeth (variations (3 or 1))
  - Section teeth
  - Remove furcation bone
  - Partial alveolotomy

Technique – Extraction forceps

- Forceps must fit curvature of tooth fragment
  - Require different shaped forceps for different tooth fragments
  - We cut teeth making unusual shapes – make sure the forceps fit

Alveolotomy or not

- Three rooted teeth
  - Same as for 2 rooted
  - For maxillary carnassials remove furcation bone between mesial roots after extraction of the mesio-buccal root

Technique – Extraction forceps

- Firmly grasp the tooth fragment
- Apply an intrusive force
  - Gently rotate clockwise, then anti-clockwise whilst maintaining intrusive force
- Apply extrusive force
  - Gently rotate clockwise and anti-clockwise to deliver tooth fragment
- NO WRIGGLING

Technique - Extraction forceps

- If unable to deliver the fragment repeat the intrusive force action and attempt the extrusive action
- If still not delivered luxate and elevate further
- It may be necessary to remove some bone which may be impeding the delivery of the root from the alveolus
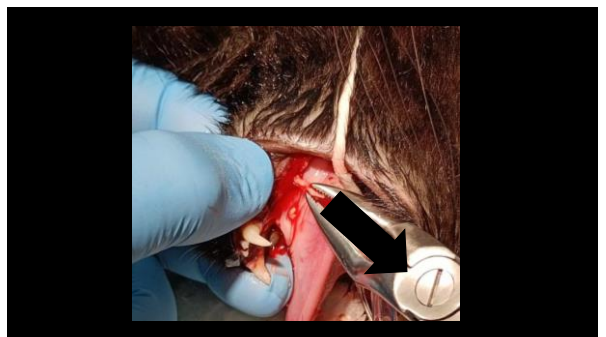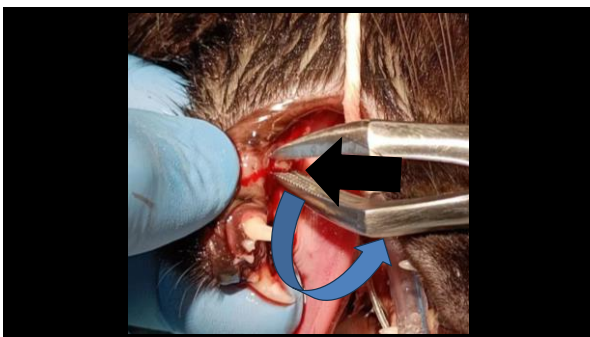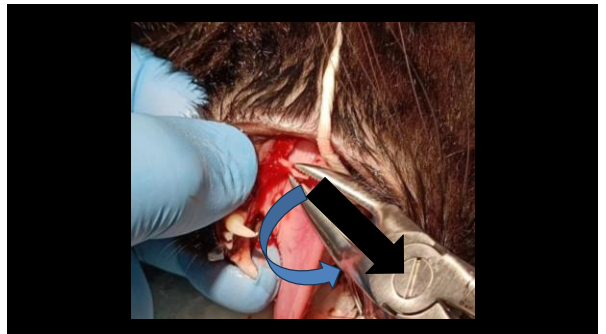
Closed extraction technique

Incisor extraction – use a luxator

Luxation

- Engage the periodontal ligament
- Direct the blade of the luxation device towards the root apex
- Drive the luxation device into the periodontal ligament space – as deeply as possible – sideways rocking action
  - Allow 5-10 seconds for adjacent ligament fatigue
  - Apply rotation force in one direction only

Careful around adjacent teeth
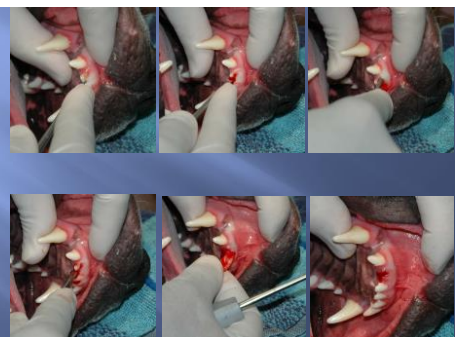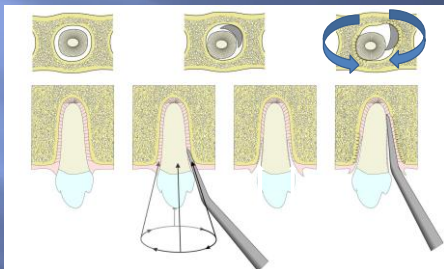
Exodontics

- Radiography is an essential component of exodontics
  - Sub-gingival fractures
  - Abnormal root shape
  - Variation in root number
  - Root resorbtion and replacement
  - Periodontitis associated compromise of the jaw
  - Pre-existing jaw fractures

Exodontics

- Closed extraction technique
  - Following radiographic evaluation and diagnosis
    - Sever gingival attachment circumferentially around the tooth
      - Luxator® or scalpel blade
    - Sever the periodontal ligament using a Luxator® or winged elevator

EXODONTICS

- Closed extraction
  - No flap raised may need to suture closed

- Open extraction
  - Flap raised and sutured closed

- Crown amputation techniques
  - Flap raised and sutured closed

Exodontics

- Closed extraction technique
  - Use an elevator / winged elevator of appropriate size to apply rotational leverage to the tooth root
  - Deliver the tooth using the Luxator®, elevator / winged elevator or extraction forceps

Exodontics

- Closed extraction (cont.)
  - Equipment
    - Scalpel blade (15 or 15c) and handle
    - Dental luxation instrument
    - Dental elevator / Couplands chisel / winged elevator
    - (Dental extraction forceps)

    - Needle holder, suture material, iris scissors, Adsons tissue forceps, suture scissors

Exodontics

- Open extraction technique
  - Additional equipment required
    - Periosteal elevator
    - Soft tissue retractor
    - Sharp/sharp tissue scissors
    - High and/or low speed dental hand pieces

Open extraction technique

- Teeth must be cut into as many pieces as there are roots

  - 2 rooted – cut into 2 parts

  - 3 rooted – cut into 3 parts

Maxillary P4 – mesial parts

Sectioning cat carnassials

- Maxillary P4

- 1. From the furcation rostrally to the middle of the mesial part of the tooth – halfway from gingiva to incisal edge
- 2. Between the two mesial cusps

Sectioning cat carnassials

- Mandibular M1

- From the furcation to incisal edge – parallel to the distal margin of the tooth

Maxillary P4 – divide mesial and distal

Start at furcation

Mandibular M1

Mandibular M1

Maxillary P3

Mandibular M1

Maxillary P3 and P4

Sectioning completed

Maxillary P3

Remove a
v-shaped piece

Mandibular P4

Remove a
v-shaped piece

Mandibular P4

Luxation technique

- Unless the luxator enters the ligament space it will not loosen the tooth.

- Check the angle of the luxator tip compared to the handle
  - Luxator tips are in line with the concave side
  - Winged elevators are aligned with the (convex) back of the head

Mandibular P4
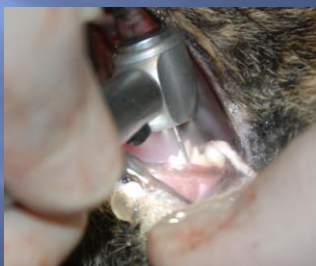
Luxator vs winged elevator

Luxator

Winged elevator

Winged elevator
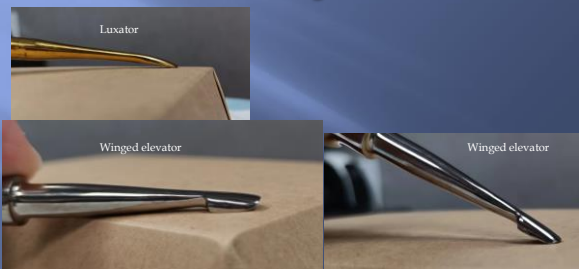
Mandibular P4
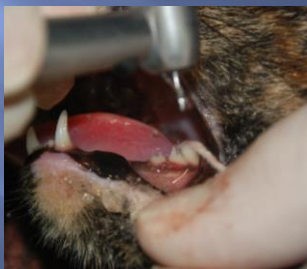
Luxation technique

- Luxating small fragments
  - Use finger force to apply rotational force
  - When indicated remove surrounding bone
  - Use a root tip elevator

Chronic gingivo-stomatitis

- When roots are present
  - Raise a continuous flap to access all affected sites
  - May need to remove some surface bone to expose roots
  - Magnify radiographs if necessary
  - Wear loupes or spectacles with magnification
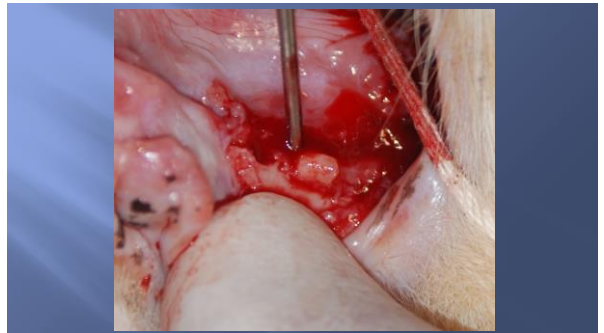
Chronic gingivo-stomatitis

- Use sharp instruments
- Be careful and work in a controlled manner
- If needed remove bone circumferentially around root – use 0.25 round bur, fine tapered bur

- Use a root tip elevator
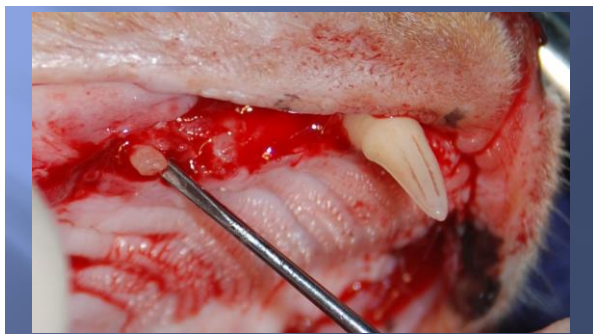
Suture material

- Ideal material
  - Keep tissues apposed long enough for healing then disappear
  - Not cause irritation or trauma to tongue etc
  - Not cause inflammation
- Monofilament, synthetic, absorbable
- suaged-on reverse cutting needle

Suture patterns and tying
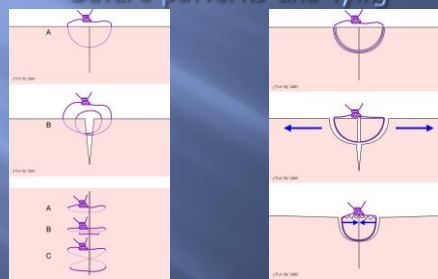
Tooth resorption

- Tooth resorption
  - Two types of tooth resorption commonly seen
    - **Type 1** – Inflammatory resorption
    - **Type 2** – Idiopathic (replacement) resorption

Extracting teeth affected by Tooth resorption

Dental radiography

is required to confirm the type and stage of tooth resorption

Tooth resorption

- Type 1 (inflammatory) resorption
  - 1. Associated with gingivitis and periodontitis
  - Some visible at the gingival margin
  - 2. Periapical pathology – endodontic disease
  - Gingiva not usually involved

  - Affected teeth must be completely extracted or where periodontally sound but the pulp is dead undergo root canal treatment, if indicated

Tooth resorption

Treatment decisions are based on

Dental radiography
And radiological interpretation

Tooth resorption

- **Type 1**

1.
  - Extraction of the whole tooth and its root/s is essential
  - The gingiva may or may not be sutured closed – may already be undergoing healing

Internal resorption
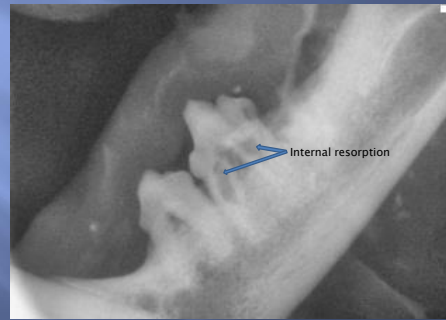
Tooth resorption

- **Type 1** (inflammatory) resorption

2.
  - The tooth has a dead pulp with periapical resorption
  - The tooth should undergo root canal therapy
  - Once the dead pulp is removed and the filling placed, the resorption around the root tip should cease and new bone will fill in around the root
  - Follow-up dental radiographs will be required at 3-6 month intervals to evaluate response to treatment

Tooth resorption

- **Type 2** (idiopathic) resorption

  - Idiopathic root resorption begins below the surface of the gingiva
  - Begins in the cementum
  - Root substance is destroyed and replaced with bone-like material
  - Ankylosis may be part of the process

Tooth resorption

- **Type 1** (inflammatory) resorption

  2. **(variant)**
  - The tooth has pulpitis and on radiography there is internal resorption
  - Treatment is
    - RCT if not severe
    - If severe, extraction

Tooth resorption

- **Type 2** (idiopathic) resorption

  - Stages of resorption
    - 1. Affecting cementum only
    - 2. Affecting cementum and dentine (Dentine/Pulp complex)
    - 3. Affecting the pulp cavity - root canal or pulp chamber
    - 4a. Crown and roots equally affected
    - 4b. Crown more affected than roots
    - 4c. Roots more affected than crown
    - 5a. Crown present but no roots
    - 5b. Crown absent and "no roots"
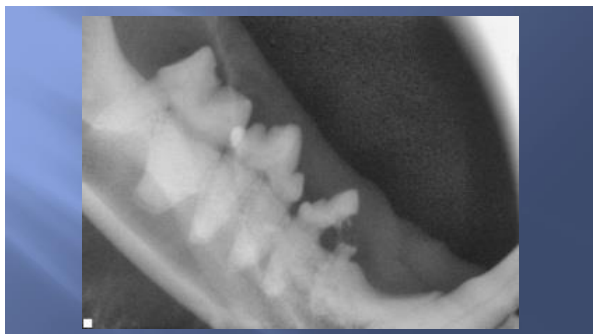
Tooth resorption

- Type 2 (idiopathic) resorption

Crown missing
- no roots

Tooth resorption

- Type 2 (idiopathic) resorption

- Mainly root affected

Canine root resorbed and
replaced by bone-like material

Tooth resorption

- Type 2 (idiopathic) resorption

  - Where no roots remain the crown should be amputated
  - If crown / root fragments remain and puncture the gingiva they should be removed

Tooth resorption

- Type 2 (idiopathic) resorption

- Root and crown affected
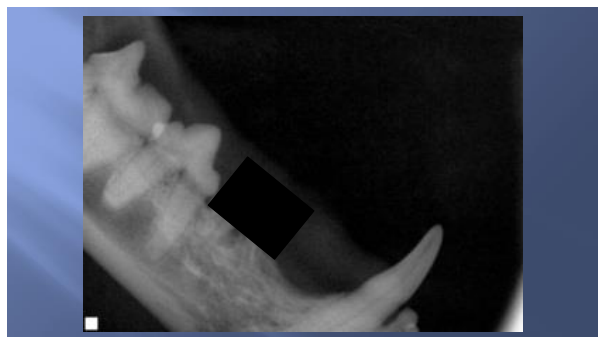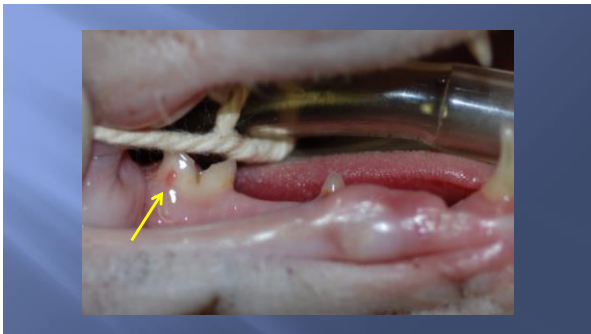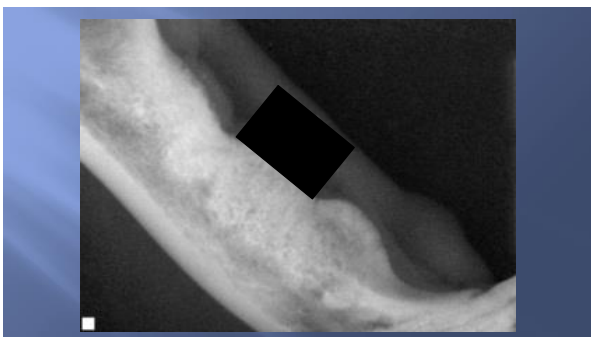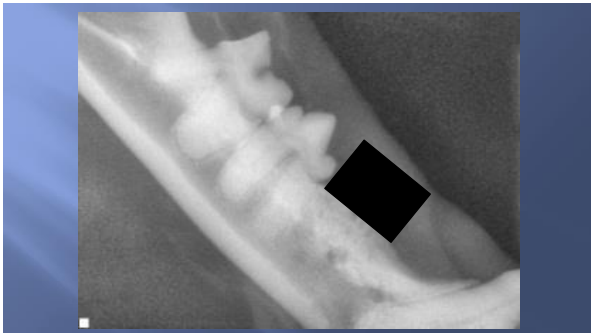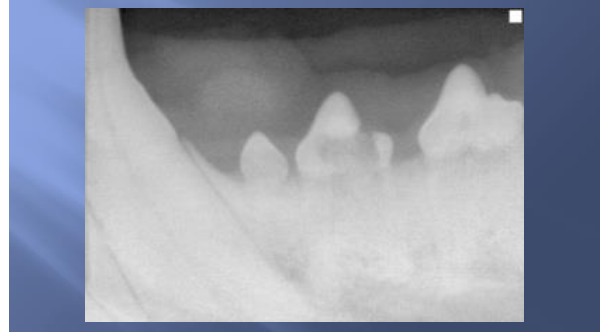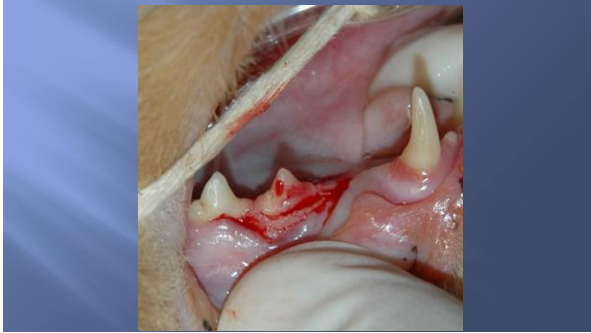
Complications of extraction

- Local anaesthesia
  - Self trauma
  - Technique – ocular trauma

- Surgery
  - Soft tissue trauma
    - Instrument slip
    - Bur trauma to flap

Complications of extraction

- Surgery
  - Bur trauma of healthy tooth
  - Fracture of healthy tooth – fulcrum

  - Root tip transportation
    - Into the nasal passages
    - Mandibular canal
    - Orbital fat pad

Complications of extraction

- Wound dehiscence
  - Excessive tension on the suture line
  - Compromised blood supply to flap
  - Biopsy site – apposition of tumour edges

Complications of extraction

- Surgery
  - Bur trauma
    - Into infra-orbital canal
    - Into mandibular canal
      - ?? Oro-facial pain syndrome??

Oral surgery

- The enemies of oral surgery
  - Impatience!
  - Epithelium
  - Tissue
    - Viability, Blood supply, Tension
  - Suture
    - Type
    - Tension
  - Instruments and tissue handling

Complications of extraction

- Surgery
  - Transportation of the luxator
    - Ocular trauma
    - Palate trauma
    - Brain trauma

Oral surgery
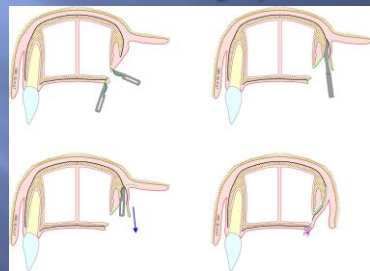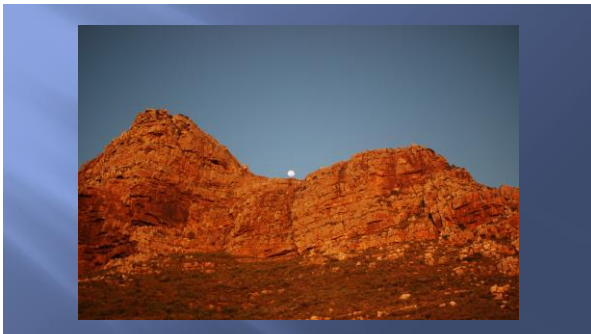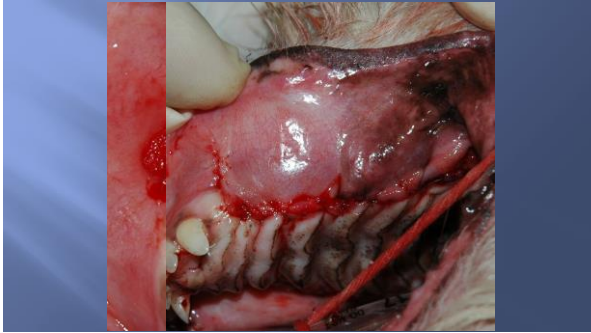
CHRONIC GINGIVOSTOMATITIS IN DOGS AND CATS

Cedric Tutt

BVSc(Hons), MMedVet(Med),
Diplomate EVDC, MRCVS

www.theveterinarydentist.com

CAPE ANIMAL
DENTISTRY SERVICE

Periodontium

- Gingiva
  - Covers the jaws, protecting the bone and rest of periodontium

  - Perforated by the teeth protruding into the oral cavity

Periodontium

- Gingiva
- Alveolar bone
- Periodontal ligament
- Cementum

Root apex
Periodontal ligament
Root canal
Cemento-enamel junction
Pulpal chamber
Alveolar bone
Cementum
Pulpal tissue
Dentine
Enamel
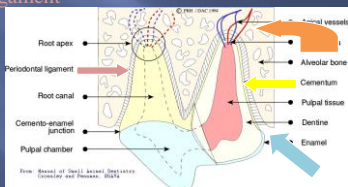
Periodontium

- Gingiva
  - Free gingiva
    - Forms a soft tissue collar
    - Potential space - sulcus
    - Probing depth <0.5 mm in cats, <3mm in dogs

  - Attached gingiva
    - Attached to the tooth by hemidesmosomes
    - Inseparable from the periosteum
    - Attached to alveolar bone

Periodontium

- The periodontium:

  - Cementum (root surface)
  - Periodontal ligament
  - Alveolar bone
  - Gingiva

- Keeps the tooth securely attached in the jaw. Provides nutrition.

Attached gingiva
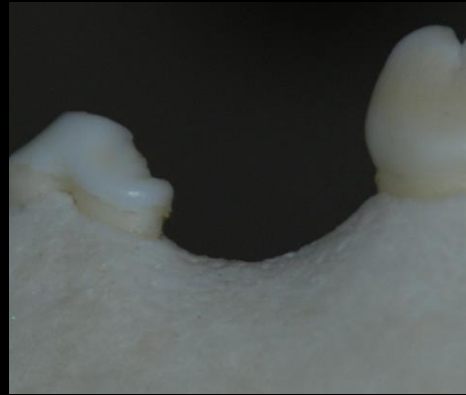
Periodontium

- Gingiva
  - Attached gingiva – in health
    - Junctional epithelium attached apical to the Cemento-enamel junction (CEJ)
    - Lymphocytes and plasmacells found here in radiologically normal alveolar bone
    - Connective tissue rich in collagen

Periodontium

Periodontal ligaments
Gingival fibres

Hemidesmosomes

Sulcus
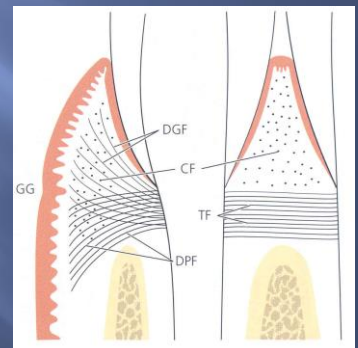
Periodontium

- Alveolar bone
  - Alveolus – socket in which the tooth resides
  - Edentulous parts of the jaw
    - Do not develop alveolar bone proper (jaw smooth)
      - No alveolus
    - No free gingiva – only attached gingiva
    - No periodontal ligament

Periodontium

Periodontal ligament fibres

Alveolar crest
  Anti-lux
Horizontal
  Stability
Oblique
  Anti-intrusion
Apical
  Anti-lux
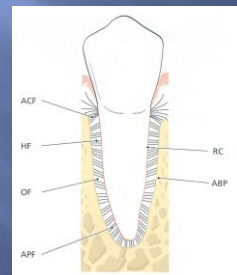
Root cementum

Alveolar bone proper

Periodontium

- Cementum
  - Living structure into which ligament is fixed
  - Can regenerate
  - Can become thickened
    - Decreasing ligament space
    - Enlarging apical diameter of root
    - Causing ankylosis

Periodontitis

- Periodontal disease in animals of same age and breed differs
  - Some are more susceptible than others!

- Immunological mechanisms may be involved

Periodontitis

- Periodontitis
  - Progression from gingivitis - superficial
  - Periapical lesions - radiographs
  - Peri-radicular lesions - radiographs

  - Traumatic
  - "Infectious"

  - Periodontal disease can be associated with swelling and other signs of inflammation

Juvenile gingivitis / periodontitis
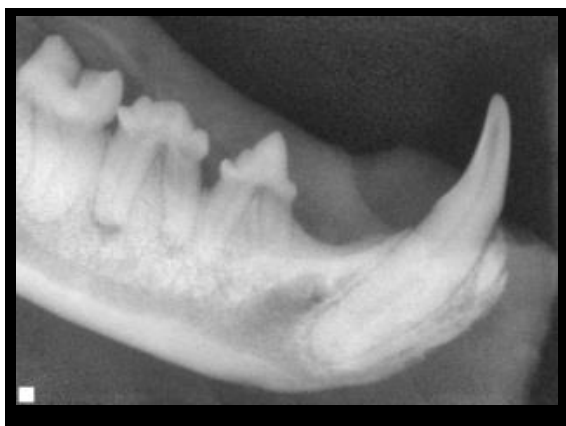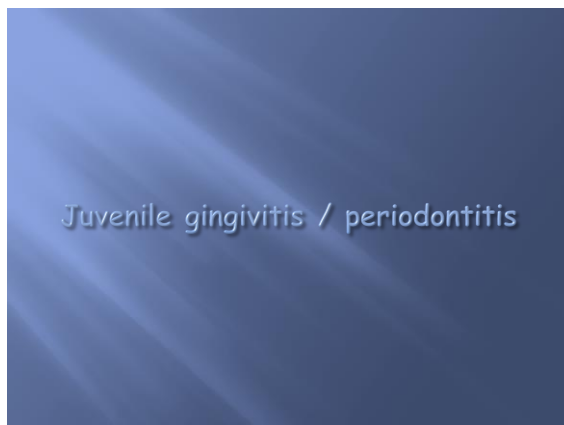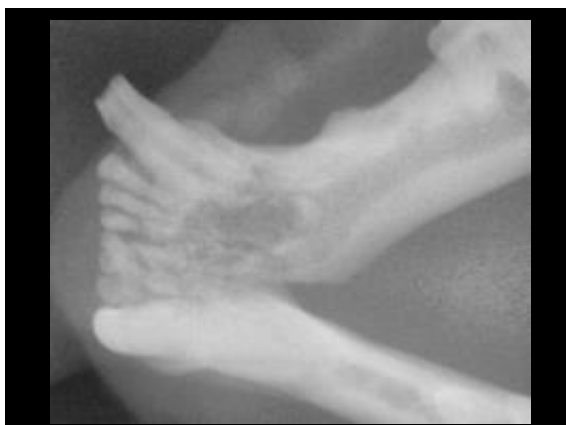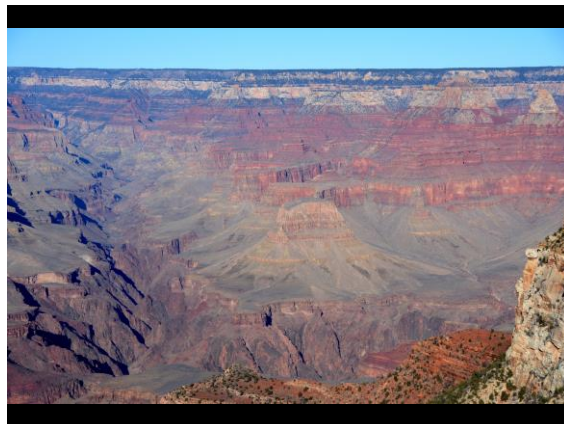
Stomatitis

- Oral mucosa
  - Alveolar mucosa
  - Buccal mucosa
  - Caudal oral mucosa
  - (Fauces)
  - Lingual
    - Glossitis
  - Lip
    - Cheilitis

Feline Chronic Gingivo-stomatitis

- Multi-factorial
  - Bacterial
    - Anaerobes
      - *Bacteroides*
    - Spirochaetes
      - *Borrelia*
  - Viral
    - FHV1
    - FCV
    - FIV
    - FeLV

Gingivo-stomatitis

- Gingivitis

  - May affect:
    - Free gingiva

    - Free and attached

    - Reversible
      - Tooth brushing

Feline Chronic Gingivo-stomatitis

- FHV1
  - Ulcers
    - Tongue
    - Lips

Feline Chronic Gingivo-stomatitis

- FIV
  - No stomatitis in SPF colonies with experimentally infected FIV positive cases

  - Naturally infected cases
    - Up to 50%
    - Ulcero-proliferative stomatitis

    - Immune response – chronic antigenic stimulation

Feline Chronic Gingivo-stomatitis

- FCV
  - In experimental infections cannot induce stomatitis

  - In cats with severe stomatitis majority positive for FCV

  - Treated animals may eliminate the virus

Stomatitis

- May be isolated to one area
- May be symmetrical
- Alveolar mucosa
- Glossitis
- Salivary gland

Feline Chronic Gingivo-stomatitis

- FeLV
  - Cats with CGS less likely positive FeLV
  - Cats with FeLV more likely have CGS

FeLV   CGS

Salivary adenitis

Buccal stomatitis

Feline Chronic Gingivo-stomatitis
Differentiate from SCC

Chronic gingiva-stomatitis

Exposure of cheek muscles

Caudal stomatitis and faucitis

Bone height within 1-2mm of alveolar margin

May affect all teeth

May only affect some teeth

Vertical bone loss predominates in some cases
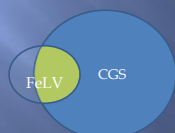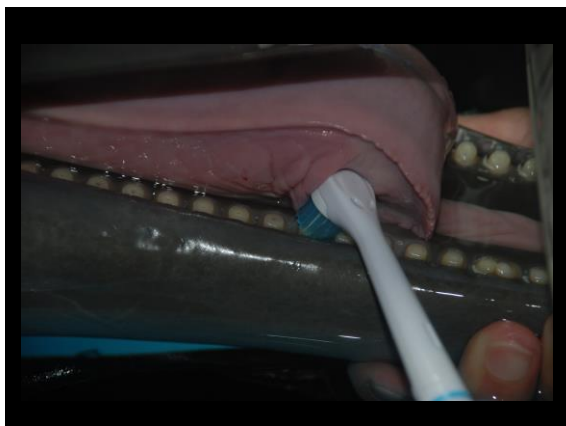
Chronic Gingivo-stomatitis

- Primary Treatment
- Always
  - Begin with scale and root debridement and polishing
  - Survey full-mouth radiographs
  - Where indicated antibiotic and anti-inflammatory medication
  - Institute thorough home-care regimens
  - Regular follow-up examinations

Vertical and horizontal bone loss and root separation

Chronic Gingivo-stomatitis

- Initial Treatment

  - Extract teeth affected by periodontal disease
    - Debride compromised gingiva
    - Suture flaps to encourage first intention healing

  - Partial gingivectomy where indicated

  - Biopsy soft tissue

Chronic Gingivo-stomatitis

- Subsequent treatment

  - Evaluate previous extraction sites
    - Completely healed – good prognosis for complete cure when all teeth extracted

    - Incomplete healing – may be too early. Additional treatment required
  - If tissue adjacent to existing teeth is inflamed, then extract more teeth

Chronic Gingivo-stomatitis

- Recently shown that extraction of all teeth vs extraction of all teeth excluding canines – no difference

- Begin by extracting remaining teeth and if canines and incisors not affected keep them

- If incisors affected – extract incisors

Chronic Gingivo-stomatitis

- When extracting all cheek teeth

  - ALWAYS extract maxillary molar 1 first

  - May be covered by exuberant gingiva
  - Crown may be missing
  - Take radiographs

cd oral

severe

Faucitis

Glossitis

Glossitis, stomatitis, faucitis

Chronic gingivo-stomatitis

- Additional treatment

  - Intra-lesional triamcinolone

  - Cyclosporine

  - Lactoferrin - Oral Relax (plus Piroxicam)
    - In some cases institute this treatment earlier
    - Shown to be effective in cats which still have teeth

Therapeutic Management of Feline Chronic Gingivostomatitis: A Systematic Review of the Literature *Jenna N. Winer, Boaz Arzi and Frank J. M. Verstraete*

Feline lymphoplasmacytic stomatitis

FELINE LYMPHOCYTIC-PLASMACYTIC GINGIVITIS STOMATITIS A CLINICAL TRIAL

Shih-Chieh Chang (張仕杰), D.V.M., Ph.D.

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Director, Veterinary Medical Teaching Hospital
Head of Clinical Oncology, Veterinary Medical Teaching Hospital
College of Veterinary Medicine, National Chung Hsing University
Taiwan College of Veterinary Surgeons (TCVS)

Experimental design
Grade 1
Double blind study

Evidence
Grade A
Histological evidence

Feline lymphoplasmacytic stomatitis

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Bovine lactoferrin and piroxicam as an adjunct treatment for lymphocytic-plasmacytic gingivitis stomatitis in cats

Yi-Ping Hung [a,1], Yi-Ping Yang [b,1], Hsien-Chi Wang [a,b], Jiunn-Wang Liao [c], Wei-Li Hsu [d], Chao-Chin Chang [d], Shih-Chieh Chang [a,b,*]

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b Veterinary Medical Teaching Hospital, College of Veterinary Medicine, National Chung Hsing University, 250 Kuo-Kuang Road, Taichung 40227, Taiwan
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d Graduate Institute of Microbiology and Public Health, College of Veterinary Medicine, National Chung Hsing University, 250 Kuo-Kuang Road, Taichung 40227, Taiwan

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This is evidence based medicine for treatment of
FCGS

308 Post Exod
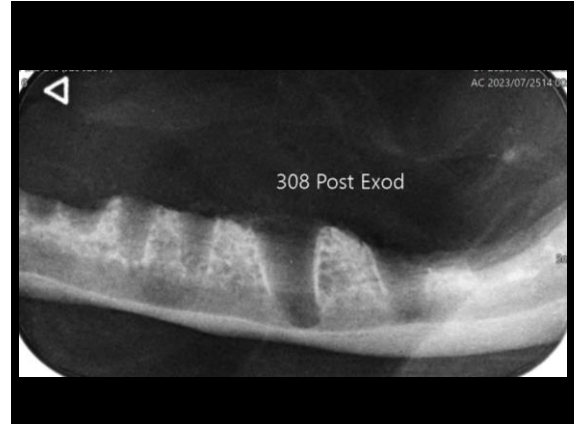
Commonly seen lesions in dogs

409 Pre Exod

308 Pre Exod

403 Pre Exod
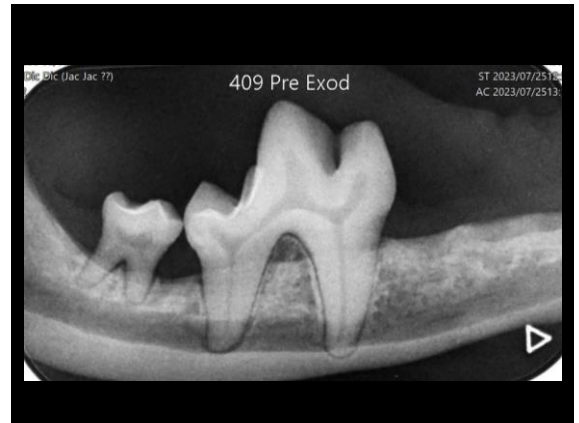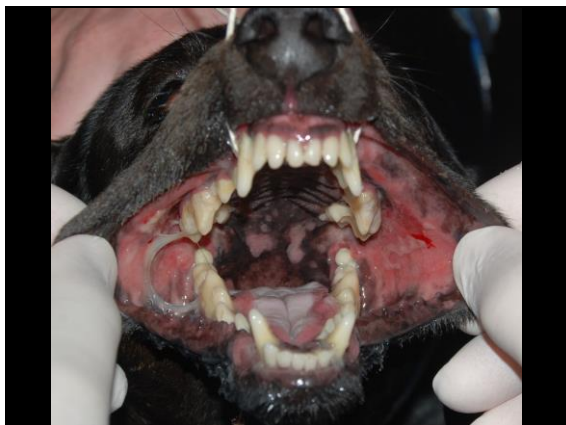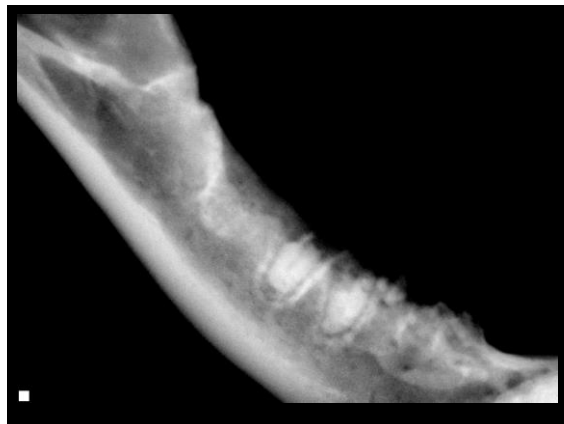
Chronic gingivo-stomatitis

▫ When presented with a case that has had "all teeth extracted" but inflammation persists

- Full mouth radiographic survey
- Repeat radiographs where unclear
- Investigate for root remnants

Chronic gingivo-stomatitis

▫ When roots are present

- Raise a continuous flap to access all affected sites
- May need to remove some surface bone to expose roots
- Magnify radiographs if necessary
- Wear loupes or spectacles with magnification
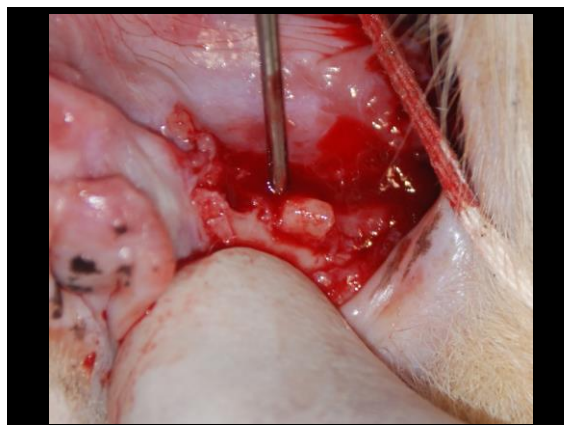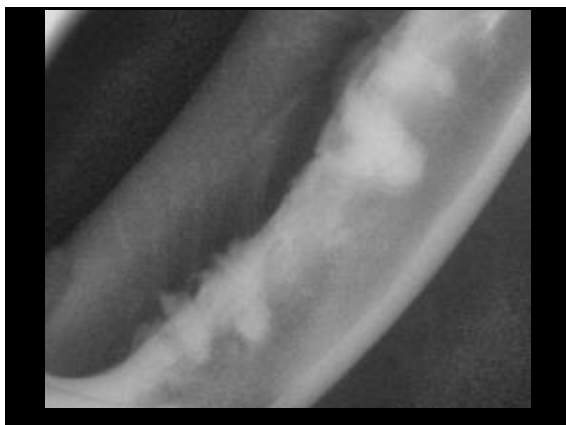
Chronic gingivo-stomatitis

- Use sharp instruments

- Be careful and work in a controlled manner

- If needed remove bone circumferentially around root – use 0.25 bur, fine taper bur

- Use a root tip elevator
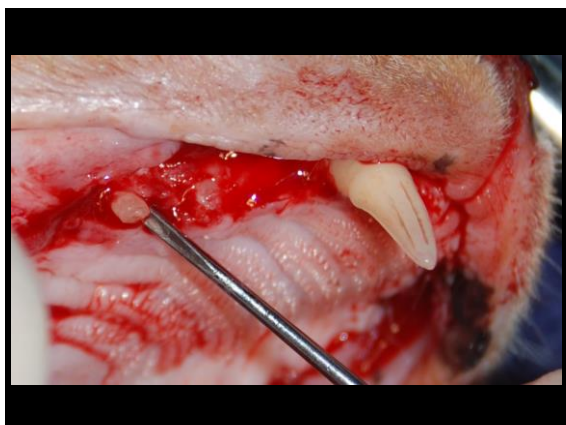
Chronic gingivo-stomatitis

- Analgesics

- IF appropriate
  - Antibiotics

- Oral rinse

Feline Chronic Gingivo-stomatitis

In severe cases where all teeth were extracted:
66-80% healed in 60 days
13-19% took up to 2 years to heal
7-15% did not heal and required ongoing medical treatment
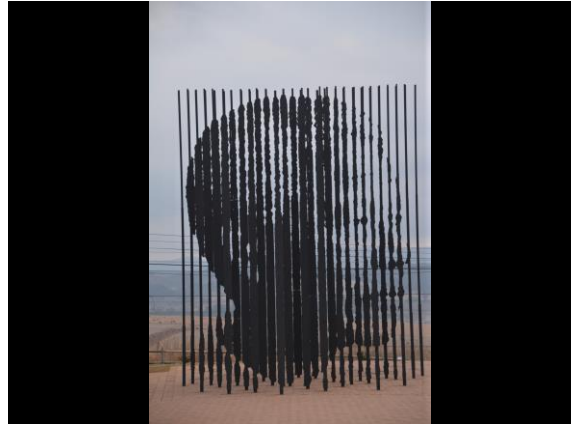
Oral tumours and cysts

Cedric Tutt

Diplomate European Veterinary Dental College

Oral tumours and cysts

- Not all "swellings" are tumours
  - But all are worth investigating
  - If we rule out a tumour, the clients are always happy
  - If we diagnose a tumour early on, usually the surgery is less complicated

Oral tumours and cysts

- Essentials:

  - CT / CBCT

  - Biopsy, biopsy, biopsy!!

Oral / facial swelling

- Differentiate acceptable norms from lesions
  - Breed differences in head shape, coat, size
- Trauma – usually history
- Inflammation / infection
- Sinus tracts – moisture, blood
- Malocclusion
- Lymph adenopathy

Oral tumours and cysts

- Both may present as swellings

- Cysts may be mistaken for oral tumours

- Cysts may result in pathological fractures

Oral examination

- History
  - General behaviour
  - Eating
  - Salivation – reduced swallowing / excess production
  - Haemorrhage
  - Halitosis

- Symmetry
  - Head – masticatory muscles
  - Facial
  - Mandibular bodies

Oral examination

- Lips
  - Muco-cutaneal junctions
  - Lip folds
  - Commissures
  - Chin
  - EGC
- Do the canine teeth protrude below the lips?
  - Do they puncture the lip?

Oral examination

- Incisive papilla
- Palatal mucosa
- Soft palate
- Tonsils
- Larynx

- Cursory look at teeth

Oral examination

- Palpate lymph nodes
  - Parotid
  - Mandibular
  - (retro-pharyngeal)
  - (infra-orbital)
- Palpate salivary glands
  - Parotid
  - Mandibular
  - Sublingual monostomatic
  - Buccal
  - (zygomatic - exophthalmos)

Oral examination

- Under GA
  - Focus on abnormality
  - Review symmetry

- Plan
  - Diagnostic imaging
  - Radiography
    - Dental
  - Computed tomography
    - Standard CT
    - CBCT
  - MRI
  - Biopsy

Oral examination

- Examine "normal side" first
  - Tongue
    - Dorsum, margin
    - Sublingual structures
      - Salivary puncta
  - Buccal mucosa
    - Salivary puncta
      - Parotid
      - Zygomatic
      - Buccal glands
    - Glands

Diagnostics

- Plan (cont.)
  - Staging
    - Lymph nodes
      - Palpation
      - FNA
      - Biopsy – FNA, wedge vs excisional
    - Thoracic radiographs
    - Thoracic CT
      - With contrast

Diagnostics

- Staging

- WHO staging: TNM

  - To – no sign of tumour
  - T$_1$ - < 2cm
  - T$_2$ – 2-4 cm
  - T$_3$ - >4 cm

Diagnostics

- Staging (cont.)
  - Node
    - Palpably normal
    - Enlarged
    - Fixed
  - Metastases
    - None
    - Local
    - Distant

Oral cysts

- Odontogenic cysts
  - structures lined by odontogenic epithelium

  - Periapical / Radicular cysts
    - Tooth with exposed pulp
      - associated with apex or lateral canal
    - Inflammation stimulates cell rests of Malassez in periodontal ligament
    - Periapical granuloma develops
    - Ischaemic degeneration
    - Granuloma develops into a cyst – can't differentiate radiographically

Diagnostics

- Tumour Biopsy
  - FNA
  - Incisional
  - Intra-lesional
  - Multiple, representative samples

  - Excisional ??

Oral cysts

- Periapical cyst treatment
  - Endodontic therapy on affected tooth
  - Remove during extraction of affected tooth
  - Debride apical alveolus

Oral cysts

- Residual cyst
  - Site of previously extracted tooth
  - Remnant of periapical cyst

  - Treatment residual cyst
    - Debridement and curettage of alveolus via surgical flap
    - Histopathology
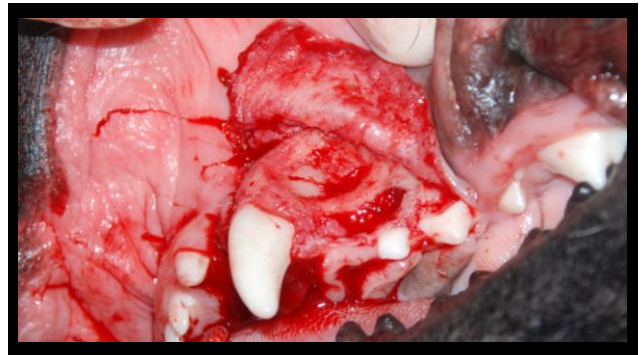
Oral cysts

- Dentigerous cysts
  - Unerupted tooth (missing tooth, supernumerary)
  - Fluctuant mass
  - Mandibular / maxillary expansion

  - Diagnosis
    - Fluctuant mass in mouth (bluish)
    - Incidental finding on radiography
    - Cystic lesion surrounding unerupted tooth

Oral cysts

- Dentigerous cysts – very uncommon in cats

Oral cysts

- Dentigerous cysts (cont.)

  - Commonly found in Boxer dogs (PM1), Shih Tzus (I)
  - Border Collie, Labrador retriever
  - Potential for pathological fracture

Oral cysts

- Treatment dentigerous cysts
  - Surgical approach
  - Raise flap
  - Bone window
  - "Shell out" the complete structure
  - Debride cavity – canine, other teeth may be exposed
  - Remove tooth
  - Release flap – close without tension
  - Histopathology – rule out SCC

Oral cysts

- Salivary accumulation
- Treament
  - Marsupialization ??
  - Salivary gland resection

- Salivary gland tumours
- Necrotising sialadenitis

Oral cysts

- Intruded teeth may be associated with a cyst

  - Gingival inclusion cyst

Oral cysts

- Salivary *"cysts"* (accumulation)
  - Submandibular }   trauma
  - Cranial cervical }   collars, grooming, sialoliths
  - Sublingual   - sialoliths
    - Ranula
  - Pharyngeal   - may be life threatening

Oral tumours

- Account for about 6% of tumours in dogs

- ALL excisions must be submitted for histopathology!
- Divided into
  - Odontogenic
    - Tumours of the tooth producing tissues
  - Non-odontogenic

- Odontogenic
  - Benign
    - Acanthomatous ameloblastoma / epulis of dogs
    - Fibromatous epulis of PDL origin / Peripheral Odontogenic Fibroma (dd gingival overgrowth)
    - Ossifying fibroma (dd gingival overgrowth)

Oral tumours

- Account for about 3-12% of benign and malignant tumours in cats

- ALL excisions must be submitted for histopathology!
- Divided into
  - Odontogenic
    - Tumours of the tooth producing tissues
  - Non-odontogenic

- Odontogenic
  - Benign
    - Feline ameloblastoma
    - Ossifying fibroma (dd gingival overgrowth)
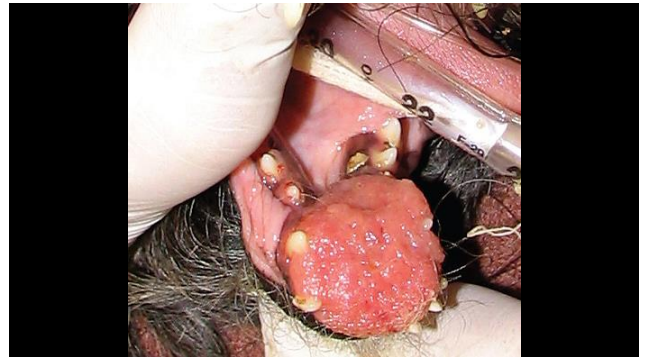
Feline Ameloblastoma

- In cats >6 years
- 2 variants: follicular pattern and keratinizing pattern
  - Does occur
  - Very rare
  - Excision with margins

Oral tumours

- Acanthomatous ameloblastoma (epulis of dogs)
  - Benign but locally invasive
  - Tooth displacement
  - Slow growing
  - About 5 years of age
  - (transformation following radiation therapy)
  - Treatment
    - Surgical excision with margins (5-10mm)

Oral tumours

- Peripheral Odontogenic Fibroma / Fibromatous epulis of periodontal ligament origin
  - Locally invasive
  - Rapid regrowth if incompletely excised

  - Treatment
    - Tooth extraction with complete PDL

Feline inductive odontogenic tumour

- Previously called Inductive Fibroameloblastoma

- Affects younger cats <3 years

- Excision with margins

Oral tumours

- Gingival overgrowth
  - Plaque associated
  - Excision
  - Cold blade / fluted or diamond bur
  - Gingivectomy and gingivoplasty
  - Haemostasis
  - Histopathology

Internet photo

DOI: https://doi.org/10.21873/invivo.13071

iv.iiarjournals.org
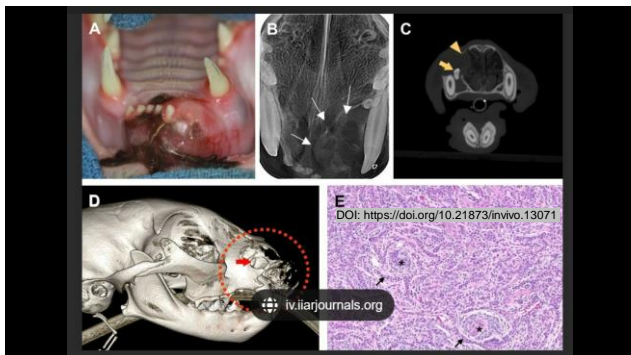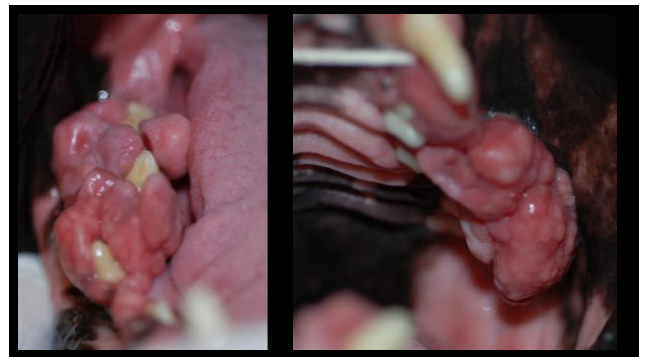
Oral tumours

Feline Juvenile gingivitis / periodontitis

Gingival overgrowth

Oral tumours

- Odontoma treatment

  - Marginal excision
  - Usually a large resultant defect
    - close without tension

Oral tumours

- Odontogenic (cont.)
  - Benign (cont.)
  - Hamartomas
  - Odontoma
    - Compound
      - Small teeth - Denticles
    - Complex
      - Tooth components - Enamel, dentine, cementum

Oral tumours

- Non-odontogenic

Differential diagnoses

- Malignant melanoma (melanotic / amelanotic)
- Squamous cell carcinoma
- Fibrosarcoma

- Osteosarcoma
- Osteoblastic chondrosarcoma
- Mastcell tumour
- Epitheliotropic T-cell lymphoma
- Lymphoma
- EGC

Oral tumours

- Malignant melanoma in cats

  - Rare
  - Usually Melanotic
  - Surgical excision
  - Staging NB
  - Palliative surgery??
  - Melanoma vaccine not effective

Oral tumours

- Malignant melanoma
  - Most common malignant oral tumour in dogs
    - About 40% of malignant oral tumours
  - Generally 6-9 months from diagnosis
  - Early metastasis
  - Very poor prognosis, one year 0%
  - (Increased risk in pigmented dogs)
  - Enter the Melanoma "vaccine"!

Oral tumours

- Squamous cell carcinoma
  - Papillary SCC – initially young dogs but has recently been described in older dogs too – excision curative

  - SCC more common in older animals (8-10 yrs)
  - Generally the more caudal the poorer the prognosis

Oral tumours

- Malignant melanoma (cont.)
  - Melanotic or amelanotic
  - Surgical excision
  - Staging NB
  - Palliative surgery
  - Melanoma vaccine (<Stage 2-3), budget
    - Possibly prolonged survival
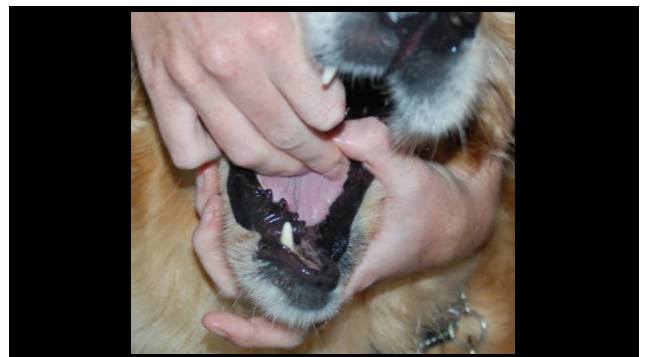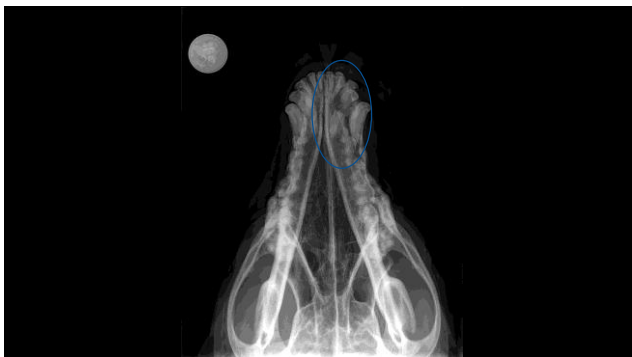
Oral tumours

- Squamous cell carcinoma
  - Tonsillar SCC
    - Poor prognosis
    - Enter accelerated radiation Rx protocols
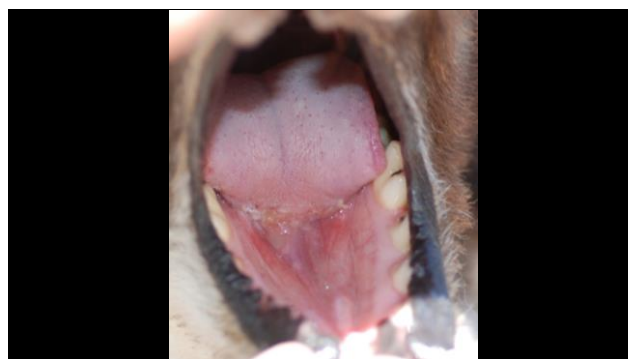
Oral tumours

- Squamous cell carcinoma

- Lingual SCC not uncommon
  - Differentiate lingual Mastcell tumour
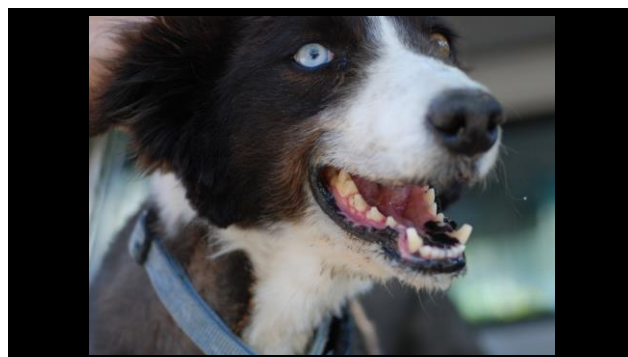
Oral tumours

- Squamous cell carcinoma

  - SCC more common in older animals (8-10 yrs)
  - Generally the more caudal the poorer the prognosis
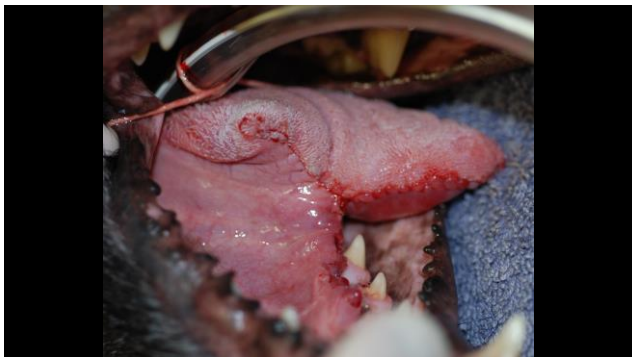
Oral SCC

Oral tumours

- Squamous cell carcinoma in cats

  - Accounts for majority (>75%) of oral tumours

  - Lingual SCC common
    - Differentiate lingual Mastcell tumour
    - Trauma
    - EGC
  - Often includes the jaws

FCGS
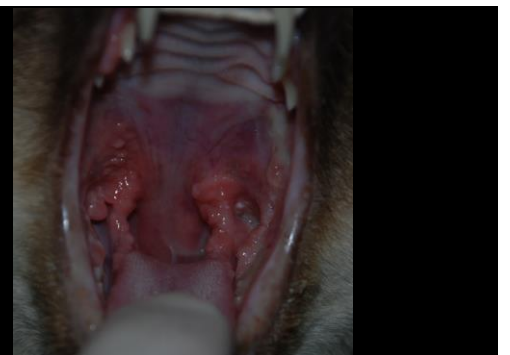
Sublingual lesions

Oral tumours

- Fibrosarcoma
  - Large breed dogs

  - Palate
  - Mandibles
  - Some metastasize, 57% recurrence rate, one year 50%
  - Histologically low grade, biologically high grade
    - Labrador retrievers
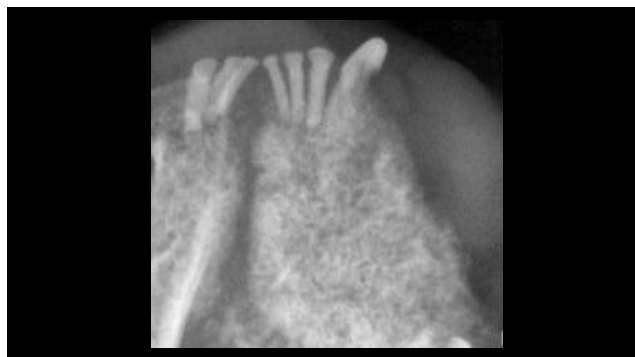
Oral tumours

- Middle aged dogs (7-9 yrs)
- Treatment
  - Depends on type
    - Schwannoma, leiomyosarcoma, rhabdomyosarcoma etc.
  - IHC staining required

  - 2cm margin required

  - Many with "clean margins" regrow
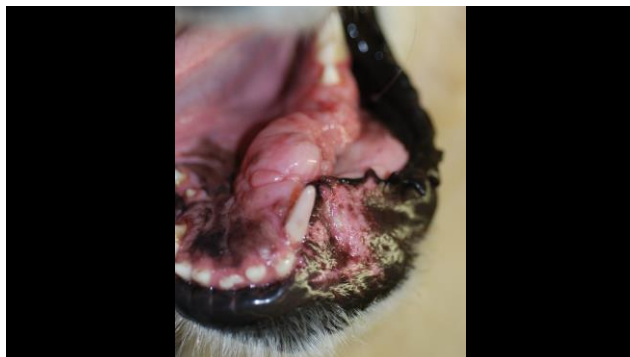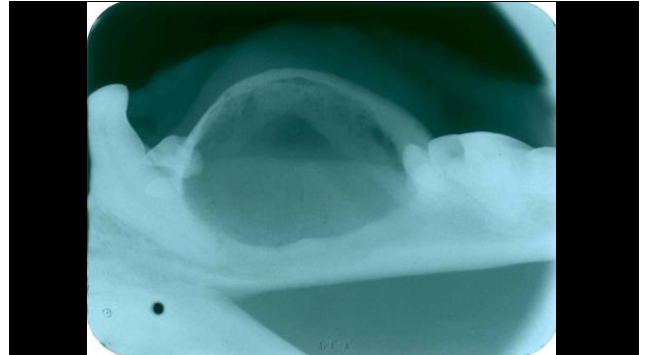
Oral tumours

- Fibrosarcoma in cats

  - Second most common oral tumour
  - Excision with margins

Oral tumours

- Osteosarcoma
  - Younger dogs
  - May be very aggressive lesions
  - May be "Multi-cystic"
  - Displaces teeth
  - Rule out dentigerous cyst

Oral tumours

- Less common

- Lymphosarcoma
  - Can destroy bone
  - Tooth displacement

  - Treatment
    - Wide excision
    - Chemotherapy
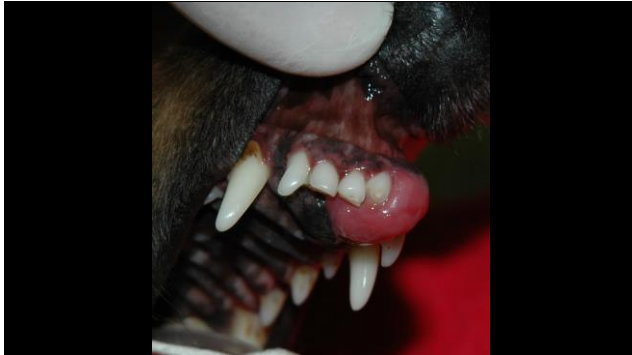
Oral tumours

- Osteoblastic chondrosarcoma
  - Moderate growth rate
  - Aggressive regrowth
  - Poor prognosis

Oral tumours

- Plasmacytoma
  - Rare
  - Locally invasive
  - Excision with narrow margins

Oral tumours

- Epitheliotropic T-cell lymphoma
  - Resembles very severe periodontitis clinically
  - Gingiva - bluish due to extravasation
  - Differential stains required (B vs T cell)
  - Prognosis very poor
  - May be confused with Erythema multiforme
  - Refractory to treatment
  - Lomustine may be beneficial

Oral tumours

- Mast cell tumour
  - Not uncommon
  - Differentiate for SCC
  - May occur on tongue margin
  - Gingiva
  - Lip
  - Palate

Oral tumour-like lesions

- Eosinophilic plaques
  - Soft palate lesions in Cocker Spaniels
  - Severe pain
  - Difficulty swallowing
  - Steroid responsive

Oral tumours

- Papillomas
  - Commonly immunocompromised young animals
  - Self-limiting
  - Control secondary infection
  - Excise if causing problems

Oral tumour-like lesions

- Eosinophilic granuloma complex in cats

  - Biopsy – require a diagnosis to institute treatment
  - Often associated with trauma - self
  - Does not appear to be painful although lesions are extensive
  - Steroid responsive

  - Remove inciting cause.

EGC

EGC

Other oral lesions
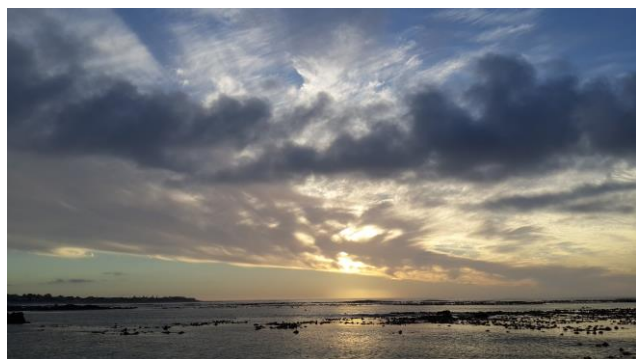
Other oral lesions

Other oral lesions

Other oral lesions

Other jaw lesions

- Craniomandibular osteopathy

  - Scottish Terriers
  - West Highland White Terriers
    - Heritable in this breed

    - May be self-limiting
    - May be progressive – poor prognosis

Other jaw lesions

- Alveolar bone response to resorptive lesions
  - Subgingival alveolar bone becomes thickened
  - Gingiva becomes pronounced
  - Radiographic diagnosis
  - May require extraction

- Buccal alveolar bone expansion

CMO

- Treatment
  - NSAIDS
  - Corticosteroids
  - Antibiotic therapy ??

  - Remove from breeding pool
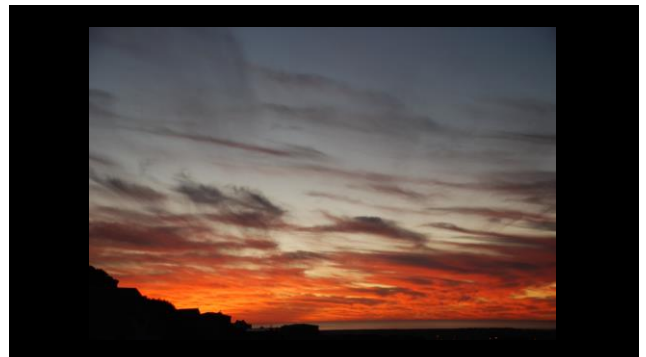
Renal Secondary hyperparathyroidism

- Rubber jaw
- Demineralisation of the jaws
  - Often with periodontally sound teeth

  - Can also be due to parathyroid tumour

African lioness

- > 200kg
- 8 men
- Table too short
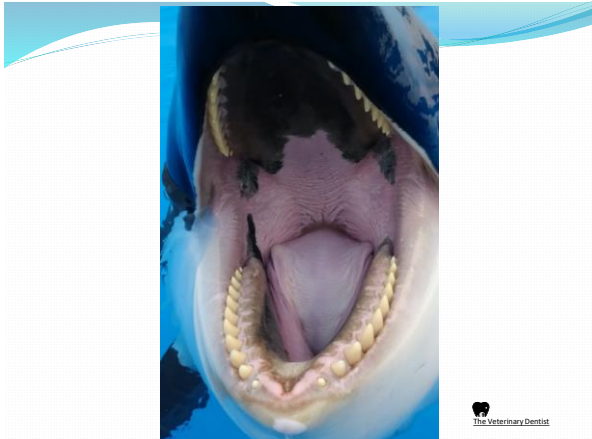
Large cats

- Sharda
  - Africa lioness
    - About 11 years old
    - Circus lion
    - Abandoned
    - Rescued
    - "Retired"

Sharda

- Fracture
  - Complicated
  - Sub-gingival
  - Malodour

- Radiography
  - "Immature" tooth
  - Thin dentinal walls
  - Transverse apex

Sharda

- Options
  - RCT – however an immature tooth so not indicated
  - Surgical extraction

- Surgical extraction
  - Luxated and elevated – delivered by forceps
  - Periosteal release - advancing flap
  - "Soft" food
  - Antibiotic Rx
  - Analgesics

The Veterinary Dentist
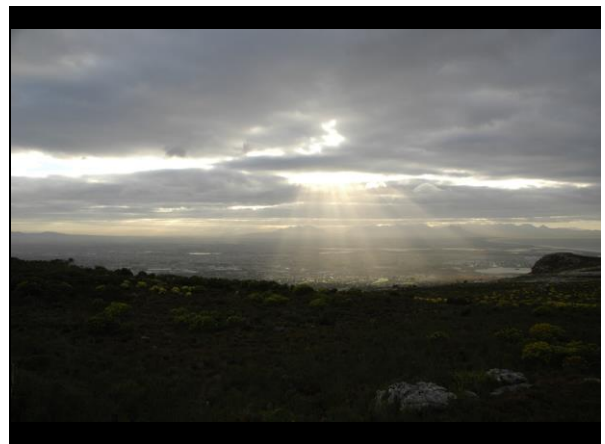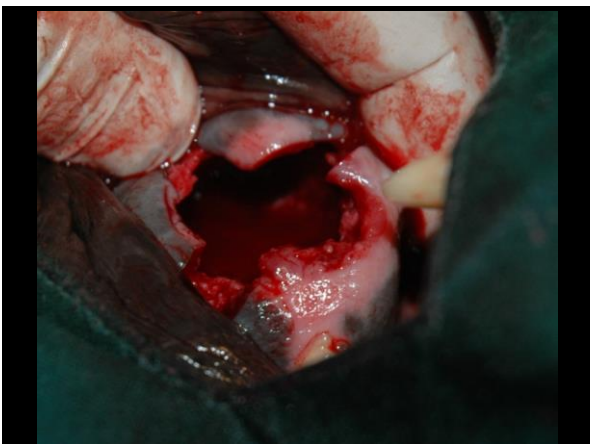
Tiger

- Spotted Bengal Tiger
- About 8 years old
- Circus tiger

- "Sold", rescued

Tiger

- Recurrent sinus tract/swelling left rostral mandible
- Swelling decreased on antibiotic therapy
- Recurred as soon as therapy interrupted

Tiger

- Crown 304 height approximated 404
- Tip missing – exposed pulp chamber
- Radiograph – wide apex apex
  - Apical bridge/opacity
  - Tooth 8.5 cm long

Tiger

- Options – RCT, extract

- Instrumented to 80mm – large bore
- Walls curettaged
- Required second access – lentulo short
- Necrotic content
- Flushed hypochlorite
- Rinsed polyionic fluid

Tiger

- Root canal and pulp chamber dried with "designer" paper points
- Obturated
- Restored access sites with GI and compomer
- Crown tip shaped to prevent tongue trauma
- Varnished with Optiguard

The Veterinary Dentist
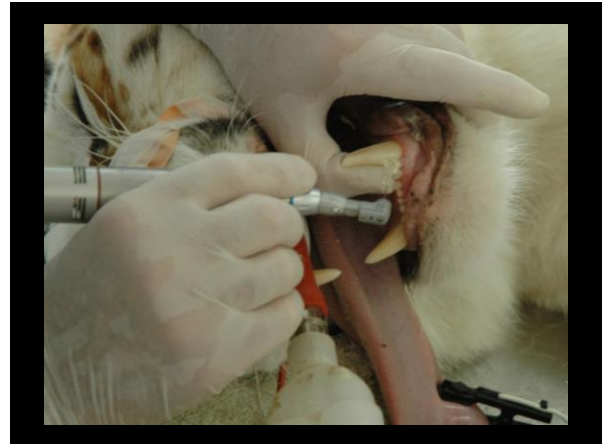
Tiger

- Complications
  - Radiography – processing chemicals soon exhausted due to temperature
  - Lentulo too short for canal length
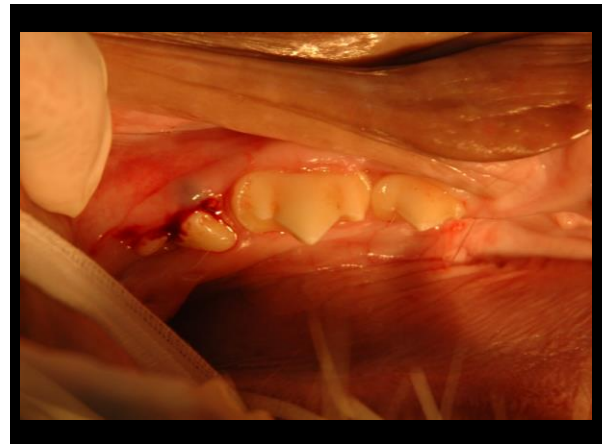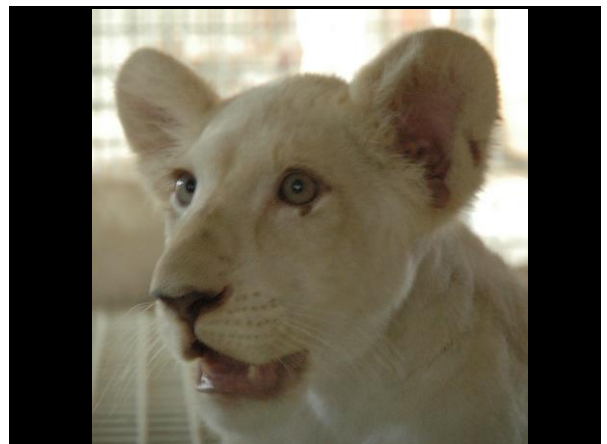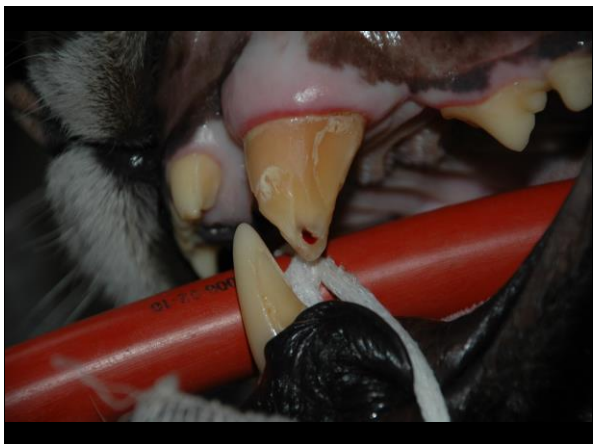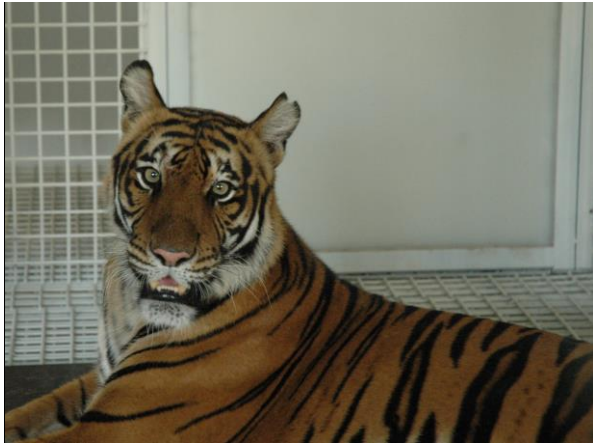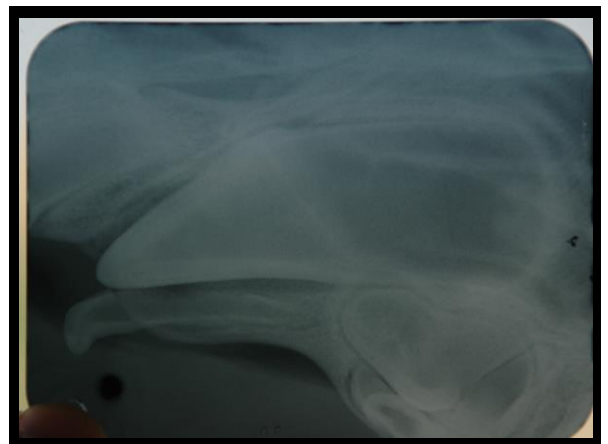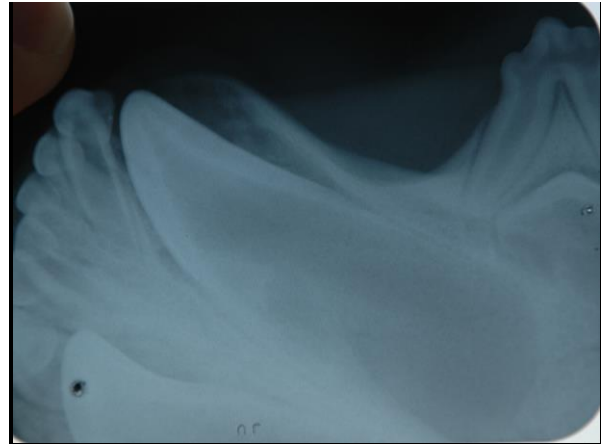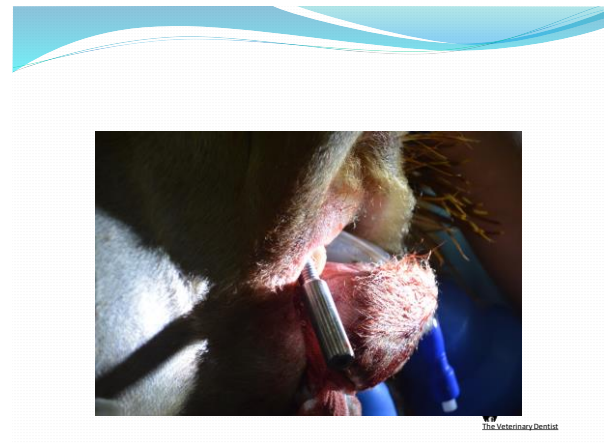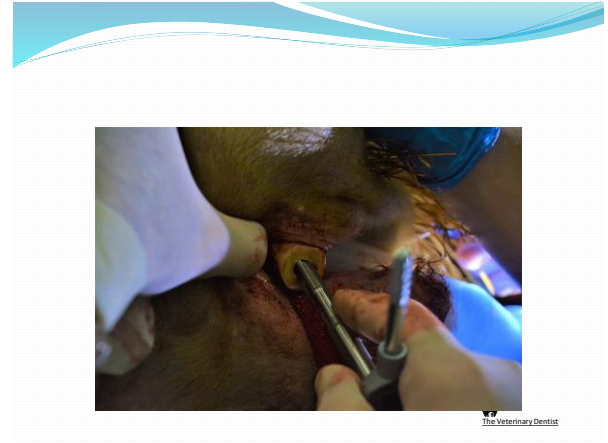
The Veterinary Dentist
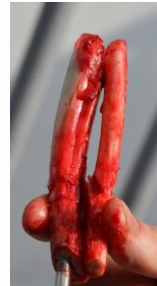
Local block
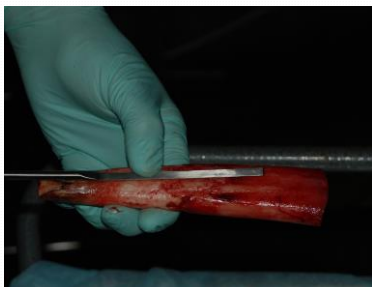
Prevost squirrel

Taking an impression of a tusk

Size does matter

Operator
Animal
Equipment

Orang Utan

Sea lion

Seal

Tiger

Bear

Jaguar

Bear

Dolphin endodontics

Elephant tusk extraction

Fossa – Madagascan arboreal predator

Prepare well

Hyena
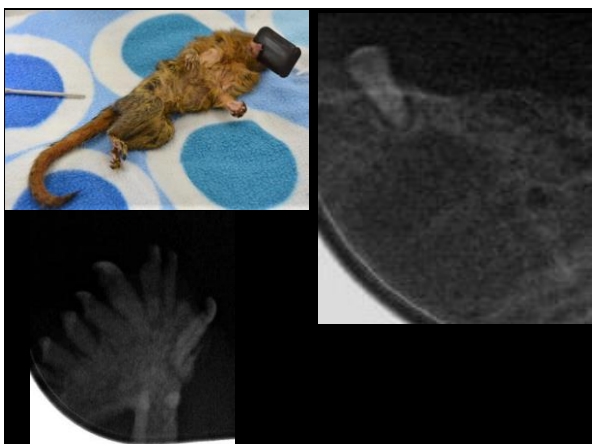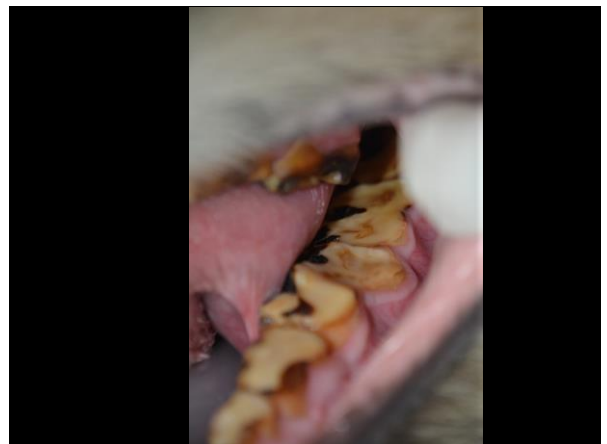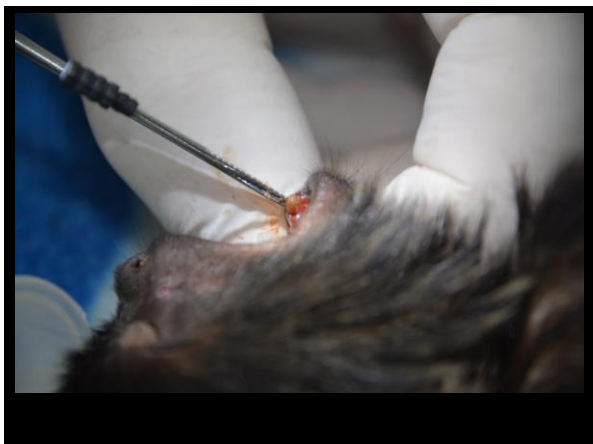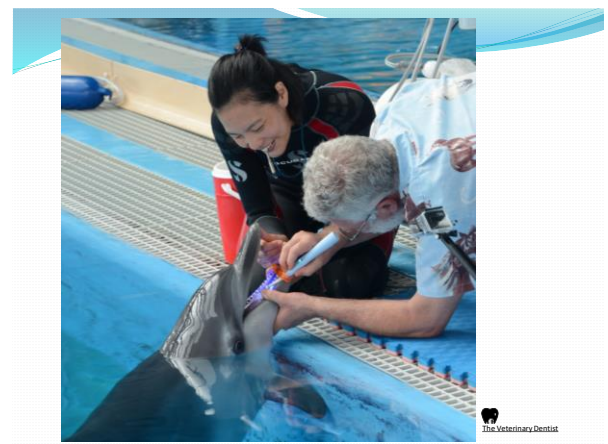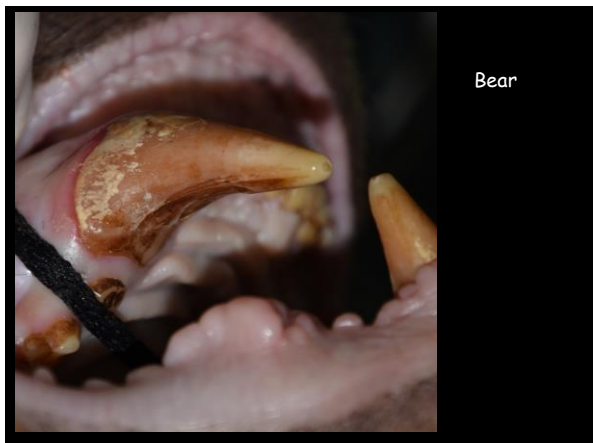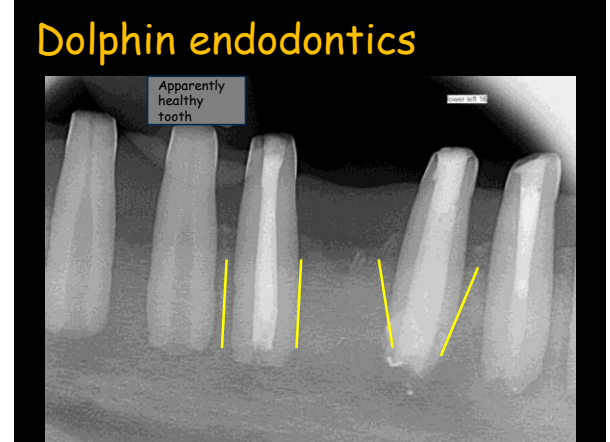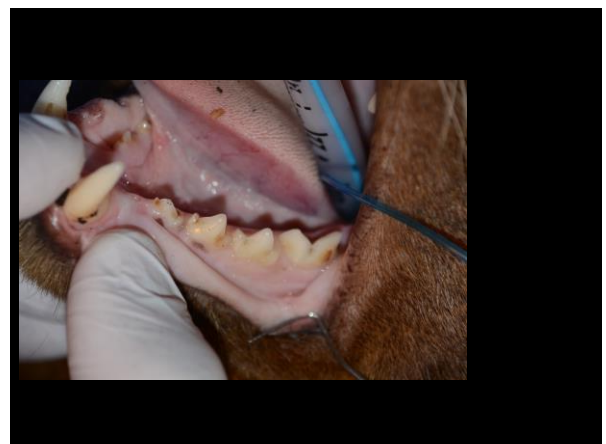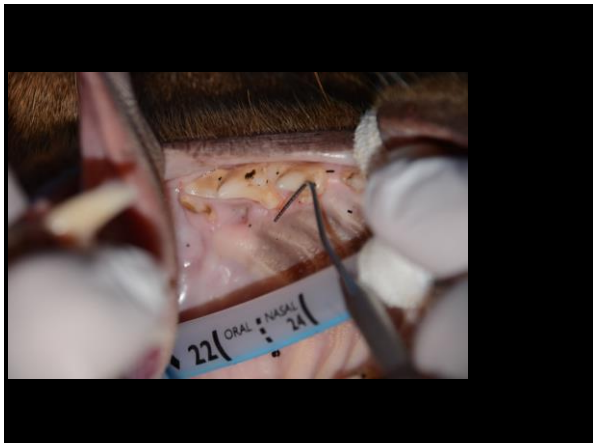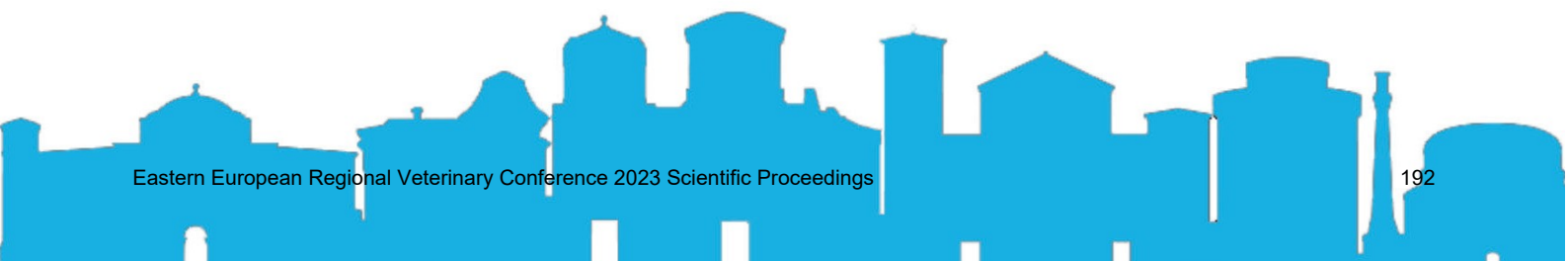
Dermatology

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(Dermatology)

DVM University of California, Davis, USA in 2001
Residency (2003-2004), then Partner (2004-2011): Animal Dermatology Clinic in San Diego, California, USA
Founded Tierdermatologie Dr. Wildermuth, a private veterinary dermatology practice in 2012 with my wife, who is also a veterinary dermatologist
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Member-at-Large, World Association for Veterinary Dermatology (WAVD) since 2015

CANINE PEMPHIGUS FOLIACEUS

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Pemphigus foliaceus (PF) is a pustular autoimmune skin disease characterized by acantholysis or loss of adhesion between keratinocytes. It is said to be the most common autoimmune skin disease of the dog and cat. Clinical lesions are due to autoantibodies primarily against desmocollin 1, the major autoantigen, which is part of the complex of molecules (desmosomes) holding the keratinocytes together.[1] This damage to the desmosomes leads to keratinocytes pulling apart before they can mature, forming acantholytic cells (Figure 1). At the clinical level these affected areas take the form of pustules that easily break open to form crusts. When the crusts break apart/age, underlying erosions, ulcerations, or epidermal collarettes are seen.

Chow chows and the Akita Inu breeds are predisposed to the disease, but it is seen in a large number of other breeds and mixed-breed dogs. It often idiopathic but can be drug-induced via systemic or topical medications.[2,3,4]

Pemphigus foliaceus can be classified into the classic facial form or trunk-dominant form.[5] The classic facial form has lesions typically on the periocular areas, the bridge of the nose (+/- the planum nasale) and pinnae (Figure 2). Often the trunk and the footpads are involved. In rare cases lesions may be limited to the footpads. The trunk-dominant phenotype group has lesions on the trunk with little to no facial involvement. The paw pads may be affected. The therapy and prognosis are the same for the two forms, but the truncal form can be mistaken for pyoderma. Both forms can have a secondary pyoderma component. When PF is generalized or severe, fever and lethargy are common and mild to moderate pruritus may be present.

The diagnosis of PF is made by a combination of the clinical appearance and aided by the presence of acantholytic cells upon cytology but the most definitive test is a skin biopsy. As dermatophytosis (*Trichophyton spp.*) can also cause acantholysis (loss of adhesion of keratinocytes) it is important to rule out this disease with a fungal culture or fungal PCR as part of the workup. Changes on a CBC and Chemistry panel may reflect inflammation, but are non-specific.

The prognosis for pemphigus foliaceus is variable and depends upon the extent and severity of the lesions, the response to and tolerance of therapy, cost of medications and monitoring, as well as the clinician's individual experience. Some suggest a very guarded prognosis in dogs and others more favorable. Most dogs need long-term treatment with one or more immunosuppressive drugs to remain in complete or partial remission, however the disease can occasionally be cured. The first drug of choice is prednisolone with a dose of 1mg/kg twice daily as it works most consistently and fast. As high-dose steroids have a long-list of short and long-term side-effects, the goal after several weeks, when the disease allows, is to slowly reduce the steroid with the goal of achieving an every other day dosing regimen. This is critical to avoid iatrogenic Cushings. Also due to the high-chance and severity of steroid-side effects, a second immunosuppressive medication is commonly needed and often started at the same time as glucocorticoids, with the idea that this second medication is "steroid-sparing". The most common treatment combination remains prednisolone and azathioprine. Ciclosporin or more newly, oclacitinib can be tried in combination with prednisolone as steroid-sparing medications, but do not generally work well as sole-therapy for canine PF. Neither work as well or with steroids as azathioprine in the author's experience. Additional treatment options for the dog include mycophenolate mofetil or chlorambucil.

Dogs with mild, focal disease or systemic disease with some lesions refractory to oral therapy, may be treated topically. Triamcinolone cream 0.1% or tacrolimus 0.1% ointment can be applied twice

daily to the affected areas. The owner should be advised to wear gloves and care must be taken that pets do not ingest the medication in large amounts.
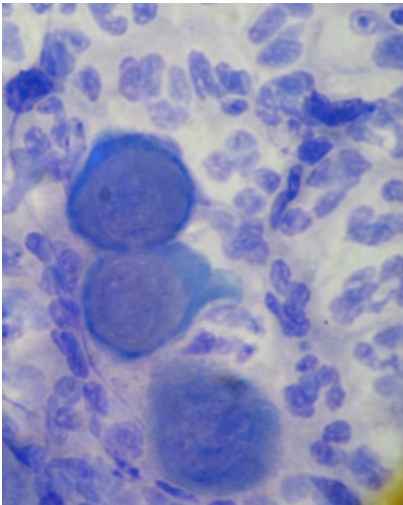
Figure 1: Acantholytic cells and neutrophils in PF

Figure 2: Classic facial Pemphigus foliaceus

References
1. Bizikova, P., et al., Cloning and establishment of canine desmocollin-1 as a major autoantigen in canine pemphigus foliaceus. Vet Immunol Immunopathol, 2012. 149(3-4): p. 197-207.
1. Oberkirchner, U., et al., Metaflumizone-amitraz (Promeris)-associated pustular acantholytic dermatitis in 22 dogs: evidence suggests contact drug-triggered pemphigus foliaceus. Vet Dermatol, 2011.
2. Bizikova P, Linder KE, Olivry T. Fipronil-amitraz-S-methoprene-triggered pemphigus foliaceus in 21 dogs: Clinical, histological and immunological characteristics. Vet Dermatol. 2014;25(103–11):e29–30.
3. Bizikova P, Moriello KA, Linder KE, Sauber L. Dinotefuran/ pyriproxyfen/permethrin pemphigus-like drug reaction in three dogs. Vet Dermatol. 2015;26:206–8. e45-6.
4. Bizikova P, Linder K, Mamo LB. Trunk-dominant and classic facial pemphigus foliaceus in dogs – comparison of anti- desmocollin-1 and anti-desmoglein-1 autoantibodies and clinical presentations. Vet Dermatol. 2022;33:414–25.

AUTOIMMUNE DERMATITIS IN PUPPIES

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Autoimmune dermatitis in puppies is rare, but does occur and presents slightly different challenges as compared to mature dogs. With respect to the diagnosis and determining if an immune-mediated disease is drug induced, this can be difficult as puppies receive a multitude of preventative therapies in a short time: multiple vaccinations, deworming, and flea/tick preventative. With respect to therapy, puppies are still developing and if they are very young, their liver may not be ready to metabolize medications as effectively as an adult dog. Polyuria and polydipsia from glucocorticoids can be even more of a problem for a dog who is not yet or just newly housebroken. With respect to co-morbidities, puppies' immune-systems are still developing and diseases such as juvenile demodicosis and papilloma virus can complicate therapy. Along these lines, puppies coming from shelters or breeding facilities where many animals are housed have an increased chance of having internal or external parasites or dermatophytosis, which could worsen under immunosuppressive therapy.

The most well-known autoimmune dermatitis in puppies is juvenile cellulitis. It is also known as puppy strangles but the best term for the disease is probably juvenile sterile granulomatous dermatitis and lymphadenitis. Microscopically, the disease is dominated by granulomatous to pyogranulomatous dermal inflammation, which clinically takes the form of a sudden onset of bilaterally symmetric edema around the lips, eyelids, pinnae and bridge of the nose.[1,2] These areas may be erythematous, moist, ulcerated or crusted.[1] A suppurative otitis and swelling of the submandibular lymph nodes is common, along with fever. Onset is typically between 3 weeks and 3 months of age. The diagnosis is based on signalment, history and clinical signs. Cultures can be helpful to rule out other diseases, and a biopsy is supportive of the diagnosis when culture and special stains are negative. Prognosis is good with dogs responding to prednisone or prednisolone at 1-2mg/kg twice daily for 1 week, then the dose is tapered over the following weeks and can be stopped.[1] Cyclosporine has been reported as an adjunctive therapy when needed.[3]

Other autoimmune diseases reported primarily in puppies include canine familial dermatomyositis (< 6 months of age) as well as juvenile-onset ischemic dermatopathy. Of the lupus dermatoses, exfoliative cutaneous lupus erythematosus (ECLE) of the German Shorthair Pointer, Hungarian Vizsla, and Hungarian Wirehaired Vizsla tends to occur in young adults but also before 1 year of age.[4] Epidermolysis Bullosa Aquisita and Acquired Junctional Epidermolysis Bullosa,[4] diseases resulting in separation of the epidermis from the dermis as well as Pemphigus foliaceus have been reported in puppies.[5]

References

1. Gauguere E, Prelaud P, Craig M. A Practical Guide to Canine Dermatology. Italy: Kalianxis. 2008; 104-105.
2. Gross TL, Ihrke PJ, Walder EJ et al. Skin Diseases of the Dog and Cat: Clinical and histopathologic diagnosis, 2nd edition. Oxford: Blackwell Publishing. 2005; 49–52.
3. Park C, Yoo J, Kim H, Kang B, and Park H. Combination of cyclosporin A and prednisolone for juvenile cellulitis concurrent with hindlimb paresis in 3 English cocker spaniel puppies. Can Vet J. 2010 Nov; 51(11): 1265–1268.
4. Halliwell R. Autoimmune and Immune-mediated Dermatoses. In: Miller B, Griffin C, Campbell. Muller & Kirk's Small Animal Dermatology 7th edition. St. Louis: Elsevier. 2013. 432-500. K.
5. Christa Horvath C, Neuber A, Litschauer B. Pemphigus foliaceus-like drug reaction in a 3-month-old crossbreed dog treated for juvenile cellulitis. Vet Dermatol. 2007 Oct;18(5):353-9.

APOQUEL FOR TREATING NON-ALLERGIC SKIN DISEASE

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Oclacitinib (Apoquel ®) is a selective Janus-kinase 1 inhibitor, approved in the EU in 2013 for the treatment of pruritus associated with allergic dermatitis and the clinical manifestations of atopic dermatitis in dogs.[1] Oclacitinib's main effect is a reduction of the itch molecule IL-31, but additional cytokines involved in allergic inflammation and the immune response are also inhibited to a certain degree: IL-2, IL-4, IL-6, and IL-13.[2] With respect to auto-immune diseases, oclacitinib can inhibit the activation of receptors of several cytokines: IL-2 as noted above, as well as IL-15, IFN-α and IFN-γ.[3] The recommended dose for pruritus is 0.4-0.6mg/kg twice daily for 2 weeks, and if therapy is to be continued, then this same dose is reduced to once daily. Long-term twice daily use is not approved, and studies at this dose are very limited.[4] Due to oclacitinib's good short and long-term tolerability, veterinary dermatologists have been slowly attempting to use oclacitinib as a sole-therapy or more commonly an adjunct-therapy for auto-immune dermatoses of the dog and sometimes the cat. Below is a table of non-allergic skin diseases that have been reported in the literature to have responded to therapy with oclacitinib.

Author	Disease	Number of Patients	Sole-therapy?
Aymeric et al 2017[5]	Presumed autoimmune subepidermal blistering dermatosis	1	Yes
Levy et al 2019[6]	Ischaemic dermatitis	4	Yes/No
High et al 2020[7]	Hyperkeratotic erythema multiforme	2	Yes/No
Colombo et al 2021[8]	Ear tip ulcerative dermatitis	22/25 improved	Yes
Aslan et al 2021[9]	Epitheliotrophic T-cell Lymphoma	1 (partial remission)	Yes
Harvey et al 2023[10]	Perianal fistula	2	Yes
Harvey et al 2023[3]	Cutaneous lupus erythematosus (DLE: 4, MCLE: 2, ECLE: 1)	7	Yes
Martinez et al 2022[11]	Pemphigus vulgaris	1	No
Carasco et al 2021[12]	Feline pemphigus foliaceus	1	Yes

References

1. https://www.ema.europa.eu/en/medicines/veterinary/EPAR/apoquel
2. Gonzales AJ et al. Oclacitinib (APOQUEL(®)) is a novel Janus kinase inhibitor with activity against cytokines involved in allergy. J Vet Pharmacol Ther. 2014 Aug;37(4): 317-24.
3. Harvey RG et al. Effective treatment of canine chronic cutaneous lupus erythematosus variants with oclacitinib: seven cases. Vet Dermatol. 2023;34: 53–8.
4. Denti D et al. Prolonged twice- daily administration of oclacitinib for the control of canine atopic dermatitis: a retrospective study of 53 client-owned atopic dogs. Vet Dermatol. 2022;33: 149-e42.
5. Aymeric E, Bensignor E. A case of presumed autoimmune subepidermal blistering dermatosis treated with oclacitinib. Vet Dermatol 2017; 28: 512–e123.
6. Levy BJ et al. The role of oclacitinib in the management of ischaemic dermatopathy in four dogs. Vet Dermatol 2019; 30: 201–e6.

7. High EJ et al. Rapid response of hyperkeratotic erythema multiforme to oclacitinib in two dogs. Vet Dermatol. 2020; 31: 330-e86.
8. Colombo, S et al. Ear tip ulcerative dermatitis treated with oclacitinib in 25 dogs: a retrospective case series. Vet Dermatol. 2021; 32: 363–e1009.
9. Aslan J et al. Treatment of canine cutaneous epitheliotropic T-cell lymphoma with oclacitinib: a case report. Vet Dermatol 2021; 32: 398–e113.
10. Harvey R, Horton H. Successful treatment of perianal fistulas in two dogs with oclacitinib. Vet Dermatol. 2023;00: 1–4.
11. Martinez N et al. A case report of the beneficial effect of oclacitinib in a dog with pemphigus vulgaris. Vet Dermatol. 2022;33:237-e65.
12. Carrasco I, et al. Beneficial effect of oclacitinib in a case of feline pemphigus foliaceus. Vet Dermatol 2021; 32: 299–301.

THE DERMATOLOGICAL EXAM - IS IT ALLERGY?

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There is no one specific test for the diagnosis of atopic Dermatitis (AD) in the dog. It is a clinical diagnosis which is based on having a combination of a compatible history, signalment, clinical examination and by ruling out other pruritic diseases. Often referred to as "allergy tests", a serum antibody (IgE) test or an intradermal test for environmental allergens cannot be used to rule AD in or out. Allergic dogs can have negative results, and non-allergic dogs positive results, which indicates sensitization but not clinical disease. It is recommended that these tests are used to select allergens for allergen-specific immunotherapy (desensitization) rather than to establish a diagnosis. Thus, the lack of a gold-standard test for AD makes the taking of a thorough history and completion of a thorough dermatological exam extremely important for a correct diagnosis.

The most recent criteria to aid in the diagnosis of allergy was published by Favrot in 2010 and includes information from the history and clinical examination:[1]

- Age of onset < 3 years
- Mostly Indoor
- Corticosteroid-responsive pruritus
- Chronic or recurrent yeast infections
- Affected front feet
- Affected ear pinnae
- Non-affected ear margins
- Non-affected dorsal lumbar area

When 5/8 of these criteria are met, the sensitivity for the diagnosis of AD is 85.4%, and the specificity 79.1%. They are not perfect, but these criterion are quite helpful. Pruritic dogs with ear margin disease are more likely to be infested with Sarcoptes than have AD. Pets with an affected dorsal lumbar area are more likely to have flea allergy dermatitis. Other top differential diagnoses for AD (food-induced or non-food induced), depending on the clinical presentation are other parasites that cause itch: *Sarcoptes scabiei*, *Cheyletiella* spp., *Trombicula autumnalis*, and lice.[2] Dermatophytosis or epitheliotrophic lymphoma may also to be considered. Demodicosis is not a top differential diagnosis for AD as it does not commonly cause pruritus.

The first stage of AD is normal appearing, but pruritic skin. Additional lesions that may be present depending on the stage of disease or individual animal are: alopecia (mainly via pruritus), scaling, erythema, papules, pustules (mainly from secondary bacterial overgrowth), excoriations (via scratching), and dark staining of the haircoat from licking. Seborrhea sicca (dry, scaly skin/haircoat) or seborrhea oleosa (greasy skin/haircoat) may be present. When lesions are chronic, the skin can become lichenified (thickened) or hyperpigmented. Secondary Otitis externa (bacteria or yeast) and secondary pyoderma or Malassezien dermatitis are also very common.

The most commonly affected sites for allergy are where topical allergens are more likely to encounter the skin directly. The largest study of 843 AD cases (both food and non-food induced AD) showed the most commonly affected sites were front paws (79%), rear paws (75%), abdomen/inguinal region (66%), pinna (58%), genitalia/ventral tail (43%), lips (42%), eyelids (32%), chest (32%) face other than lips & eyelids (31%) and both front and rear legs other than paws (31%).[1]

References

1. Favrot C, Steffan J, Seewald W, Picco F. A prospective study on the clinical features of chronic canine atopic dermatitis and its diagnosis. Vet Dermatol. 2010;21(1):23–31.
2. Hensel, P., Santoro, D., Favrot, C. et al. Canine atopic dermatitis: detailed guidelines for diagnosis and allergen identification. BMC Vet Res 11, 196 (2015).

WHAT'S NEW IN SERUM ALLERGY TESTING?

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Serum Allergen-specific IgE Testing has long been available to help guide the therapy of atopic dermatitis in veterinary medicine. An important fact that has not changed and that every practitioner needs to keep in mind, is that both normal dogs and cats, as well as those with clinical symptoms of environmental allergy, can have positive test results (IgE). Therefore, it is recommended that the test be used to help identify allergens for avoidance or for treatment with allergen-specific immunotherapy, and not to obtain a diagnosis. The diagnosis of environmental allergy is a clinical diagnosis, made by having a combination of a compatible history and clinical signs as well as by ruling out other common causes of itch (mainly parasites and food allergy). There have been a few relatively recent breakthroughs to help increase the accuracy with which serum allergy tests identify allergens as well as increase our knowledge about molecular allergology in veterinary medicine.

1) Cross-reactive carbohydrate determinants (CCDs) are carbohydrates found on the cell surface of plants and insects, against which serum IgE can be produced.[1] This type of IgE against CCDs is clinically irrelevant for the patient, but if not accounted for (removed) during a serum allergy test, it can lead to false positive results leading the clinician to select allergens for avoidance or desensitization that are irrelevant.[1,2,3] For the last couple of years, laboratories are using CCD-blockers to remove this anti-CCD IgE, which leads to a decrease increase in the amount of false positive results. Historically, in veterinary medicine, intradermal allergy test and serum allergy tests from the same patients do not match, but when CCD blockers are used, their correlation improves, but does not match completely.[4]

2) PAX® – Pet Allergy Xplorer serum test for the dog, horse and cat from Nextmune tests for the presence of IgE against allergen extracts, similar to traditional tests, but also tests for IgE against known molecular components.[5] For example a sample will be tested for the presence of IgE against *Dermatophagoides farinae* extract, but also for IgE against the molecular allergy components Der f 1, Der f 2 and others. Testing with purified or recombinant molecular allergens increases the reproducibility of the test, as compared to using crude extracts, which contain a variable rather than a standardized amount of the important allergen to be tested. The test cartridge allows for a large number of extracts and molecular components (> 200) to be tested with a small amount of serum. Molecular allergy testing should help maximize finding the most relevant allergens to include in an immunotherapy mixture, which should increase the chance for success. As more and more samples are tested, the test will help guide the identification of new molecular components causing allergy and the test subsequently updated.

References
1. Levy BJ, DeBoer DJ. A preliminary study of serum IgE against cross-reactive carbohydrate determinants (CCD) in client-owned atopic dogs. Vet Dermatol. 2018;29: 243-e90.
2. Piccione ML, DeBoer DJ. Serum IgE against cross-reactive carbohydrate determinants (CCD) in healthy and atopic dogs. Vet Dermatol. 2019;30:507-e153.
3. Lee KW, McKinney BH, Blankenship KD, Morris DO. Detection and Inhibition of IgE for cross-reactive carbohydrate determinants evident in an enzyme-linked immunosorbent assay for detection of allergen-specific IgE in the sera of dogs and cats. Vet Dermatol. 2020;31:439-e116.
4. Gedon NKY, Boehm TMSA, Klinger CJ, Udraite L, Mueller RS. Agreement of serum allergen test results with unblocked and blocked IgE against cross-reactive carbohydrate determinants (CCD) and intradermal test results in atopic dogs. Vet Dermatol. 2019;30:195-e61.
5. https://nextmune.com/product/pax-serum-test/

SELECTING ALLERGENS FOR IMMUNOTHERAPY

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What is immunotherapy? Also known as desensitization or allergen specific immunotherapy (ASIT), it is the administration of increasing quantities of allergen extracts, selected based on specific individual sensitivities, to an allergic subject to develop immune tolerance.[1] For pets with atopic dermatitis (AD) due to environmental allergies it is the only therapy that is aimed at redirecting the patient's immune response away from an allergic response, and it is the only therapy that can potentially cure an allergy, although cure is rare.

When is it time to do an allergy test? It is recommended to perform a serum or intradermal test for environmental allergens when a patient has a history & clinical signs suggestive of AD, parasitosis and food allergy have been ruled out, and the **main goal** is to identify allergens for either avoidance or to try ASIT to control the disease long-term. Both normal dogs and cats, as well as those with clinical symptoms of environmental allergy, can have positive or negative results on either test. Therefore the test does not confirm or rule out an allergy.

How do you interpret the allergy test results? Once an allergy test has been performed, the first rule of interpretation is to see if the positive allergens fit with the clinical symptoms of the pet with respect to the season. If the pet's symptoms are year round, then for the results to fit, giving the best chance for success with ASIT, the test should be positive for a year-round allergen such house dust mites. If the only positive allergen was grass pollen, which is present from spring through fall, then there would be no allergen to explain this pet's itch in winter time. If the test result does not fit, then a second allergy test can be performed (either an intradermal test or serum test, whichever had not yet been performed) to see if these results do match. Some pets with AD test negative on both tests (intrinsic atopy). Year round allergens include house dust mites, food mites (which are also/more present in the environment than food), epithelia (such as cat dander), the molds Aspergillus, Mucor & Penicillium and Malassezia yeast. Seasonal allergens include grasses (spring through fall), weeds (end of spring through fall), trees (mainly springtime) and the molds Alternaria & Cladosporium (spring through fall).

Which allergens to select first? The number of allergens that can be included in an ASIT solution is generally dictated by the company who prepares the bottle. The more allergens that are in the mix, the more diluted each allergen is, so there is a limit to how many allergens can and should be included. For an allergen to be important and cause clinical symptoms, it must be in the pet's environment. The allergens on a serum or intradermal test have been selected and modified over the years by each company to include the most relevant allergens. There is no standard protocol for allergen selection, as it is very individual, and greatly dependent on the pet's history and the test results. Generally I will start with adding 1-2 house dust or food/storage mites (for pets with year-round allergens) first as they are always present in the environment where a person lives & sleeps.

Next, I will include 1 (or more) grasses as grass pollen is present from spring to fall (long season) and dogs walk on grass nearly every time they go outside. Among the pollen, grasses cross-react with each other the most, meaning including one grass allergen in the solution will often be enough to cover for others even if the pet reacted to several different types of grass. With respect to the level of cross-reactivity the different pollen have with each other within a group, different types of grass have the most cross-reactivity, followed by weeds and then trees. After including a grass pollen, I will look and try to include a few tree & weed pollen, paying attention to cross-reactions (see below) to cover for as many allergens as possible. After this Malassezia and molds, will be my final selections. Epithelia are to be included if the pet will have close contact with the animal dander in question, for example cat or feathers.

Grass cross reactivity:[2]
- Pooideae family
    - Meadow fescue
    - Timothy
    - Orchard
    - Perennial rye
    - Kentucky bluegrass
    - Red top
- Chloridoideae family
    - Bermuda
- Panicoideae family
    - Johnson

Weed cross reactivity:[2]
- Chenopodiaceae
    - Scale
    - Lamb's quarter
    - Russian thistle
    - Kochia
- Amaranthaceae
    - Pigweed
    - Western water hemp

Tree cross-reactivity[2]
- Cupressaceae
    - Juniper
    - Cedar
    - Cypress
- Betulaceae
    - Birke
    - Alder
    - Hazel
- Fagaceae
    - Beech
    - Oak
- Oleaceae
    - Ash
    - Olive
    - Privet
- Salicaceae
    - Cottonwood
    - Poplars
    - Aspen
    - Willow

References:
1. Reedy LM, Miller WH, Willemse T. Allergic Skin Diseases of Dogs and Cats, 2nd Ed. London: Saunders; 1997.
2. Esch RE. Allergen immunotherapy: What can and cannot be mixed. J Allergy Clin Immunol 2008: 65-660.

FELINE PYODERMA

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Feline pyoderma is thought to be less common than canine pyoderma. This may be the case, but it is also very likely that feline pyoderma is underdiagnosed. Skin cytology seems to be performed less commonly in cats as compared to the dog. Another reason may be that feline pyoderma appears to respond better to therapy directed at the primary disease, without local or systemic antibiotic therapy as compared to the dog.

The diagnosis of feline pyoderma is made by performing cytology on a lesion: a papule, pustule, crust, plaque, erosion, or ulceration, for example, and finding bacteria in the presence of neutrophils. The more strict definition for diagnosis would require the observation of phagocytosis of bacteria by neutrophils. Allergic skin diseases, including flea allergic dermatitis, food allergy and feline atopic skin syndrome (FASS, the current term for feline atopic dermatitis) are common causes of pyoderma. Feline reaction patterns that have been reported to have a pyoderma component are miliary dermatitis, eosinophilic plaques, and lip ulcers.[1,2,3]

Since resistance to antibiotics in human and veterinary medicine is increasing we need to be selective about their use. Before a cat is treated systemically for pyoderma it is important to confirm the diagnosis with cytology and start a treatment directed at the primary disease: elimination diet, treating for parasites, or reducing pruritus with glucocorticoids, for example. If therapy against the primary disease is not successful or the pyoderma-component at the start is severe, than systemic therapy with amoxicillin clavulonic acid (15-25 mg/kg bid), cefalexin (20-25 mg/kg bid) or clindamycin (10 mg/kg once daily or 5mg/kg twice daily) can be recommended as first-line options. It is highly recommended that **fluoroquinolones and cefovecin, although they are more practical, as a once daily therapy and injection, respectively, be kept as reserve antibiotics** to minimize resistance in the veterinary population. Systemic antibiotics, in particular clindamycin in the cat can cause Antibiotic Associated Gastrointestinal Signs: AAGS which can be chronic.[4] Local antimicrobial therapy is an option (shampoos, creams and ointments), but is less practical as compared to the dog.

References
1. Wildermuth BE, Griffin CE, Rosenkrantz WS. Response of feline eosinophilic plaques and lip ulcers to amoxicillin trihydrate-clavulanate potassium therapy: a randomized, double-blind placebo-controlled prospective study. Vet Dermatol. 2012;23(2):110-8.
2. Wildermuth BE, Griffin CE, Rosenkrantz WS. Feline pyoderma therapy. Clin Tech Small Anim Pract. 2006;21(3):150-6.
3. Yu HW, Vogelnest LJ. Feline superficial pyoderma: a retrospective study of 52 cases (2001-2011). Vet Dermatol. 2012;23(5)448-e86.
4. Whittemore JC, Stokes JE, Laia NL, Price JM, Suchodolski JS. 2018. Short and long-term effects of a synbiotic on clinical signs, the fecal microbiome, and metabolomic profiles in healthy research cats receiving clindamycin: a randomized, controlled trial. PeerJ 6:e5130.

UNIQUE FELINE CASES

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Case 1: Chilli-Pepper-Jones

- Signalment: 4 year old MC DSH, brown tabby

- History:
  - Adopted about 3 months ago
  - Lives in Germany, 100% Indoors, no travel outside of Germany
  - 2 other cats in the house with no pruritus
  - Pruritus for years, non-seasonal, at least partially steroid responsive (owner wants to avoid steroids
  - Additional Previous Therapy: did not improve with Ivermectin trial two times
  - Novel ingredient diet trial Kangaroo for 3 months did not help
  - Stool is normal, no vomiting or diarrhea, appetite normal
  - PU/PD

- Clinical Examination:

- Differential Diagnosis?

- Chilli Day 1

  - Diagnostic Plan?
  - Therapy Plan?

- Final Diagnosis?

Case 2: Elli

- Signalment:
    - 4 year old FC Turkish Angora
    - Lives in Germany, 100% Indoors, No travel outside of Germany

- History:
    - Crusts with licking (only these spots) for 1.5 years
    - Left side, shoulder abdomen, same lesions for longtime
    - Lives in an Elizabethan collar
    - No reponse to antibotics, Elimination Diet

- Clinical Examination:

- Differential Diagnosis?

- Elli Day 1

    - Diagnostic Plan?
    - Therapy Plan?

- Final Diagnosis?

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Kerstin graduated from Swedish University of Agriculture (SLU). She is a specialist in dogs and cats dermatology, and a Diplomate of the European College of Veterinary Dermatology since 2004. She is working as a dermatologist in a private practice and she is also a professor at Swedish University of Agriculture where she teaches subjects related to small animal and equine dermatology in the veterinary program at SLU.

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Her current research is related to basic disease mechanisms, genetic background and improved diagnostics and treatment, with a focus on immune-mediated skin diseases such as allergies and autoimmune/immune-mediated diseases.

CANINE OTITIS EXTERNA – HOW DO I TREAT, AND WHY?

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Otitis externa is very commonly seen in canine patients in veterinary practice and up to 20% of the canine population is affected. Although often benign initially, recurrent otitis can become chronic and lead to the development of irreversible tissue changes and antimicrobial resistant infections and thus need to be handled with respect.

Factors that can lead to development of otitis externa and those that affect the prognosis need to be identified and addressed. Predisposing factors confer a risk, but don´t necessarily lead to disease. Among those are conformation of the ear canal, abundant hair growth, humidity, excessive cerumen production, polyps and excessive care inducing skin lesions. Primary factors do always lead to an inflammatory reaction. Presence of foreign body, otoparasitosis (*Otodected cynotis*, otodemodicosis), keratinization defects, skin diseases affecting the inner pinna or the skin in the ear canal and neoplasias are examples of primary causes. The most common is though allergic inflation. Failure to identify and correct the primary factor will lead to chronic or relapsing otitis externa with the development of perpetuating factors. If perpetuating factors are present, this will hinder the resolution of the otitis, for example secondary infections, pathologic tissue changes that over time might become irreversible and otitis media. To successfully manage otitis externa identification of any perpetuating factor is critically important.

All cases of otitis externa should be thoroughly examined with the aim to look for primary factors and cytology and otoscopy need to be performed. The result of the cytological examination, with eventual findings of *Malassezia* overgrowth, bacteria (cocci or rod shaped bacteria), presence of neutrophils and eventual biofilm production will guide the treatment protocol. The use of antibiotics is only recommended for bacterial infections that cannot be cured without antibiotics. In many cases the use of an ear cleanser and treatment with a topical corticosteroid to control the inflammation is effective. In case of presence of rod shaped bacteria a culture and sensitivity test is strongly recommended. Systemic antibiotic use is usually not helpful. If antibiotics are needed, a topical application will reach a much higher concentration at the site of the infection. If possible, ask for a antibiogram for antibiotics that are available for topical use. To be remembered is that presence of neutrophils hamper the in vivo activity of polymyxin B and gentamycin. If biofilm is present that can lead to a clinivally relevant increase in MIC values. The use of acetylcystein is effective o break biofilm.

In case the ear canal is stenotic, systemic corticosteroids, prednisolone 1mg/kg/day for 7-14d should be administered to evaluate if the stenosis is still reversible.

References:
1. Angus JC. Otic cytology in health and disease. Vet Clin North Am Small Anim Pract 2004; 34: 411–424
2. Eriksson C, Bergvall K. *Malassezia* otit hos hund. Examensarbete 2007:62 ISSN 1652-8697
3. Henneveld et al. Corynebacterium spp. in dogs and cats with otitis media: A retrospective study J Am Anim Hosp Assoc 2012;48: 320-326.
4. Hnilica KA. Otitis Externa Small Animal Dermatology: A Color Atlas and Therapeutic Guide. 3rd ed. St. Louis, Missouri: Elsevier Saunders; 2011.
5. Malayeri HZ, Jamshidi S, Salehi TZ. Identification and antimicrobial susceptibility patterns of bacteria causing otitis externa in dogs. Vet Res Commun. 2010;34:435–444.
6. Saridomichelakis MN, Farmaki R, Leontides LS, Koutinas AF. Aetiology of canine otitis externa: A retrospective study of 100 cases. Vet Dermatol. 2007;18:341–347.

CANINE OTITIS EXTERNA – HOW CAN WE PREVENT RELAPSES?

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Canine otitis externa can be a single episode event, if caused by for example *Otodectes cynotis* or a foreign body. It is though very common as a consequence of an underlying disease, which means that if this primary condition is not addressed, the patient will experience more or less frequent relapses leading to chronic inflammatory changes, tissue abnormalities and resistant infections.

The most common underlying disease is canine atopic dermatitis (CAD) and inflammation of the ear is included in the diagnostic criteria for CAD. One possible cause of allergic inflammation being responsible for otic inflammatory reactions is the distribution of mast cells in canine skin, with ear and paw skin having the highest mast cell counts per mm^2. As Staphylococcal adherence and *Malassezia* populations are higher on atopic vs healthy skin, secondary infections commonly develop in ears of allergic dogs. To prevent the progression of chronic lesions, which in atopic ears includes stenosis, calcification of the tissue, otitis media and antimicrobial resistant ifections a proactive treatment approach is crucial. Important factors in the development of *Pseudomonas* spp infection are dysbiosis and topical antimicrobials selecting for resistant strains of bacteria. Topical treatment with glucocorticoids, as a proactive treatment, is able to prevent development of flare in atopic dogs and frequently used in problem areas as for example paws, axilla and groin, but should also be used in the ears of atopic dogs. The use of topical corticosteroids as proactive treatment has been shown to be unlikely to increase the risk of secondary microbial overgrowth and prolong the time to otitis externa relapse.

References:
1. Auxilia ST, Hill PB. Mast cell distribution, epidermal thickness and hair follicle density in normal canine skin: possible explanations for the predilection sites of atopic dermatitis? Vet Dermatol, Volume: 11, Issue: 4, Pages: 247-254,
2. Barnard N, Foster A. Pseudomonas otitis in dogs: A GP's guide to treatment. In Pract 2017; 39: 386–398.
3. Bizikova P, Linder KE, Paps J, Olivry T. Effect of a novel topical diester glucocorticoid spray on immediate- and late-phase cutaneous allergic reactions in Maltese-beagle atopic dogs: a placebo-controlled study. Vet Dermatol. 2010 Feb;21(1):70-9.
4. Bond R, Collin NS, Lloyd DH. Use of contact plates for the quantitative culture of
5. Malassezia pachydermatis from canine skin.J Small Animal Practice 1994;35:68-72
6. Cole GW, Silverberg NL. The adherence of Staphylucoccus aureus to human corneocytes Archives of Dermatol 1986;122:166-169
7. Favrot C, Steffan J, Seewald W, Picco F. A prospective study on the clinical features of chronic canine atopic dermatitis and its diagnosis. Vet Dermatol. 2010 Feb;21(1):23-31.
8. Léonard C. Preventive use of a topical anti-inflammatory glucocorticoid in atopic dogs without clinical sign of otitis does not affect ear canal microbiota and mycobiota. Vet Dermatol 2021 Aug;32(4):355-e98.
9. Lourenço AM, Schmidt V, São Braz B et al. Efficacy of proactive long-term maintenance therapy of canine atopic dermatitis with 0.0584% hydrocortisone aceponate spray: a double-blind placebo controlled pilot study. Vet Dermatol 2016; 27: 88–92.e25
10. McEwan NA. Adherence by Staphylococcus intermedius to canine keratinocytes. Research in Veterinary Science 2000;68:279-283
11. Olivry T; New diagnostic criteria for canine atopic dermatitis. International Task Force of Canine Atopic Dermatitis. Vet Dermatol. 2010 Feb;21(1):123-6.
12. Paterson S. Discovering the causes of otitis externa. In Pract 2016; 38: 7–11.
13. Paterson S. A study to evaluate the primary causes associated with Pseudomonas otitis in 60 dogs. J Small Animal Pract 2018; 59, 238–242

14. Ring J, Alomar A, Bieber T et al. Guidelines for treatment of atopic eczema (atopic dermatitis) part I. J Eur Acad Dermatol Venereol 2012; 26: 1045–1060 & Part II. J Eur Acad Dermatol Venereol 2012; 26: 1176–1193

15. Santoro D, Marsella R, Pucheu-Haston CM et al. Allergic dermatitis cause 60% of otitis cases. Vet Dermatol 2015; 26: 84–e25.

16. White SD, Bourdeau P, Blumstein P et al. Comparison via cytology and culture of carriage of Malassezia pachydermatis in atopic and healthy dogs. Advances in Vet Dermatol Vol 3 1998:291-298

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INSULINOMA IN CANINE PATIENTS

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Glucose is a major homeostatic component and is involved in several physiological reactions, mostly the production of energy. Its regulation is complex and depends on several mechanisms. The main regulator of hyperglycaemia is the hormone insulin, produced by the beta-cells of the pancreas.

Neoplasia of the pancreas in dogs includes beta-cell neoplasia and is characterized by an autonomous abnormal hypersecretion of insulin, independent of the glycemia. The consequences are a continuous storing and use of glucose by the tissue, as well as a reduced production of glucose by the liver. This results in hypoglycaemia, which is more easily triggered by exercise than in a normal patient[1].

Insulinomas are usually solitary tumours within the pancreas but have a metastasis rate of 45 to 65%, most commonly in the lymph nodes and in the liver.

Older dogs are affected, with a median age of 9-years, and Golden Retrievers as well as Boxers are predisposed. Specific symptoms include weight gain and polyphagia due to the hyperinsulinaemia. The nervous system – due to its unique metabolism – is particularly sensitive to hypoglycaemia (neuroglycopenia). Therefore, during phases of hypoglycaemia, dogs can present the following unspecific neurological symptoms: weakness, ataxia, epileptic seizures, collapse or changes in behaviour. Duration of symptoms is described for a median of 1 to 2 months before presentation and are described as episodic[2]. Initially, compensatory mechanisms like increased secretion of glucagon or catecholamines can help to maintain normoglycemia to an extent.

Major differentials for hypoglycaemia in older dogs include paraneoplastic hypoglycaemia due to insulin-like secretions by some tumours, sepsis, liver failure or xylitol intoxication.

The cornerstone of diagnosis of an insulinoma is hypoglycaemia with concurrent normal or increased insulinaemia. In a healthy dog, hypoglycaemia should normally be accompanied by a low level of insulin. Therefore, even a normal insulin concentration in the presence of glucose value below 3.2 mmol/L (52 mg/dL) is considered highly suspicious for insulinoma. Diagnostic imaging is another important step in the diagnosis. While ultrasound is not very sensitive for the detection of smaller pancreatic masses, computed tomography (CT) of the abdomen has a sensitivity up to 95% to detect insulinomas[3]. Definitive diagnosis requires histological analysis of the pancreatic mass after surgical resection.

Emergency treatment of the hypoglycaemic episode aims at restoring normoglycemia while avoiding hyperglycaemia at all costs. Hyperglycaemia will indeed cause a disproportionate increase in insulin secretion and further exacerbate hypoglycaemia. Conservative glucose *boli* can be used, and if needed intravenous corticosteroids and medetomidine can improve the glycaemic control. Long-term conservative therapy is mostly based on a diet with complex sugars, lots of fibres and lots of proteins, to achieve a stable blood glucose concentration over the day. Small doses of glucocorticoids can also be added. If this is not enough to maintain euglycemia, the medication diazoxide can be used and has quite good results. However, it can have marked gastro-intestinal side effects and is rather expensive. Specific chemotherapy with steptozosin is not recommended due to severe side effects. Newly, toceranib (Palladia®) has been tried and was shown to improve the overall survival time compared to conservative treatment alone[4].
For many cases, surgery remains the treatment of choice, especially in the absence of distant metastasis. Local metastasis can be removed at the same time as the primary pancreatic tumour. Pancreatitis and development of a transient or permanent diabetes mellitus are the most frequent complications. Median survival time (MST) post-surgery is reported to be up to 350 to 500 days[5].

Outcome is better for non-metastatic disease. Negative prognostic factors include younger age and persistent hypoglycaemia after surgery[6].

References:

1.   Nelson RW. Chapter 9 - Beta-Cell Neoplasia: Insulinoma. In: Feldman EC, Nelson RW, Reusch CE, et al. (eds) *Canine and Feline Endocrinology (Fourth Edition)*. St. Louis: W.B. Saunders, 2015, pp.348-375.
2.   Ryan D, Pérez-Accino J, Gonçalves R, et al. Clinical findings, neurological manifestations and survival of dogs with insulinoma: 116 cases (2009-2020). *The Journal of small animal practice* 2021; 62: 531-539. 2021/03/17. DOI: 10.1111/jsap.13318.
3.   Robben JH, Pollak YW, Kirpensteijn J, et al. Comparison of ultrasonography, computed tomography, and single-photon emission computed tomography for the detection and localization of canine insulinoma. *Journal of veterinary internal medicine* 2005; 19: 15-22. 2005/02/18. DOI: 10.1892/0891-6640(2005)19<15:coucta>2.0.co;2.
4.   Alonso-Miguel D, García-San José P, González Sanz S, et al. Evaluation of palliative therapy, alone or in combination with toceranib phosphate, in dogs diagnosed with metastatic or recurrent beta-cell neoplasia. *N Z Vet J* 2021; 69: 234-239. 2021/05/05. DOI: 10.1080/00480169.2021.1905569.
5.   Cleland NT, Morton J and Delisser PJ. Outcome after surgical management of canine insulinoma in 49 cases. *Vet Comp Oncol* 2021; 19: 428-441. 2020/06/20. DOI: 10.1111/vco.12628.
6.   Del Busto I, German AJ, Treggiari E, et al. Incidence of postoperative complications and outcome of 48 dogs undergoing surgical management of insulinoma. *Journal of veterinary internal medicine* 2020; 34: 1135-1143. 2020/03/27. DOI: 10.1111/jvim.15751.

ADDISON DISEASE IN DOGS

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Hypoadrenocorticism (or Addison's disease) is a rare endocrine disease in dogs. The clinical signs can be vague and confusing, and it is therefore sometimes called "the great pretender".
Glucocorticoids (GC, mainly cortisol) and mineralocorticoids (MC, mainly aldosterone) are produced in the cortex of the adrenal glands. The principal stimulus for cortisol secretion is adrenocorticotropic hormone (ACTH) which is produced by the hypophysis. Glucocorticoids are important among others for the integrity and the health of the gastro-intestinal mucosa and for the maintenance of blood pressure and glycemia. For the MC, aldosterone is a key substance, and its production is controlled by the renin-aldosterone-angiotensin system (RAAS) and the serum potassium concentration. Decrease circulating blood volume is a major stimulator for renin production and therefore aldosterone release. Hyperkalaemia is a direct stimulus for aldosterone release. Aldosterone stimulates the reabsorption of sodium in the renal tubuli and therefore water, increasing the blood volume. as Aldosterone also directly stimulates potassium reabsorption in the tubuli[1].
Dogs with hypoadrenocorticism can present with the so-called "typical" version of the disease, where the adrenal glands do not produce neither GC nor MC. However, some dogs have an "atypical" hypoadrenocorticism where the adrenals do not produce GC but the secretion of MC is intact. Some of those dogs progress toward a typical form of the disease over time.
Dogs with hypoadrenocorticism are usually young to middle-aged and females are more frequently affected than males[2]. Predisposed breeds include Poodle, West Highland White Terrier, Portuguese Water Dog, Labrador Retriever and Bobtail. Symptoms are described as unspecific, "waxing and waning" and include apathy, dysorexia, weight loss, chronic diarrhoea and chronic vomiting. These can be exacerbated after a stressful event or an intense exercise. With MC deficiency, polyuria-polydipsia is present due to hyponatremia and medullary washout. During an Addisonian crisis, dogs present with the characteristic hypotensive shock accompanied with bradycardia due to severe hyperkalaemia.
Common haematological findings in dogs with hypoadrenocorticism include absence of a stress leukogram or eosinophilia[1]. In the biochemistry, in case of typical hypoadrenocorticism, there is a hyponatremia and/or a hyperkalemia[3]. A Na/K ratio below 25 is suspicious although not pathognomonic for hypoadrenocorticism. Pre-renal azotaemia with an urine specific gravity below 1.030 is also a typical finding[2]. Ultrasound of the abdomen usually does not reveal any anomaly, except for small adrenal glands, which are usually smaller than 3 mm in length.
Use of a single measurement of plasma cortisol is recommended to rule out hypoadrenocorticism. When the value is above 2 mcg/dL (55 nmol/L), hypoadrenocorticism is ruled out[4]. However, if the value is below 2 mcg/dL, it is NOT a confirmation of hypoadrenocorticism. Gold standard for the diagnosis of hypoadrenocorticism consist of the injection of ACTH to stimulate the production of cortisol by the adrenal gland (so-called ACTH stimulation test). In case of Addison's disease, there is no production of cortisol after the injection of ACTH.
Treatment of an Addisonian crisis should be focused on an aggressive fluid therapy and correction of electrolyte disorders. If hyperkalaemia does not resolve with fluid therapy alone, a protocol of insulin and glucose injections can be used. An ACTH stimulation test should be performed as soon as possible. Afterwards, substitution of corticoids should be initiated quickly. In case of emergency, a protocol with a continuous rate infusion of hydrocortisone has been described[5] and is very efficient and practical. As hydrocortisone has both an GC and MC effect, it is therefore suited for an emergency treatment. Alternatively, an injection of dexamethasone (equivalent of 0.5 to 1 mg/kg of prednisolone) can be used to substitute GC. MC can be replaced by administration of oral fludrocortisone or subcutaneous deoxycorticosterone pivalate (DOCP). Dogs usually improve quickly after a few days.
Long-term management is lifelong. It aims at substituting GC only in case of an atypical hypoadrenocorticism or both GC and MC in case of typical hypoadrenocorticism. GC can be replaced with oral prednisolone, usually at very low doses (0.1 to 0.2 mg/kg daily). MC can be

replaced with oral fludrocortisone (0.01 mg/kg twice daily) or with subcutaneous monthly DOCP injections[6]. In times of stress (anesthesia, surgery, visit to the veterinarian etc…) it is recommended do double the dosage of GC as the dog may need more cortisol as usual.

Monitoring dogs under treatment for hypoadrenocorticism consist of monitoring signs of under dosage of GC (chronic gastrointestinal signs, apathy, weight loss) or over dosage (polyuria-polydipsia, polyphagia, weight gain…). The MC dosage can be monitored with regular measurement of sodium and potassium plasma concentrations, with the goal of achieving a Na/K ratio between 29 and 32. As dogs with atypical Addison can still develop typical disease overtime, it is also recommended to monitor electrolytes concentrations in those patients.

The long-term prognosis is excellent.

References:

1.   Scott-Moncrieff JC. Chapter 12 - Hypoadrenocorticism. In: Feldman EC, Nelson RW, Reusch CE, et al. (eds) *Canine and Feline Endocrinology (Fourth Edition).* St. Louis: W.B. Saunders, 2015, pp.485-520.

2.   Peterson ME, Kintzer PP and Kass PH. Pretreatment clinical and laboratory findings in dogs with hypoadrenocorticism: 225 cases (1979-1993). *Journal of the American Veterinary Medical Association* 1996; 208: 85-91. 1996/01/01.

3.   Schofield I, Woolhead V, Johnson A, et al. Hypoadrenocorticism in dogs under UK primary veterinary care: frequency, clinical approaches and risk factors. *The Journal of small animal practice* 2021; 62: 343-350. 2021/02/09. DOI: 10.1111/jsap.13285.

4.   Lennon EM, Boyle TE, Hutchins RG, et al. Use of basal serum or plasma cortisol concentrations to rule out a diagnosis of hypoadrenocorticism in dogs: 123 cases (2000-2005). *Journal of the American Veterinary Medical Association* 2007; 231: 413-416. 2007/08/03. DOI: 10.2460/javma.231.3.413.

5.   Gunn E, Shiel RE and Mooney CT. Hydrocortisone in the management of acute hypoadrenocorticism in dogs: a retrospective series of 30 cases. *The Journal of small animal practice* 2016; 57: 227-233. 2016/04/22. DOI: 10.1111/jsap.12473.

6.   Sieber-Ruckstuhl NS, Reusch CE, Hofer-Inteeworn N, et al. Evaluation of a low-dose desoxycorticosterone pivalate treatment protocol for long-term management of dogs with primary hypoadrenocorticism. *Journal of veterinary internal medicine* 2019; 33: 1266-1271. 2019/03/14. DOI: 10.1111/jvim.15475.

PULMONARY HYPERTENSION IN SMALL ANIMALS

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Pulmonary hypertension (PHT) is an under-recognized syndrome in small animals that can have a wide variety of aetiologies. It is not a single disease but rather an abnormal haemodynamic state and its work-up necessities a multi-disciplinary approach.

Pulmonary hypertension is defined as an abnormal increase in pressure within the pulmonary vasculature. This increase in pressure can be due to several mechanisms[1]:

- Increase in pulmonary blood flow – in case of increased right cardiac output
- Increase in pulmonary vascular resistance – in case of vascular wall changes or abnormal blood composition
- Increase in pulmonary blood pressure – usually in case of increase left heart venous return

Dogs with pulmonary hypertension are usually small breed, middle-aged to older dogs but the signalment reflects the underlying disease they are having. Exercise intolerance, cough, cyanosis, and crackles at auscultation are common findings. A split of the second heartbeat during auscultation should raise suspicion of pulmonary hypertension.

For further work up: echocardiography alone is not diagnostic for PHT but is rather a tool that one can use to evaluate the probability that a patient has PHT, in the light of the clinical signs as well as the other diagnostic findings. The goals of echocardiography are to 1. estimate the pulmonary arterial pressure through measurement of the tricuspid regurgitation 2. search for cardiac changes that are secondary to PHT. Those cardiac changes are at three anatomical localisations: right ventricle and interventricular septum, pulmonary artery, right atrium with the *vena cava caudalis*. The probability of the presence of PHT will then be determined depending on the number of anatomical localisations that present changes suggestive of PHT and the peak velocity of the tricuspid regurgitation[1]. The severity of the PHT is described depending on the severity of the clinical signs, and no longer on the severity of the regurgitation.

PHT in small animals is newly classified in six different groups[1]:

- Group 1: "primary" pulmonary hypertension, that in small animals mostly involves PHT due to cardiac shunts, like *patent ductus arteriosus* or intracardiac shunts.
- Group 2: PHT secondary to left heart disease, which is the most frequent cause of PHT in dogs.
- Group 3: PHT secondary to respiratory disease and/or hypoxemia. Diseases in this group includes brachycephalic obstructive airway syndrome (BOAS), chronic bronchitis, bronchial collapse, pulmonary fibrosis or other lower respiratory diseases.[2]
- Group 4: PHT secondary to pulmonary thromboembolism (PTE).
- Group 5: PHT secondary to parasitic disease, namely heartworms (*Dirofilaria immitis*) or lungworms (*Angiostrongylus vasorum*[3]).
- Group 6 regroups unclear or multifactorial aetiologies for PHT.

Echocardiography should be performed in dogs that have clinical signs suspicious for pulmonary hypertension and radiographic changes that are suggestive (tortuous pulmonary vessels, dilated pulmonary trunk and right-sided cardiac enlargement are the most commonly seen changes). It should also be performed in dogs that have disease that can cause PHT and in which classical treatment fails to cure respiratory signs. Other diagnostic work-ups are indicated depending on the underlying aetiology for the PHT.

Treatment of pulmonary hypertension has three goals[1]:

1. Decrease progression or complications
2. Treat - when possible - the underlying aetiology

3. PHT-specific treatment

The first aim of the therapy can be achieved by moderating exercise, by avoiding non-necessary anaesthetic procedures and by avoiding respiratory infections.

The second aim of the therapy includes all treatment for the underlying aetiologies, for instance deworming in case of parasitic disease or surgery in case of BOAS. Unfortunately, some causes are not curable or progressive despite treatment, and more difficult control of PHT is to be expected.

Specific treatment for PHT consist of the administration of a phosphodiesterase 5 inhibitor, mainly the molecule sildenafil. In dogs with diverse causes of PHT, sildenafil successfully decreased the intensity of the clinical signs and improved the quality of life[4], as well as improving the radiographic changes[5]. It is thus recommended in dogs with Group 3 PHT and to be considered in dogs with parasitic disease and PTE. In dogs from Group 1, if there is no specific treatment, sildenafil may also be considered. In dogs with left-sided heart disease, sildenafil may be considered in dogs free of left-sided heart failure and with symptoms that fail to respond to specific treatment.

Monitoring of dogs with PHT is mainly based on clinical signs. Indeed, repeated echocardiography may not be useful, as measurements may not improve (particularly the tricuspid regurgitation) even if the clinical symptoms improve[4].

References:

1. Reinero C, Visser LC, Kellihan HB, et al. ACVIM consensus statement guidelines for the diagnosis, classification, treatment, and monitoring of pulmonary hypertension in dogs. *Journal of veterinary internal medicine* 2020; 34: 549-573. 2020/02/18. DOI: 10.1111/jvim.15725.

2. Jaffey JA, Wiggen K, Leach SB, et al. Pulmonary hypertension secondary to respiratory disease and/or hypoxia in dogs: Clinical features, diagnostic testing and survival. *The Veterinary Journal* 2019; 251: 105347. DOI: https://doi.org/10.1016/j.tvjl.2019.105347.

3. Borgeat K, Sudunagunta S, Kaye B, et al. Retrospective evaluation of moderate-to-severe pulmonary hypertension in dogs naturally infected with Angiostrongylus vasorum. *The Journal of small animal practice* 2015; 56: 196-202. 2014/12/09. DOI: 10.1111/jsap.12309.

4. Johnson LR and Stern JA. Clinical features and outcome in 25 dogs with respiratory-associated pulmonary hypertension treated with sildenafil. *Journal of veterinary internal medicine* 2020; 34: 65-73. 2019/12/10. DOI: 10.1111/jvim.15679.

5. Kellihan HB, Waller KR, Pinkos A, et al. Acute resolution of pulmonary alveolar infiltrates in 10 dogs with pulmonary hypertension treated with sildenafil citrate: 2005-2014. *J Vet Cardiol* 2015; 17: 182-191. 2015/08/22. DOI: 10.1016/j.jvc.2015.04.002.

PLATELET DISORDERS IN SMALL ANIMALS

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Platelets are very important cells for primary haemostasis. Platelet disorders are frequent in small animals, with thrombocytopenia being the most frequent one.

After endothelial injury, unmasked von Willebrand factor (VWF) binds to platelets and collagen, which initiates platelet activation. Platelet activation leads to an increase surface of aggregation, recruitment of further platelets and initiation of fibrin synthesis, by the activation of some coagulation factors. Therefore, a decrease in platelet number (thrombocytopenia) or function (thrombopathia) can lead to coagulation disorders, mainly hypocoagulability.

Thrombocytopenia is the most frequent platelet disorders in dogs, but also in cats, although there are much less frequent in the latter species. Thrombocytopenia is manifested by surface bleedings, with petechiae, ecchymoses and hematomas. Sometimes these can be the only clinical sign that the animal is presenting. Patients can also manifest abnormally prolonged bleeding after an injury or bleeding from other surfaces (melena, haematochezia, epistaxis, haemoptysis…). Severe bleeding can lead to clinical anaemia.

A manual thrombocyte count on a blood smear is necessary to confirm the thrombocytopenia because automatic counts can be unreliable.

Differential diagnoses for thrombocytopenia in small animals include:

- immune-mediated destruction
  - primary when no other causes are found.
  - secondary to a tumour, infection, mediation etc
- major utilisation of thrombocytes
  - disseminated intra-vascular coagulation.
  - major thrombosis
- bone-marrow suppression of thrombocyte production (multiple possible bone marrow diseases).

Diagnostic work-up of thrombocytopenia in dogs must include: assessment for other cytopenia, assessment for coagulation disorders or severe bleeding, assessment of possible drug intake or infectious disease, as well as exploration of a possible paraneoplastic cause. If every other cause of thrombocytopenia is excluded or unlikely, a diagnosis of primary immune-mediated thrombocytopenia (IMT) can be made.

Treatment of IMT consist of immunosuppression, classically achieved with high doses of corticosteroids. Most dogs respond well to this treatment alone. However, in refractory cases, it is possible to add a second immunosuppressive. Cyclosporine and mycophenolate mofetil (MMF) have the same success rate but MMF tend to have less side effects than cyclosporine[1]. One injection of intra-veinous vincristine on top of the glucocorticoid treatment can also improve the efficiency for platelet normalization as well as reduce the hospitalisation time[2]. Regular monitoring – whith a manual thrombocyte count – should be performed after normalization of the platelet count on a 3-week schedule and treatment should be deescalated on -25% reduction steps. The short-term prognosis of primary IMT in dogs is good with a 80-90% survival at discharge[3] and the long-term prognosis is also good with a 85% survival in one long-term study[4] over at least one year.

Thrombocytosis is less frequent in small animals (incidence less than 5%[5]) but nevertheless its finding remains clinically important. It is mostly associated with neoplasia and inflammation/infections[5-7]. More severe thrombocytosis commonly associated with neoplastic disease[7].

Von Willebrand disease is the most frequent inherited bleeding disorder in dogs. Depending on the vWF plasma concentrations and the array of multimers present, there are 3 types of Von Willebrand disease, with different severities of bleeding tendencies. Clinical signs include bleeding tendencies after surgery or trauma and surface mucosal bleedings. Von Willebrand disease can be suspected in a dog with clinical bleeding but normal thrombocyte count and coagulation times (PT and PTT). Buccal mucosal bleeding time is prolonged (more than 4 minutes). Diagnosis can be confirmed by

measurement of VWF antigen plasma concentration. Prevention or control of bleeding can be achieved by administration of desmopressin subcutaneously or by administration of blood products that contain good amounts of VWF (fresh whole blood, fresh frozen plasma, cryoprecipitate).

References:

1.   Cummings FO and Rizzo SA. Treatment of presumptive primary immune-mediated thrombocytopenia with mycophenolate mofetil versus cyclosporine in dogs. *The Journal of small animal practice* 2017; 58: 96-102. 2017/02/06. DOI: 10.1111/jsap.12621.
2.   Rozanski EA, Callan MB, Hughes D, et al. Comparison of platelet count recovery with use of vincristine and prednisone or prednisone alone for treatment for severe immune-mediated thrombocytopenia in dogs. *Journal of the American Veterinary Medical Association* 2002; 220: 477-481. 2002/02/28. DOI: 10.2460/javma.2002.220.477.
3.   O'Marra SK, Delaforcade AM and Shaw SP. Treatment and predictors of outcome in dogs with immune-mediated thrombocytopenia. *Journal of the American Veterinary Medical Association* 2011; 238: 346-352. 2011/02/02. DOI: 10.2460/javma.238.3.346.
4.   Simpson K, Chapman P and Klag A. Long-term outcome of primary immune-mediated thrombocytopenia in dogs. *The Journal of small animal practice* 2018; 59: 674-680. 2018/08/14. DOI: 10.1111/jsap.12912.
5.   Neel JA, Snyder L and Grindem CB. Thrombocytosis: a retrospective study of 165 dogs. *Vet Clin Pathol* 2012; 41: 216-222. 2012/03/07. DOI: 10.1111/j.1939-165X.2012.00416.x.
6.   Woolcock AD, Keenan A, Cheung C, et al. Thrombocytosis in 715 Dogs (2011-2015). *Journal of veterinary internal medicine* 2017; 31: 1691-1699. 2017/09/13. DOI: 10.1111/jvim.14831.
7.   Athanasiou LV, Polizopoulou ZS, Papavasileiou EG, et al. Magnitude of reactive thrombocytosis and associated clinical conditions in dogs. *The Veterinary record* 2017; 181: 267. 2017/08/07. DOI: 10.1136/vr.104042.

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CUSHING'S SYNDROME IN DOGS

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Introduction:
Cushing's syndrome (CS) is a frequent endocrine disorder of middle-aged and older dogs and is characterized by the presence of excessive concentration of glucocorticoids in circulation.[1] Hypercortisolemia may be caused by excessive secretion of adrenocorticotropic hormone (ACTH-dependent hyperadrenocorticism), by excessive secretion of cortisol due to a tumor in the adrenal gland (ACTH-independent hyperadrenocorticism), or also by iatrogenic chronic administration of glucocorticoids.[2] Majority of dogs (>89%) with CS have pituitary-depended hyperadrenocorticism (PDH), whilst some with CS have hyperadrenocorticism due to adrenal tumor (AT).[3] Most common clinical signs are polydipsia/polyuria (90%), polyphagia (70%), abdominal enlargement and excessive panting (60%) and systemic hypertension. Less common clinical signs in 20-50% cases are alopecia, lethargy, muscle weakness, hyperpigmentation and muscle atrophy. Clinical presentation in <20% are thromboembolism, recurrent UTI, calcinosis cutis and facial nerve paralysis.[4-6] Most common laboratory abnormalities in CBC in dogs with CS are stress leukogram, thrombocytosis and mild erythrocytosis. Biochemistry will usually show increased alkaline phosphatase, alanine aminotransferase and hypercholesterolemia. Specific gravity of urine is usually hypo- or isosthenuric and proteinuria is common.[4-7]

Screening tests:
ACVIM Consensus Panel recommends performing diagnostic tests for CS in case of[8]:
1. Compatible history and physical examination findings. The greater the number, the stronger the suspicion. Laboratory changes alone are not indication for test.
2. Pituitary macrotumor.
3. Diabetic dog with persistent poor response to high dosage of insulin not attributed to another causes, including owner issues.
4. Adrenal mass.
5. Persistent hypertension (the Panel did not reach consensus on this indication).

No test has 100% diagnostic accuracy.[8] Low-dose dexamethasone suppression test (LDDST) is a test of choice for naturally-occurring CS in Cosensus panel ACVIM 2012.[8] In veterinary medicine, reported sensitivity and specificity of the LDDST range from 85 to 100% and from 44 to 73%, respectively.[6,9,10] Diagnosis of CS is supported by 8-hour post dexamethasone plasma concentration above laboratory cutoff.[11] Lack of suppression confirms the diagnosis of CS and has a highest positive predictive value. Results of LDDST can be affected by concurrent non adrenal disease. The ACTH stimulation test assesses adrenocortical reserve and dogs with CS have increased reserve, so post-ACTH cortisol concentration is greater than the reference range. Because of its low sensitivity, its diagnostic usefulness as a screening test for spontaneous CS is inferior to the LDDST.[8] However ACTH stimulation test is less affected by nonadrenal illness. Urine cortisol-to-creatinine ration (UCCR) can be used to rule out (due to high sensitivity of almost 100%), but not to rule in the disease.[11] Any dog with high UCCR should be further tested with ACTH stimulation test or LDDST. After confirming CS in a dog, differentiating between PDH and AT should be performed in order to provide adequate treatment modality. Laboratory tests (endogenous ACTH, LDDST, HDDST) or imaging (CT, MRI, ultrasound abdomen) could be used to differentiate PDH and AT.

Treatment:

Adrenalectomy is a treatment of choice for an AT. It is technically difficult, serious intra and postoperative complications are common and mortality can exceed 25%.[11] Hypophysectomy (transsphenoidal) could be a choice of treatment for PDH. Advantage of this treatment is that it is effective long-term treatment for dogs with CS since the tumor is completely removed. However, this procedure requires special facilities and most common complications are central diabetes insipidus, hypernatremia, keratoconjunctivitis sicca and secondary hypothyroidism.[13] Radiation therapy can reduce tumor size and improve neurologic signs. This treatment is effective only for PDH macrotumors.[11] Today medical choice of treatment is trilostane - an inhibitor of steroid synthesis. Trilostane is well tolerated and has a low prevalence of side effect comparing to previous used mitotane. Trilostane is effective resolving signs of CS in about 75-85% of cases. Starting dose is 0.5-1mg/kg PO q12 (preferred over 2mg/kg q24h). Dogs whose trilostane dose is actively managed tend to live longer.[12]

Monitoring:

After starting trilostane dogs should be re-examined at 7-14 days, 30 days and then every 90 days thereafter. There is no gold standard test for evaluating trilostane treatment. ACTH stimulation test should be performed 2-4h after trilostane tablet. Pre-pill cortisol measurements is newer monitoring test for CS. Two cortisols are measured in 1h apart just before administration of trilostane (11-13h after last trilostane tablet if q12h or 23-25hif q24h). Regardless of the method chosen the most important aspect of monitoring is close owner observation for sign of hyper and hypoadrenocorticism.

References:
1. Caragelasco D, Kogika M, Cínthia, et al. Urine protein electrophoresis study in dogs with pituitary dependent hyperadrenocorticism during therapy with trilostane. *Pesq. Vet. Bras*; 37(7):734-740, 2017.
2. Peterson M.E. 2007. Diagnosis of hyperadrenocorticism in dogs. *Clin Tech Small Anim Pract*;22(1):2-11, 2007.
3. Gallelli MF et al.: A comparatice study by age and gender of the pituitary adenoma and ACTH and alpha-MSH secretion in dogs eith pituitary-dependent hyperadrenocorticism, Res Vet Sci 88:33,2010.
4. Owens JM, Drucker WD. Hyperadrenocorticism in the dog: Canine Cushing's syndrome. Vet Clin North Am 1977;7:583–602.
5. Ruckstuhl NS, Nett CS, Reusch C. Results of clinical examinations, laboratory tests, and ultrasonography in dogs with pituitary-dependent hyperadrenocorticism treated with trilostane. Am J Vet Res 2002;63:506–512.
6. Reusch CE, Feldman EC. Canine hyperadrenocorticism due to adrenocortical neoplasia. Pretreatment evaluation of 41 dogs. J Vet Int Med 1991;5:3–10.
7. Ortega TM, Feldman EC, Nelson RW, et al. Systemic arterial blood pressure and urine protein/creatinine ratio in dogs with hyperadrenocorticism. J Am Vet Med Assoc 1996;209:1724– 1729.
8. Behrend NE, Kooistra SH, Nelson R et al. Diagnosis of spontaneous canine hyperadrenocorticism: 2012 ACVIM consensus statement (small animal);27(6):1292304, 2013.
9. Kaplan AJ, Peterson ME, Kemppainen RJ. Effects of dis- ease on the results of diagnostic tests for use in detecting hyper- adrenocorticism in dogs. J Am Vet Med Assoc;207:445–451,1995.
10. 22. Chastain CB, Franklin RT, Ganjam VK, Madsen RW. Evaluation of the hypothalamic pituitary-adrenal axis in clinically stressed dogs. J Am Anim Hosp Assoc;22:435–442,1986.
11. Behrend NE, Canine hyperadrenocorticism in: Feldman EC, Nelson RW, Reusch EC et al. Canine & Feline Endocrinology, St.Louis, Missouri, 2015, pp- 315-347.
12. Schofield I, Brobdelt DC, Wilson ARL et al, Survival analysis 219 dogs with hyperadrenocorticism attending primary care practice in England. Vet Rec 186,328, 2020.
13. Hanson JM, et al: Efficacy of transsphenoidal hypophysectomy in treatment of dogs with pituitary-dependent hyperadrenocorticism , J Vet Intern Med 19:687, 2005.

IDIOPATHIC IMMUNE MEDIATED POLYARTHRITIS

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Pathogenesis:
Polyarthritis is characterized by neutrophilic inflammation in 2 or more joints.[1] Polyarthritis may be divided into[1]:
- Infectious (rickettsia, bacteria, Mycoplasma, L-form bacteria, fungi, viruses)
- Secondary to distant immunogenic stimulus (non-joint infectious and inflammatory focus, drugs, neoplasia, post-vaccinal)
- Primary immune-mediated:
  - Non-erosive (Systemic lupus erythematosus, breed associated: Shar-Pei, Akita, idiopathic immune-mediated)
  - Erosive (breed-associated: Greyhound, Rheumatoid arthritis, periosteal proliferative polyarthritis).

Idiopathic immune-mediated polyarthritis (IMPA) is the most common form of the polyarthritis, accounting for approximately 50–65% cases.[8] Immune-mediated nonerosive polyarthritis is believed to be driven by type III hypersensitivity reaction where immune complexes antigen - antibody accumulate in the joint space. Implicated antigens are typically found in the systemic circulation, but can originate from within the joint space itself.[2,3] The presence of immune complexes in the joint space activates complement along the synovial membrane and within the synovial fluid. Complement fixation results in tissue damage and the release of cytokines, some of which attract neutrophils.[4]

Clinical signs and diagnosis:
Affected dogs are usually young adults (2.5 - 4.5 years) and there is no sex predisposition. Large breeds are commonly affected, more concretely Labrador Retriever, Golden Retriever, German Shepherd, Cocker Spaniel and American Eskimo.[5-7] Clinical signs can be diverse, although most common reported are: fever, lethargy, weakness, reluctance to walk, a stiff or stilted gait, lameness, swelling of multiple joints and pain on palpation of the joints.[5-8] Clinicians should be aware that sometimes there are no obvious localized pain or joint changes. IMPA has been also reported as one of the most common causes of fever of unknown origin in dogs.[9] It is necessary to exclude all causes that can make secondary polyarthritis (e.g., infectious diseases, neoplasia, inflammation, drugs, vaccination) to diagnose IMPA. Good clinical examination should be performed with palpation of all joints (swelling, pain, range of motion and instability). A minimum database should include a complete blood count (CBC), serum chemistry panel, urinalysis, and urine culture. Common CBC and blood chemistry findings noted in dogs with IMPA include leukocytosis, mild nonregenerative anemia, mild hypoalbuminemia and increase C-reactive protein (CRP). Thoracic radiographs, joint radiographs and abdominal ultrasonography are most useful to exclude other diseases. Antinuclear antibody and rheumatoid factor serologic titar may be evaluated.[1] Titar for tick-borne disease (Lyme disease, bartonellosis, ehrlichiosis, anaplasmosis, Rocky Mountain spotted fever) should be performed to help distinguish the cause of polyarthritis. If serology is negative, PCR testing should be performed to exclude acute disease. Blood culture, urine and synovial fluid may help to identify a possible local or systemic bacterial infection. Septic arthritis should also be ruled out before starting an immunosuppressive therapy.[10] Evaluation of the heart valves via echocardiography may also be necessary to screen for endocarditis, particularly if a new or progressive murmur is auscultated. Endocarditis can lead to either a sterile reactive immune polyarthritis or a true infective arthritis via hematologic spread of organisms to one or more joints.[11]

Arthrocentesis is fundamental to diagnose inflammatory joint disorders. Samples should be taken from at least 4 joints.[1] Small joints are mostly affected (carpi, tarsi) by IMPA. Procedure should be performed sterile to minimize possibility for iatrogenic septic arthritis. The clinician should minimize blood contamination by avoiding superficial vessels. Once the joint space is entered, the syringe

plunger should be gently drawn back and the needle hub carefully observed. In healthy dogs, there is <0.25 mL of synovia that can be sampled from small joints. If >0.5 mL is collected, the joint is considered likely to have the disease.[12] If there is enough synovial fluid, samples should be submitted in ethylenediaminetetraacetic acid (EDTA). If there is a small amount of synovial fluid (about 0.2 mL), cytology slides should be prepared. Normal canine synovial fluid contains <3,000 cells/mL.[12] Greater than 90% of these cells are mononuclear and <5% are mature, nondegenerate neutrophils. Degenerative joint disease, trauma and previous ligament injury are associated with mononuclear inflammation (<10% neutrophiles).[1] Immune-mediated and infectious disease are associated with >10% neutrophiles. If infectious agents are excluded on direct cytologic examination of joint fluid, neutrophilic inflammation (>10% neutrophiles in synovial fluid) can be diagnosed as IMPA.

Treatment:
Treatment of polyarthritis should target the underlying cause (if applicable) and concurrently address pain and inflammation.[10] Immunosuppressive therapy, primarily with glucocorticoids, is the cornerstone of therapy of IMPA. Prednisolone 2mg/kg PO q24h is a starting dosage. Disease should be completely in remission (CRP normal, clinical examination normal) to reduce prednisolone 25%. The dose can be tapered by 25% every 2-3 weeks if the disease is still in remission. If remission cannot be achieved only with prednisolone second immunosuppressive drug like mycophenolate mofetil or leflunomide should be considered. Pain management is also important and pain medication like gabapentin, tramadol, amantadine could be used. Regularly rechecks are important before tapering immunosuppressive drug. If tick-borne disease is positive, especially Lyme disease and rickettsia infection, treatment with doxycycline 10mg/kg PO q24h for 4 weeks should be started.

Prognosis:
Most cases (90%) showed rapid response with immunosuppressive drugs. Some dogs (10%) fail to respond and suffer with continued lameness and progressive joint damage.[1] Some dogs that relapsed required life-long therapy to remain in remission, whereas others can be finally cured.[5]

References:
1. Stone M, Immune-Mediated Polyarthritis and Other Polyarthritides in: Textbook of Veterinary Internal Medicine 8th Edition, St. Louis, Missouri, Elsevier, 2017.
2. Taylor SM. Part Ten: joint disorders. In: NelsonRW, CoutoCG, eds. Small animal internal medicine. 4th ed. St Louis (MO): Mosby Elsevier; 2009:1119–41.
3. Kohn B. Canine immune-mediated polyarthritis. European Journal of Companion Animal Practice;17(2):119–24, 2007.
4. Johnson CK, Mackin A, Canine immune-mediated polyarthritis: part 1: pathophysiology. J Am Anim Hosp Assoc, 48(1):12-7, 2012
5. Clements DN, Gear RNA, Tattersall Jet al. Type I immune-mediated polyarthritis in dogs: 39 cases (1997–2002). J Am Vet Med Assoc, 224(8):1323–7, 2004.
6. Stull JW, Evason M, CarrAPet al. Canine immune-mediated polyarthritis: clinical and laboratory findings in 83 cases in western Canada (1991–2001). Can Vet J ;49(12):1195–203, 2008.
7. Jacques D, Cauzinille L, Bouvy Bet al. A retrospective study of 40 dogs with polyarthritis. Vet Surg;31(5):428–34, 2002.
8. Rondeau MP, Walton RM, Bissett Set al. Suppurative, nonseptic polyarthropathy in dogs. J Vet Intern Med 2005;19(5):654–62.
9. Dunn KJ, Dunn JK, Diagnostic investigations in 101 dogs with pyrexia of unknown origin, J Small Anim Pract;39 (12):574–8, 1998.
10. Johnson CK, Mackin A. Canine immune-mediated polyarthritis: part 2: diagnosis and treatment. J Am Anim Hosp Assoc.48(2):71-82,2012.
11. Sykes JE, Kittleson MD, Pesavento PA et al. Evaluation of the relationship between causative organisms and clinical characteristics of infective endocarditis in dogs: 71 cases (1992–2005). J Am Vet Med Assoc; 228 (11): 1723-3, 2006.
12. Mac Williams PS, Friedrichs KR. Laboratory evaluation and interpretation of synovial fluid. Vet Clin N Am Small Anim Pract; 33:153-78, 2003.

DIAGNOSTIC APPROACH TO PU/PD

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Physiology:

Polyuria / polydipsia (PU/PD) are common clinical symptoms in dogs and cats. These are broad symptoms with many differential diagnosis, therefore a systematic approach is very important. Normal daily water intake and urine output in dogs and cats are influenced by many factors: nutrients, minerals, water content of the diet, high environmental temperature, exercise… Normal water intake should not exceed 90 mL/kg/day in dogs and 45 mL/kg/day in cats. Normal urine output ranges from 20 to 45 mL/kg/day in dogs and cats.[1] Urine production and water production are controlled by the interaction among kidneys, pituitary gland and hypothalamus. Neurohypophysis is producing vasopressin - AVP or antidiuretic hormone (ADH). Most important stimulus for AVP secretion is increased plasma osmolality. It is also stimulated by high-pressure arterial baroreceptors and low-pressure volume receptors.[2] 1% increase in osmolality, as well as 10-15% decrease in either blood pressure or volume are sufficient to stimulate AVP secretion. Other factors like pain, stress, nausea, drugs and structural brain disease can stimulate secretion of AVP. AVP works on V_2 receptors on renal collecting duct epithelia where it opens water channels, allowing re-absorption of H_2O and making urine concentrated.[3] In addition, AVP has a vasoconstrictive action mediated through V_1 receptors on blood vessels.[3] To get properly concentrated urine there is a need for proper AVP secretion and action. In addition, there need to be adequate osmolality in the renal medulla. Primary polyuria is much more common than primary polydipsia. Most common differential for primary polydipsia are psychogenic polydipsia, abnormalities in the center of thirst and metabolic disorders.

Differential diagnosis PU/PD[4]:

Central diabetes insipidus (CDI)
- Primary diabetes insipidus
- Secondary diabetes insipidus (trauma induced, neoplastic, cushing's syndrome, drugs, polycythemia)

Primary nephrogenic diabetes insipidus (NDI)

Secondary nephrogenic diabetes insipidus (NDI)
- Liver disease
- Hyperadrenocorticism
- Hypoadrenocorticism
- Hyperthyroidism
- Pyelonephritis
- Pyometra/E. Coli endotoxemia
- Hypokalemia
- Hypercalcemia
- Erythrocytosis
- Acromegaly
- Leiomyosarcoma
- Drug induces (glucocorticosteroids, phenobarbital)

Osmotic diuresis
- Diabetes mellitus
- Post obstructive diuresis
- Chronic kidney disease
- Primary renal glucosuria
- Fanconi syndrome
- Drug administration (osmotic diuretic)
- High salt diet

Low renal medullary tonicity
- Renal medullary washout
- Low protein diet
- Hepatic impairment

Other/unknown mechanism
- Polyureic phase of acute kidney injury
- Syndrome of inappropriate ADH secretion
- Splenic hemangiosarcoma
- Pheochromocytoma

Diagnostic approach

Owner should be asked to measure exact water intake in 24h. First logical step in diagnostic is a random urine sample for determination of urine specific gravity (USG). If USG is >1.030 other differentials, that can be confused with PU/PD (like urine incontinence or dysuria), should be further examined for exclusion. Many causes of PU/PD can be ruled out with database consisting of complete history (age, breed, duration of clinical signs, possible medication) and physical examination (nutritional status, palpation of lymph nodes, dermatological changes, vaginal discharge, thyroid palpation, abdominal palpation, rectal examination). Complete blood count and biochemistry with ideally ionized calcium und urinalysis with urinary culture should be performed. In older cats, measurement of serum thyroid hormone is important to rule out hyperthyroidism. Next step is a diagnostic imaging like chest radiographs and abdominal ultrasound. If the cause for PU/PD is not found, further tests should take place like excluding hyperadrenocorticism (LDDST, ACT stimulation test), other hormonal testing (T4, PTH, PTH-rp) and water deprivation test and ADH response test. Diagnostic tests to confirm and differentiate among CDI, primary NDI and psychogenic polyuria are water deprivation test, random plasma osmolality determination and clinical response to vasopressin analogue DDAVP treatment.[3] In water deprivation test animals require careful monitoring. The test should not be performed if there is renal function impairment, or it should be stopped when animal lose more than 5% of body weight. The modified deprivation test is time consuming, labor intensive and associated with risk of sever hypertonic dehydration, which can be fatal. For this reason, more common trial therapy with DDAVP is used.

References:
1. DiBartola S, Clinical approach to polyuria and polydipsia in: Fluid, Electrolyte and Acid-Base Disorders in Small Animal Practice, 4th Edition, St.Lousi Missouri Elsevier, 2006.
2. Trasher TN, Baroreceptor regulation of vasopressin and renin secretion: low-pressure versus high-pressure receptors, Front Neuroendocrinol 15(2):157,1994.
3. Nelson RW, Water Metabolism and Diabetes Insipidus in: Feldman EC, Nelson RW, Reusch EC et al. Canine & Feline Endocrinology, St.Louis, Missouri, pp 1-36, 2015.
4. Shiel RE, Polyuria and Polydipsia in: in: Textbook of Veterinary Internal Medicine 8th Edition, St. Louis, Missouri, Elsevier, 2017.

DIABETIC KETOACIDOSIS

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Pathogenesis:

Diabetic ketoacidosis (DKA) is the most common life-threatening hyperglycemic emergency in patients with diabetes mellitus. Early diagnosis and management are most important to improve patient outcome.[1] Insulinopenia and increased concentration of counterregulatory hormones like glucagon, catecholamines cortisol and growth hormones are main pathomechanisms in DKA. Due to cellular starvation (because of reduced peripheral tissue glucose use) hepatic glucose production is increased by gluconeogenesis and glycogenolysis. Insulin is a powerful inhibitor of lipolysis, fat oxidation and stimulator of peripheral glucose and ketones use. Insulin deficiency increases lipolysis and elevate free fatty acids (FFA), as well as glucose and ketones bodies (acetoacetate, β-hydroxybutyrate and acetone) in bloodstream.[2] Protein catabolism is also increased as a consequence of counterregulatory hormones.[3] The first formed ketone body in liver is acetoacetat (AcAc), which is later converted to β-hydroxybutyrate (BHB) and acetone. The initial formation of ketone bodies and their utilization as an energy source is a protective mechanism against cellular starvation. All this processes: insulin resistance, ketogenesis and gluconeogenesis worsen hyperglycemia and lead to clinical manifestation of DKA.

Clinical signs and diagnosis:

Most important clinical signs are results of absolute insulin deficiency, hyperketonemia and hyperglycemia. It often occurs in animals with previously untreated diabetes or in case of inadequate insulin dosing. Insulin deficiency and ketonemia leads to enhanced water and electrolyte urine excretion. Increased blood glucose exceeds renal threshold for complete reabsorption and is lost in urine, inducing osmotic diuresis.[2] Excretion of ketones in urine is responsible for loss of ions like sodium, potassium, calcium and magnesium. Elevated ketones production overwhelmed body's buffering system causing increased arterial hydrogen ion concentration and decreased bicarbonate, which makes state of metabolic acidosis. Worsening of general condition due to metabolic acidosis results in vomiting, diarrhea and lack of fluid intake further leading to water loss, dehydration and increase plasma osmolality. Water is shifting from intracellular to extracellular space which causes cellular dehydration, obtundation and coma. Life-treating causes of DKA are: dehydration, metabolic acidosis, osmotic diuresis, electrolyte derangements and hyperosmolality. Diagnosis is made based on typical clinical signs (PU/PD, dehydration, vomiting, diarrhea, polyphagia, weight loss), hyperglycemia, increased ketone bodies and metabolic acidosis. Ketone bodies can be measured in urine or blood. Common nitroprusside reagent strips for ketonuria measure only AcAc and acetone and not β-hydroxybutyrate, therefore urine ketone test may be negative and should not be used to exclude DKA. Portable ketone meters are validated in cats and dogs and are measuring BHB. There is a good agreement between capillary and venous blood BHB and good overall correlation of the portable meter with the reference method.[4,5] The magnitude of increase in serum BHB concentration correlates with severity of metabolic acidosis.[6] Studies have showed that sensitivity of plasma ketone dipstick is 100% which indicates that negative result can be used to exclude DKA in cats.[7]

Typical blood changes are: hemoconcentration or anemia, leukocytosis, hyperglycemia, hypercholesteremia, increased liver enzymes (due to decreased perfusion, hepatic lipidosis), azotemia (pre-renal or renal), hyponatremia, hypochloremia, hypokalemia, metabolic acidosis, hyperosmolality and ketonemia. Urinalysis usually shows glycosuria, ketonuria, isosthenuria, hyposthenuria or hypersthenuria. Dogs and cats with DKA often have concurrent diseases like urinary tract infection, pancreatitis, pyelonephritis, chronic kidney disease, hepatic lipidosis, cholangiopathy.

Treatment:
First step in treatment of these patients is fluid therapy to restore water and electrolyte losses. Insulin should not be started in a hypovolemic animal, since it can worsen already depleted intravascular volume. Fluid therapy alone contribute to decrease in glucose, ketones and counterregulatory hormones by increasing glomerular filtration rate (GFR) and urinary excretion.[1,8] The initial volume and rate of fluid administration are defeminated by assessing the degree of shock, the dehydration deficit, the animal's maintenance requirements, plasma protein concentration and presence or absence of cardiac disease.[2] Most dogs and cats have net deficit of total body potassium due to osmotic diuresis. Sometimes potassium concentration can be normal or even elevated. Potassium should be supplemented according to guidelines and should not exceed 0.5 mmol/kg/h.[9] Serum phosphor can be decreased, normal or increased depending on the duration of illness and kidney function. Usually, phosphor concentration severely drops after starting insulin treatment due to intracellular shift of phosphorus with glucose. Phosphor can be supplemented as potassium phosphate and should not be mixed with calcium. Frequent re-checks are necessary to avoid under-supplementation or iatrogenic hyperphosphatemia. Metabolic acidosis usually resolves with fluid and insulin administration and bicarbonate supplementation is not always necessary. Hypomagnesemia is a common in dogs and cats with DKA and it can worsen during initial treatment. To date there are no clinical studies that have yielded guidelines for magnesium replacement in dogs and cats. Insulin treatment is critical for ketoacidosis resolution. Insulin treatment should be postponed until animal is well perfused and has stable potassium and phosphorus values.[1,8] Insulin treatment should be started in 3-6h of rehydration therapy. Early (<6h) vs late (>6h) insulin therapy has been associated with shorter resolution of DKA without associated increase in complication rates.[10] Regular insulin and short-acting insulin (lispro, aspart) can be used.[11,12] There are many different protocols for intravenous and intramuscular insulin administration. To minimize occurrence of complications and to improve chance of successful response to therapy close monitoring of serum glucose concentration, urine production, plasma ketones, blood gases and electrolytes should be monitored every 2-8h.

Prognosis:
DKA remains one of the most difficult metabolic therapeutic challenges in veterinary medicine.[2] Reported mortality ranges between 5% and 30%.[1,13,14]

Hyperosmolar hyperglycemic state (HHS):
HHS is defined as a sever hyperglycemia (600mg/dl), hyperosmolality (>320mOsm/kg) and dehydration but without significant or detectable ketonemia or ketonuria. It is believed that small amount of insulin is present, thus preventing the development of ketosis by inhibiting lipolysis.[15] Hyperglycemia tends to be more severe than hyperglycemia in DKA, probably because of low to undetectable concentration of ketones. Ketone bodies are important and early contributors to clinical signs.[1,15] Usually HHS progress for a longer time.[2] The goal therapy for HHS is similar like for DKA.

References:
1. O'Brien MA. Diabetic Emergencies in Small Animals. Vet Clin Small Anim 40:317-333,2010.
2. Nelson RW: Diabetic ketoacidosis in: Feldman EC, Nelson RW, Reusch EC et al. Canine & Feline Endocrinology, St.Louis, Missouri, 2015, pp- 315-347.
3. Thiebaud D, et al: Effect of long chain triglyceride infusion on glucose metabolism in man, Metabolism 21:1128, 1982.
4. Weingart C, Lotz F, Kohn B: Validation of a portable hand-held whole-blood ketone meter for use in cats. Vet Clin Pathol 41:114, 2012.
5. Zeugswetter FK, Rebuzzi L: Point-of-care β-hydroxybutyrate measurement for diagnosis of feline diabetic ketoacidemia. J Small Anim Pract 53(6):328,2012.
6. Duarte R, et al: Accuracy of serum β-hydroxybutyrate measurements for the diagnosis of diabetic ketoacidosis in 116 dogs. J Vet Intern Med 16:411, 2002.
7. Zeugwetter F, Pagitz M: Ketone measurements using dipstick methodology in cats with diabetes mellitus, J Sm Anim Pract 50:4, 2009.
8. Thomovsky E, Fluid and Electrolyte Therapy in Diabetic Ketoacidosis. Vet Clin North Am Small Anim Pract. 47(2):491-503, 2017.

9. DiBartola SP. Fluid, Electrolyte and Acid-Base Disorders in Small Animal Practice: 4th ed. Saunders Elsevier.

10. DiFazioJ, Fletcher DJ: Retrospective comparison of early-versus late insulin therapy regarding effect on time to resolution of diabetic ketosis and ketoacidosis in dogs and cats:60 cases (2003-2013). J Vet Emerg Crit Care 26(1):108, 2016.

11. Sears KW, Drobatz KJ, Hess RS: Use of lispro insulin for treatment of diabetic ketoacisodis in dogs, JVet Emerg Critic Care 22(2):211, 2012.

12. Walsh ES, Drobatz KJ, Hess RS: Use of intravenous insulin aspart for treatment of naturally occurring diabetic ketoacidosis in dogs, J Vet Emerg Critic Care 26(1):101, 2016.

13. Hume DZ, Drobatz KJ, Hess RS: Outcome of dogs with diabetic ketoacidosis: 127 dogs (1993-2003), J Vet Intern Med 20:547,2006

14. Cooper RL,et al: Retrospective evaluation of risk factors and outcome predictors in cats with diabetic ketoacidosis (1997-2007):93 cases, J Vet Emerg Crit Care 25/2):263, 2015.

15. Fayfman M, Pasquel FJ, Umpierrez GE. Management of Hyperglycemic Crises: Diabetic ketoacidosis and hyperglycemic hyperosmolar state, Med Clin North Am 101(3):587-606, 2017.

Management in Practice

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For 28 years he worked in the veterinary pharmaceutical industry, serving Animal Health and improving the business activity of veterinarians, in South Eastern countries, as Director of Business Units. Effectively participated in acquisitions and mergers processes, development of new products and services, purchases, and cross-functional projects. In April 2020, he founded Urban Vets with the aim of improving veterinary entrepreneurship.

HOW MUCH SHOULD I CHARGE FOR MY SERVICES AT MY VET CLINIC?

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Veterinarians estimate their service costs based on several factors, including the type of service or procedure being provided, the location of their practice, the specific needs of the patient, and their own business expenses. Here are some of the key factors that veterinarians consider when estimating service costs:

Type of Service or Procedure: The cost of veterinary services can vary widely depending on what needs to be done. Routine check-ups, vaccinations, and basic diagnostic tests will generally be less expensive than more complex procedures such as surgery, dental work, or specialized treatments.

Location: The cost of veterinary services can vary significantly by geographic location. Veterinarians in urban areas with higher living costs may charge more than those in rural areas. This can also be influenced by the overall cost of living and the demand for veterinary services in a particular region.

Labor and Expertise: Highly specialized procedures or services may require the expertise of veterinarians with advanced training or specialized certifications. These services may be more expensive due to the level of skill and expertise required.

Equipment and Facilities: The cost of maintaining and upgrading medical equipment and facilities can impact service fees. Veterinarians who invest in state-of-the-art equipment may charge more for their services.

Overhead Costs: Veterinarians have various overhead costs, including rent or mortgage for their clinic, utilities, insurance, and staff salaries. These costs are factored into the overall pricing of services.

Medications and Supplies: The cost of medications, medical supplies, and surgical equipment used during procedures will be included in the estimate. Some specialized medications or supplies may be more expensive.

Emergency or After-Hours Care: Veterinarians often charge more for emergency or after-hours care, as it can require additional staffing and resources.

Size and Species of the Animal: Larger animals and certain species may require more time, resources, and specialized equipment, which can result in higher service costs.

Complexity of the Case: The complexity of the medical condition or surgical procedure can impact the cost. More complicated cases may require additional diagnostic tests, treatment options, and follow-up care

Additional Services: Some veterinary clinics offer additional services such as boarding, grooming, and behavioral training. These services are typically priced separately from medical care.
Veterinarians often provide estimates or treatment plans for more involved procedures, allowing you to understand the expected costs before proceeding with treatment. Keep in mind that costs can vary from one practice to another, so it's a good idea to compare prices and consider the reputation and quality of care provided by the clinic.

I HAVE NO TIME...! – I CAN'T MAKE IT!

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Productivity, multitasking, and task-switching are all important aspects of managing one's time and responsibilities efficiently. Here's an overview of each concept:

1. Productivity:
Productivity refers to how effectively and efficiently you use your time and resources to accomplish tasks and achieve your goals. Here are some tips for improving productivity:

Time Management: Prioritize tasks, set deadlines, and create a schedule or to-do list to stay organized.

Focus on Goals: Clearly define your goals and break them down into smaller, manageable tasks.

Eliminate Distractions: Identify and minimize distractions in your workspace, such as turning off notifications or finding a quiet place to work.

Take Breaks: Short, regular breaks can help maintain focus and prevent burnout.

Delegate: If possible, delegate tasks to others to free up your time for more important responsibilities.

Use Productivity Tools: Utilize apps and tools designed for task management, time tracking, and collaboration.

2. Multitasking:
Multitasking involves performing multiple tasks or activities simultaneously. While it can be useful for handling routine or straightforward activities, it's important to be aware of its limitations:

Efficiency: Multitasking can lead to reduced efficiency because the brain needs to switch between tasks, which can result in errors or lower-quality work.

Overwhelm: Trying to do too much at once can be overwhelming and lead to increased stress.

Task Selection: Some tasks are better suited for multitasking than others. Simple, repetitive tasks may be easier to combine than complex, cognitive tasks.
Prioritization: It's essential to prioritize tasks and recognize when focused, single-tasking is more appropriate.

3. Task-Switching:
Task-switching, or context-switching, refers to shifting between different tasks or activities. While similar to multitasking, it often involves changing focus from one task to another sequentially. Here are some considerations:

Cognitive Load: Task-switching can impose a cognitive load as you need to mentally transition from one task to another, which can slow you down.
Efficiency: Frequent task-switching can decrease efficiency, as time is spent on context switching rather than completing tasks.

Batching Tasks: Whenever possible, group similar tasks together and work on them in batches to minimize the need for frequent task-switching.

In summary, productivity involves effective time management and goal-oriented work. While multitasking and task-switching can be helpful in certain situations, they should be used judiciously. It's often more efficient to focus on one task at a time, especially when working on complex or critical activities. Understanding your own work style and the demands of your tasks can help you strike the right balance between productivity, multitasking, and task-switching.

DIGITAL MARKETING FOR VETERINARY CLINICS

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Digital marketing can be a valuable tool for veterinary practices to promote their services, connect with clients, and build a strong online presence. Here are some key strategies and aspects of digital marketing that can benefit veterinary practices:

Website Development: A well-designed and user-friendly website is essential for any business, including veterinary practices. Ensure your website provides essential information such as services offered, contact details, staff bios, and client testimonials. Make it easy for visitors to schedule appointments online or request information.

Search Engine Optimization (SEO): Optimizing your website for search engines like Google is crucial to ensure that your practice appears in relevant search results. Use relevant keywords, create high-quality content, and optimize your site's technical aspects to improve search engine rankings.

Content Marketing: Regularly publish informative and engaging content on your website's blog. Topics can include pet care tips, common health issues, and updates about your practice. High-quality content can establish your practice as a trusted source of information and improve your search engine rankings.

Social Media Marketing: Maintain active social media profiles on platforms like Facebook, Instagram, and Twitter. Share educational content, pet stories, staff highlights, and engage with your audience. Social media is an excellent way to connect with your clients and showcase your expertise.

Email Marketing: Collect email addresses from your clients and use email marketing campaigns to send updates, newsletters, promotions, and appointment reminders. Email marketing can help you stay connected with your client base and promote special offers.

Online Advertising: Consider running online advertising campaigns on platforms like Google Ads or Facebook Ads. These platforms allow you to target specific demographics and geographic locations, making it easier to reach potential clients in your area.

Online Reviews and Reputation Management: Encourage satisfied clients to leave positive reviews on platforms like Google My Business, Yelp, and social media. Respond to both positive and negative reviews professionally and promptly. A strong online reputation can attract new clients.

Video Marketing: Create video content to showcase your practice, introduce your team, provide pet care tips, or explain common procedures. Video content can be shared on your website and social media channels.

Mobile Optimization: Ensure that your website is mobile-friendly, as many people access information on their smartphones. Mobile optimization can improve the user experience and help with search engine rankings.

Analytics and Monitoring: Use tools like Google Analytics and social media insights to track the performance of your digital marketing efforts. Adjust your strategies based on data to maximize effectiveness.

Online Appointment Booking: Implement an online appointment booking system to make it convenient for clients to schedule visits.
Digital marketing allows veterinary practices to reach a wider audience, engage with current clients, and establish themselves as trusted experts in pet care. It's important to have a well-thought-out

digital marketing strategy tailored to your practice's goals and target audience. Consider seeking assistance from digital marketing professionals or agencies if you're new to this area or need expert guidance.

Neurology

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Steven graduated from Ghent University in Belgium. After graduation, he performed there a Rotating Internship followed by a PhD about disk-associated cervical spondylomyelopathy ('wobbler's syndrome') in dogs. He completed his Residency in Neurology and Neurosurgery at the Royal Veterinary College (RVC), University of London.

He is now Associate Professor and Head of the RVC Neurology and Neurosurgery team. Although he is interested in all aspects of veterinary neurology, most of his research and publications focus on spinal disorders, neurosurgery and clinical reasoning. Steven has published widely and presented most of his work at international conferences. He enjoys teaching and is therefore regularly involved in continuing education events around the world.

HOW TO PERFORM A NEURO-EXAM IN PRACTICE

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Successful management of animals with suspected neurological disease can be a daunting and stressful prospect. It is however important to have a calm, structured, and logical approach when confronted with neurologically abnormal animals. A good understanding of the basic principles of the neurological examination is key to becoming more confident when evaluating neurological patients.

After performing a neurological examination, you should be able to answer the following questions: (1) Is the animal having a neurological disease, (2) Which part of the nervous system is affected, and (3) sometimes, you can determine the prognosis. Predicting the prognosis will only be possible in a minority of cases with specific clinical presentations, such as acute spinal injury and head trauma. It is important to realise that the severity of clinical signs does often NOT correlate with likelihood of recovery. This Information is crucial for obtaining a reliable list of differential diagnoses.

BEFORE PERFORMING A NEUROLOGICAL EXAMINATION

Although it is tempting to immediately perform a neurological examination, it is important to first obtain a detailed clinical history and perform a complete general physical examination. In several situations, the animal will be completely normal when presented to you. Examples of this are seizures and movement disorders. Information from the clinical history will then be the most important factor in selecting appropriate diagnostic and treatment options. Neurological abnormalities can also be caused by systemic diseases, which can only be recognized after a thorough general physical examination.

BASIC COMPONENTS OF THE NEUROLOGICAL EXAMINATION[1]

The neurological examination can be divided in the _hands-off_ and _hands-on_ examination. The hands-off examination is of great importance and often reveals key findings. The hands-off examination is unfortunately often overlooked. The neurological examination is further divided into the following 7 components; (1) Mentation and behaviour, (2) Posture and gait, (3) Proprioception, (4) Cranial nerves, (5) Spinal reflexes, (6) Spinal palpation, and (7) Nociception. It is important to start with the least invasive parts of the neurological examination and keep the more invasive parts for the end. Evaluating spinal pain and nociception/pain sensation can be considered the most invasive parts of the neurological examination.

1. _Mentation and behaviour_: Mentation and behaviour are not the same. In Neurology patients, **abnormal mentation** is most often characterised as decreased responsiveness or decreased consciousness. A larger than normal stimulus should be applied before you receive a response. Progressively decreasing levels of mentation are obtundation, stupor, and coma. Mentation can be decreased in forebrain and brainstem disorders. It is often more profoundly decreased in brainstem disorders.

   Abnormal behaviour is characterised by an inappropriate interaction with the environment Examples of abnormal behaviour include circling, compulsive pacing, and head-pressing. Abnormal behaviour is suggestive for forebrain disease. A common misconception is to consider aggression as a common sign of forebrain dysfunction. It is highly unlikely for dogs with neurological disease to have aggression-related behaviour problems as their predominant clinical sign. In endemic regions, Rabies could be an exception to this rule.

2. *Posture and gait*: abnormalities in posture include low-head carriage, kyphosis, head tilt. Abnormalities in gait include paresis, ataxia, and lameness. It is important to realize that ataxia (= loss of coordination) and paresis (= weakness) are different concepts. Animals with ataxia can have cerebellar or vestibular disease, animals with paresis can have lumbosacral or generalised neuromuscular disease, while animals with both ataxia and paresis can have spinal or brainstem disease.
Paresis is characterised by weakness and can be expressed as decreased muscle tone or increased stiffness with a shorter than normal stride.

3. *Proprioception*: This is often evaluated by hopping or paw placement responses in dogs, while visual placing, tactile placing, and wheel barrowing are useful in cats. Proprioceptive deficits are a reliable indicator for the presence of neurological disease. Proprioceptive deficits can occur in forebrain, brainstem, and spinal disease.

4. *Cranial nerves*: It is important to realise that performing a specific cranial nerve test often evaluates multiple anatomical structure and often more than one specific cranial nerve. Isolated cranial nerve deficits can be associated with specific idiopathic conditions. Certain combinations of cranial nerve deficits can be suggestive for inner ear localisations, while multiple cranial nerve deficits can occur in brainstem or generalized lower motor neuron disorders.

5. *Spinal reflexes*: Evaluation of spinal reflexes, such as the withdrawal reflex and patella reflex, is indicated to recognize focal or generalized lower motor neuron disease. It is also performed to evaluate which spinal cord segment is affected in animals with spinal cord disease. Decreased spinal reflexes indicate that a lesion is present in the local reflex arc, which includes the peripheral nerves and related spinal cord segment.

6. *Spinal palpation*: it is important to start with gentle palpation when you suspect the presence of spinal pain.

7. *Nociception*: Because this part of the examination is unpleasant, evaluation of nociception or 'pain sensation' should only be performed in paraplegic and comatose animals. It is important to realize that the response of the withdrawal reflex and nociception have a different nature and should not be confused.

DETERMINING THE NEURO-ANATOMICAL LOCALISATION[1]

The *combination* of clinical signs and findings of the neurological examination is used to determine the neuro-anatomical localisation. This will consist of one of the following; (1) forebrain, (2) cerebellum, (3) brainstem, (4) spinal cord, and (5) Neuromuscular.

1. *Forebrain:* Clinical signs include seizures, decreased mentation, abnormal behaviour, and central blindness. Additional neurological deficits include decreased menace response, decreased response after stimulation of the nasal mucosa, and proprioceptive deficits.

2. *Cerebellum:* Clinical signs include ataxia *without* paresis, hypermetria, central vestibular disease, and intention tremors. Additional neurological deficits include a decreased menace response.

3. *Brainstem:* Clinical signs include decreased mentation, generalised ataxia, hemiparesis, tetraparesis, and vestibular disease. Additional neurological deficits include proprioceptive deficits and cranial nerve deficits.

4. *Spinal cord*: Clinical signs include a *combination* of ataxia and paresis, spinal hyperesthesia, and bladder dysfunction. Additional neurological deficits include proprioceptive deficits and alterations in spinal reflexes.

5. *Neuromuscular:* The hallmark of neuromuscular disease is paresis *without* ataxia. Other clinical signs include changes in voice and regurgitation. Additional neurological deficits can include decreased spinal reflexes and cranial nerve deficits.

DETERMINING PROGNOSIS

Although prognosis for an individual animal is largely dependent on the specific diagnosis, the neurological examination can provide prognostic information in selected cases. Loss of nociception or pain sensation is the most important clinical prognostic factor in animals with spinal disease.[2] Negative prognostic factors for animals with traumatic brain injury are comatose mental status with bilateral mydriatic pupils and negative pupillary light reflexes, decerebrate rigidity, and a prolonged comatose mental status (>48hours).[3]

References

1. Garosi L, Lowrie M. The neurological examination. BSAVA Manual of canine and feline neurology. 4th Edition 2013: 1-24.
2. Olby NJ, da Costa RC, Levine JM, et al. Prognostic factors in canine intervertebral disc disease. Front Vet Sci 2020;7:596059.
3. Kuo KW, Bracek LM, Taylor AR. Head Trauma. Vet Clin North Am Small Anim Pract. 2018; 48:111-128.

HOW TO RECOGNISE THE MOST LIKELY DIAGNOSIS WITHOUT EXPENSIVE DIAGNOSTICS – CLINICAL REASONING IN FIRST OPINION PRACTICE

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It is common to feel uncomfortable and unconfident when confronted with an animal with suspected neurological disease. Although several factors can be responsible for this 'neurophobia'[1], it is often wrongly assumed that all neurology patients need to be referred to a specialty centre for advanced and expensive diagnostics, such as magnetic resonance imaging (MRI). Not all neurology patients can however be referred, not all neurologically abnormal animals need to be referred, and not all referred patients will require advanced diagnostics. Although patients with neurological disease can present with spectacular clinical signs and emotionally distressed owners, the clinical approach to these patients is not necessarily different from animals affected by other disorders. The combination of a thorough clinical history, general physical examination, and neurological examination will enable you to list the most likely differential diagnoses for the individual patient. This will serve as a starting point to discuss further diagnostics and management options with your client.

DIAGNOSTIC APPROACHES NOT SUITABLE FOR NEUROLOGICAL PATIENTS: PATTERN RECOGNITION AND "FISHING"

Experienced veterinary surgeons can rely on ***pattern recognition*** to achieve most of their clinical diagnoses. This is especially true for common diseases with unique and specific clinical signs. This diagnostic approach becomes however problematic for less experienced clinicians, uncommon diseases or disorders characterized by unspecific clinical signs. Neurological disorders are unsuitable for diagnosis by pattern recognition; not the disease itself, but the location of the disease within the nervous system will dictate the nature of clinical signs. This has two clinical consequences: (1) different diseases affecting the same location in the nervous system can cause similar clinical signs, (2) A specific disease may affect different locations in the nervous system and can therefore present with variable clinical signs.

"Fishing", diagnosis by exhaustion, or performing a variable amount of diagnostic tests in the hope to find potential abnormalities, should also be considered less ideal in neurology patients. Routine diagnostic tests, such as haematology, biochemistry, and even analysis of cerebrospinal fluid are rarely specific for a given neurological disease. Inappropriate selection of diagnostics can cause the owner to run out of money before a final diagnosis has been reached. "Fishing" for abnormal findings becomes also problematic when using the most sensitive neurodiagnostic procedure, MRI.

PROBLEM BASED CLINICAL REASONING[2]

Problem based clinical reasoning involves a logical progression through the following steps: (1) Define the problem of your patient. This can include pain, a gait abnormality, seizures, or abnormal behaviour. (2) Define which body system is affected. Neurological disorders can sometimes be difficult to differentiate from disorders affecting other body systems, (3) Define the location of the problem. For neurological disorders this can include the forebrain, brainstem, cerebellum, spinal cord or peripheral neuromuscular disease. (4) Define the lesion.[3] Now a list of likely differential diagnoses should be obtained. The answers to questions (1), (2), and (3) are answered after obtaining a thorough clinical history (what is the actual complaint?) and performing a complete general physical and neurological examination.

Define the lesion – How to get more from your neurological examination

Traditionally, a list of differentials was obtained using the VITAMIN D or DAMNIT-V scheme. Several neurological diseases can however be divided in more than one of these categories and this system does not always allow you to narrow down your list of differentials to only the most likely disorders for your individual patient. More recent developments in medical education advocate a problem-based approach following the principles of clinical reasoning. [2] More specifically, neurological disorders are associated with specific clinical characteristics and considering these specific clinical characteristics can be used to recognize the most likely differentials for an individual patient. After identifying the neuro-anatomical localisation, the most important clinical characteristics are (1) onset of clinical signs, (2) progression of clinical signs, (3) symmetry of clinical signs, (4) presence or absence of pain, and (5) patient's signalment. This diagnostic approach can also be referred to as the ***"5-finger-rule"***.

(0) Neuro-anatomical localisation

Obtaining a neuro-anatomical localisation is the starting point of obtaining a reliable list of differentials. Several neurological conditions will affect a specific or preferential part of the nervous system.

(1) Onset

 The onset of clinical signs is typically divided into peracute, acute, and chronic. It is important to consider the difference between peracute (seconds to minutes) and acute (hours to days) onset of clinical signs. Although several neurological conditions are characterized by an acute onset of clinical signs, only a few are characterized by a peracute onset. Examples of disorders with a peracute onset are vascular (for example, ischemic myelopathy) and idiopathic disorders (for example, idiopathic vestibular disease). Classical chronic conditions, such as neoplasia, can however also deteriorate acutely. This is referred to as "acute on chronic onset".

(2) Progression

Progression of clinical signs can be divided into improving, static, deterioration, waxing and waning, and episodic. The presentation of 'spontaneously improving neurological signs' might be more common than expected and can be seen in vascular disorders (for example, a cerebellar infarct), idiopathic disorders (for example, idiopathic Horner's syndrome), and pure contusive injuries (for example, acute non-compressive nucleus pulposus extrusion).

(3) Symmetry

Clinical signs can be symmetrical or strongly lateralized (asymmetrical). Examples of strongly lateralized brain conditions are neoplasia and vascular disorders. Examples of strongly lateralized spinal cord conditions are ischemic myelopathy and acute non-compressive nucleus pulposus extrusion.

(4) Pain

Neurological disorders, especially spinal disorders, can be painful. Presence of pain excludes several other conditions, such as degenerative myelopathy and ischemic myelopathy. Animals with classical painful conditions, such as compressive intervertebral disk disease, are however not always overtly painful. These conditions should therefore not be excluded if no obvious pain can be elicited on spinal palpation.

(5) Signalment

Neurological conditions commonly occurring in one species are very rare or do not occur at all in other species. Different neurological conditions should therefore be considered in dogs and

cats. Congenital and infectious disorders are more common in young animals, while neoplastic and degenerative conditions are more common in older animals. Neurological conditions can also be associated with gender and breed. Caution should however be exercised because not every neurologically abnormal Dachshund will have intervertebral disk disease.

Problem based clinical reasoning has been demonstrated to be valuable in the diagnostic approach of dogs[4] and cats[5] with spinal disease, epilepsy[6,7], vestibular syndrome [8,9], and canine cervical hyperesthesia[10]. It allows inexperienced clinicians to obtain a reliable list of differentials in animals with neurological disease.

References

1. Abushouk AI, Duc NM. Curing neurophobia in medical schools: evidence-based strategies. Med Educ Online. 2016;21:32476.
2. May SA. Clinical reasoning an case-based decision making: the fundamental challenge to veterinary educators. J Vet Med Educ. 2013;40:200-209.
3. Maddison JE, Volk HA, Church DB. Clinical reasoning in veterinary practice. 2nd Edition. Wiley Blackwell. 2022.
4. Cardy TJA, De Decker S, Kenny PJ, et al. Clinical reasoning in canine spinal disease: what combination of clinical information is useful? Vet Rec. 2015;177:171.
5. Mella SL, Cardy TJ, Volk HA, et al. Clinical reasoning in feline spinal disease: which combination of clinical information is useful? J Feline Med Surg. 2020;22:521-530.
6. Armasu M, Packer RMA, Cook S, et al. An exploratory study using a statistical approach as a platform for clinical reasoning in canine epilepsy. Vet J. 2014;202:292-296.
7. Stanciu G-D, Packer RMA, Pakozdy A. et al. Clinical reasoning in feline epilepsy: which combination of clinical information is useful? Vet J. 2017;225:9-12.
8. Harrison E, Grapes NJ, Volk HA, et al. Clinical reasoning in canine vestibular syndrome: which presenting factors are important? Vet Rec. 2021;188:e61.
9. Grapes NJ, Taylor-Brown FE, Volk HA, et al. Clinical reasoning in feline vestibular syndrome: which presenting features are the most important? J Feline Med Surg. 2021; 23:669-678.
10. Grapes NJ, Packer RMA, De Decker S. Clinical reasoning in canine cervical hyperaesthesia: which presenting features are important? Vet Rec. 2020;187:448.

HOW TO APPROACH ACUTE HIND LIMB PARALYSIS IN PRACTICE

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It is often assumed that dogs with acute hind limb paralysis have a poor prognosis and need to be referred to specialty centres for advanced and expensive diagnostics. Despite the severity of their clinical presentation, animals with acute hind limb paralysis can often be assessed and successfully treated in first opinion practice.

INITIAL ASSESSMENT OF ANIMALS WITH ACUTE HIND LIMB PARALYSIS

If an animal is presented with multiple injuries, do not immediately focus on the neurological signs. You should, if present, focus first on more life-threatening abnormalities. After obtaining a clinical history and performing a general physical examination, a neurological examination should be performed. Findings of the neurological examination will indicate if the animal has indeed spinal disease, which part of the spinal cord is affected and can offer prognostic information. The most important aspects of the neurological examination in animals with suspected spinal disease are 1) observation of gait and posture, 2) evaluation of proprioception, 3) spinal reflexes, 4) presence of spinal pain and 5) evaluation of deep pain perception or nociception.

The pathophysiology of acute spinal cord injury is complex and can be divided into primary and secondary spinal cord injury.[1] The primary injury represents immediate physical damage to the spinal cord and vasculature at the time of injury. This is followed by the secondary injury, which represents a cascade of biochemical and metabolic events initiated by the primary injury. The majority of this secondary spinal cord injury occurs in the first 24-48 hours after the primary injury. Decreased spinal cord perfusion is considered an important factor in secondary spinal cord injury. It can therefore be considered to stimulate spinal cord blood flow by providing adequate IV fluid therapy. High doses of corticosteroids have historically been considered to decrease the damaging effects of secondary spinal cord injury. Results from more recent human and veterinary studies do however not demonstrate any benefit and suggest a higher risk of potentially life-threatening complications when administering high doses of corticosteroids in patients with acute spinal cord injury.[2,3] *It is therefore no longer recommended to routinely administer corticosteroids in patients with acute spinal disease.*

TOP 4 DIFFERENTIALS FOR ACUTE HIND LIMB PARALYSIS IN DOGS

The 4 most common causes of acute hind limb paralysis in dogs are acute compressive intervertebral disc extrusion, ischemic myelopathy, acute non-compressive nucleus pulposus extrusion (ANNPE), and spinal fracture/luxation.

Acute compressive intervertebral disc extrusion[4]
Acute compressive intervertebral disc extrusion, or Hansen type I intervertebral disc disease typically affects chondrodystrophic dog breeds between 3 and 7 years old. The Dachshund and French bulldog are especially vulnerable. Clinical signs have an acute onset and are often progressive. Spinal pain is typically present, especially in the early stages of disease. Ambulatory dogs are often managed medically with a combination of strict rest, anti-inflammatory drugs and analgesia. Surgery is typically recommended in non-ambulatory dogs and is associated with a good prognosis if deep pain perception is present. If deep pain perception is absent, 50-60% of dogs will still have a good outcome.

<u>Ischemic myelopathy and acute non-compressive nucleus pulposus extrusion</u>[5,6]
Ischemic myelopathy or fibrocartilaginous embolism and ANNPE (previously also referred to as traumatic intervertebral disc extrusion and high-velocity low-volume disc extrusion) have a similar, almost identical, clinical presentation. In contrast to dogs with type I intervertebral disc disease, both disorders are associated with a peracute instead of an acute onset of clinical signs. Clinical signs typically occur in just a few seconds and are often associated with strenuous activity, such as running in a field or chasing/jumping for a tennis ball. ANNPE can also be associated with external trauma and should therefore be considered an important differential for vertebral fracture/luxation. Large non-chondrodystrophic dog breeds are most often affected. Although clinical signs can progress in the first 24 hours after onset, both disorders are typically non-progressive. It is not uncommon to see some spontaneous improvement within the first hours after onset of clinical signs. Although dogs often yelp when clinical signs occur, spinal pain is not an obvious feature during examination. Clinical signs can be dramatically lateralized and this should raise suspicion for both disorders. These are non-surgical conditions and physiotherapy/hydrotherapy forms the cornerstone of treatment. Prognosis is considered good if pain perception is present.

<u>Vertebral fracture/luxation</u>[7]
Vertebral fracture/luxation has a peracute onset of clinical signs and is most often associated with external trauma. Animals are often obviously painful. Assessment of vertebral instability and severity of clinical signs will determine if dogs can be managed medically or surgically.

HOW TO RECOGNIZE THE MOST LIKELY DIAGNOSIS?

Acute spinal disorders are associated with specific clinical characteristics and a high index of suspicion can be reached after following the principles of clinical reasoning ('5-finger rule'). This is especially important because not all dogs with acute hind limb paralysis will have a surgical condition and these non-surgical conditions are associated with the most characteristic clinical presentation. In other words, you should be able to recognise non-surgical causes of acute hind limb paralysis in first opinion practice. After identifying the neuro-anatomical localisation, the most important clinical characteristics are (1) onset of clinical signs, (2) progression of clinical signs, (3) symmetry of clinical signs, (4) presence or absence of spinal pain, and (5) patient's signalment.[8]

(1) Onset

It is important to consider the difference between peracute (seconds to minutes) and acute (hours to days) onset of clinical signs. Ischemic myelopathy, ANNPE and vertebral fracture/luxation are associated with a peracute onset of clinical signs. Acute compressive intervertebral disc extrusion is often associated with an acute onset of clinical signs.

(2) Progression

Progression of clinical signs can be divided into improving, static, deterioration, and episodic. Ischemic myelopathy and acute ANNPE are associated with spontaneously improving or static clinical signs. Acute compressive intervertebral disc extrusion can be associated with progressive clinical signs.

(3) Symmetry

Clinical signs can be symmetrical or strongly lateralized. Ischemic myelopathy and ANNPE can be associated with symmetrical or strongly lateralized clinical signs.

(4) Pain

Acute spinal disorders can be painful or non-painful. Ischemic myelopathy and ANNPE are typically not associated with obvious spinal pain. Vertebral fracture/luxation is often associated with severe spinal pain. Animals with classical painful conditions, such as compressive intervertebral disk extrusion, are however not always overtly painful. Although spinal pain or

spinal hyperaesthesia is often the predominant clinical sign early in the disease process, it is often difficult to elicit spinal pain when clinical signs progress and animals become paralysed.

(5) Signalment

Ischemic myelopathy and ANNPE occur most often in middle-aged to older non-chondrodystrophic dog breeds. Acute intervertebral disc extrusion occurs most often in young to middle-aged chondrodystrophic dog breeds.

Looking after paralysed patients and realistic expectations

Animals can make fantastic recoveries despite severe neurological signs. It is however important to have realistic expectations. Animals with acute hind limb paralysis will not recover the ability to walk in one or two days. This will be longer and animals need to be given the opportunity to demonstrate gradual and slow neurological improvement. In most acute spinal conditions, it can take up to two weeks until any obvious sign of improvement is seen. It is therefore important to be patient and provide appropriate nursing care until neurological function is restored. The cornerstone of nursing care for paralysed patients is bladder management. It should be assumed that animals unable to walk will also be unable to urinate voluntarily.

References

1. Olby NJ. The pathogenesis and treatment of acute spinal cord injuries in dogs. Vet Clin North Am Small Anim Pract. 2010;40:791-807.
2. Levine JM, Levine GJ, Boozer L, et al. Adverse effects and outcome associated with dexamethasone administration in dogs with acute thoracolumbar intervertebral disk herniation: 161 cases (2000-2006). J Am Vet Med Assoc. 2008;232:411-417.
3. Olby NJ, Muguet-Chanoit AC, Lim JH, et al. A placebo-controlled, prospective, randomized clinical trial of polyethylene glycol and methylprednisolone sodium succinate in dogs with intervertebral disk herniation. J Vet Intern Med. 2016;30:206-214.
4. Olby NJ, Moore SA, Brisson B, et al. ACVIM consensus statement on diagnosis and management of acute canine thoracolumbar intervertebral disc extrusion. J Vet Intern Med. 2022;36:1570-1596.
5. Fenn J, Drees R, Volk HA, De Decker S. Comparison of clinical signs and outcomes between dogs with presumptive ischemic myelopathy and dogs with acute noncompressive nucleus pulposus extrusion. J Am Vet Med Assoc. 2016;249:767-775.
6. De Decker S, Fenn J. Acute herniation of nondegenerate nucleus pulposus: acute noncompressive nucleus pulposus extrusion and compressive hydrated nucleus pulposus extrusion. Vet Clin North Am Small Anim Pract. 2018;48:95-109.
7. Jeffery ND. Vertebral fracture and luxation in small animals. Vet Clin North Am Small Anim Pract. 2010;40:809-828.
8. Cardy TJA, De Decker S, Kenny PJ, et al. Clinical reasoning in canine spinal disease: what combination of clinical information is useful? Vet Rec. 2015;177:171.

SPINAL DISORDERS IN FRENCH BULLDOGS AND PUGS

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The popularity of the French bulldog and pug breeds has increased sharply in recent years. The high demand for pugs and, especially, French bulldogs has been associated with an increased awareness of health and welfare concerns in small brachycephalic breeds. Although respiratory conditions have been most widely reported, both breeds are prone to specific spinal disorders. Although French bulldogs and pugs share similar phenotypic characteristics, they are affected by different spinal conditions.

VERTEBRAL MALFORMATIONS

Hemivertebra are characterised by incomplete formation of the vertebral body[1]. They occur most often in the mid-thoracic region and can be associated with an abnormal dorsoventral (i.e. kyphosis) or lateral (i.e. scoliosis) curvature of the vertebral column. Thoracic hemivertebra occur extremely common in neurologically normal French bulldogs. Up to 100% and 30% of neurologically normal French bulldogs has one or more hemivertebra and kyphosis, respectively.[2,3] This will only very rarely cause clinical signs in this breed and should be considered an incidental finding in most cases. Hemivertebra occurs in 17% of neurologically normal Pugs.[2] Hemivertebra are more likely to cause clinical signs in Pugs and when a severe degree of kyphosis is present.[4] Although selected cases can be treated medically, surgical stabilisation is the treatment of choice.[5]

Caudal articular process dysplasia is characterised by incomplete formation (hypoplasia) or complete absence (aplasia) of the caudal articular processes of one or more vertebra.[6] This condition is strongly associated with the Pug breed and >95% of neurologically normal Pugs has one or more sites of caudal articular process dysplasia along the vertebral column.[7] It was originally hypothesised that this condition could result in low-grade and repetitive instability. This could then in turn cause a reactive fibrotic reaction, characterised by constrictive fibrotic band surrounding the spinal cord.[6] This has been referred to as constrictive myelopathy or meningeal fibrosis. The causative relationship between caudal articular process dysplasia and meningeal fibrosis has however been question and the association between both conditions is currently unclear.[8]

SPINAL MALFORMATIONS

Spinal arachnoid diverticula are focal dilatations of the subarachnoid space with accumulation of CSF. These resemble cystic lesions, which can cause spinal cord compression. The French bulldog and Pug are predisposed for this spinal malformation.[9]Although 80% of affected dogs will improve after surgery, there are concerns that pugs experience a higher recurrence rate compared to other breeds.[10]

Meningeal fibrosis or constrictive myelopathy is characterised by circumferential intradural fibrotic adhesions, causing progressive constriction of the spinal cord. This condition has been heavily associated with the pug breed.[8] Although meningeal fibrosis has been associated with caudal articular process dysplasia, this spinal malformation has also been reported without any concurrent vertebral malformations.[8] Although treatment is challenging, positive outcomes have been reported after surgical stabilisation.[11]

INTERVERTEBRAL DISC DISEASE

Acute intervertebral disc extrusion (IVDE) is by far the most common spinal disorder in French bulldogs. This breed is predisposed to both thoracolumbar and cervical IVDE. Although thoracic hemivertebra with kyphosis will only rarely be the primary cause of clinical signs in French bulldogs, this malformation has been associated with a higher likelihood of thoracolumbar IVDE and a more caudal distribution of IVDE along the vertebral column.[12] There are concerns that IVDE in French bulldogs is associated with more severe disease characteristics compared to IVDE in other breeds: (1) IVDE in French bulldogs is more likely associated with extensive epidural haemorrhage, (2) French bulldogs are more likely to develop progressive myelomalacia, a devastating complication, and (3) up to 50% of French bulldogs will experience a recurrence of clinical signs after successful recovery after surgery.

References

1. Dewey CW, Davies E, Bouma JL. Kyphosis and kyphoscoliosis associated with congenital malformations of the thoracic vertebral bodies in dogs. Vet Clin North Am Small Anim Pract. 2016;46:295–306.
2. Ryan R, Gutierrez-Quintana R, Ter Haar G, De Decker S. Prevalence of thoracic vertebral malformations in French bulldogs, Pugs and English bulldogs with and without associated neurological deficits. Vet J. 2017;221:25–29.
3. Brown JD, Podadera J, Ward M, et al. The presence, morphology and clinical significance of vertebral body malformations in an Australian population of French Bulldogs and Pugs. Aust Vet J. 2021 99, 378-387.
4. De Decker S, Packer RMA, Capello R, et al. Comparison of signalment and computed tomography findings in French bulldogs, pugs, and English bulldogs with and without clinical signs associated with thoracic hemivertebra. J Vet Intern Med. 2019;33:2151-2159.
5. Mariné AF, De Risio L, Mascort J, et al. Transthoracic vertebral distraction and stabilization in 10 dogs with congenital thoracic vertebral malformations. Vet Comp Orthop Traumatol. 2021;34:367-374.
6. Fisher SC, Shores A, Simpson ST. Constrictive myelopathy secondary to hypoplasia or aplasia of the thoracolumbar caudal articular processes in Pugs: 11 cases (1993-2009). J Am Vet Med Assoc. 2013; 242:223–229.
7. Bertram S, Ter Haar G, De Decker S. Caudal articular process dysplasia of thoracic vertebrae in neurologically normal French bulldogs, English bulldogs, and Pugs: prevalence and characteristics. Vet Radiol Ultrasound. 2018;59: 396–404.
8. Rohdin C, Ljungvall I, Häggström J, et al. Thoracolumbar meningeal fibrosis in pugs. J Vet Intern Med. 2020;34:797–807.
9. Mauler DA, De Decker S, De Risio L. Signalment, clinical presentation, and diagnostic findings in 122 dogs with spinal arachnoid diverticula. J Vet Intern Medic. 2014;28:175–181.
10. Alisauskaite N, Cizinauskas S, Jeserevics J. Short- and long-term outcome and magnetic resonance imaging findings after surgical treatment of thoracolumbar spinal arachnoid diverticula in 25 Pugs. J Vet Intern Med. 2019;33: 1376–1383.
11. Tauro A, Rose J, Rusbridge C, Driver CJ. Surgical management of thoracolumbar myelopathies in Pug dogs with concurrent articular facet dysplasia. Vet Comp Orthop Traumatol Open. 2019;2:e60-e72.
12. Inglez de Souza MCCM, Ryan R, Ter Haar G. Evaluation of the influence of kyphosis and scoliosis on intervertebral disc extrusion in French bulldogs. BMC Vet Res. 2018;14:5.

HOW TO APPROACH VESTIBULAR SYNDROME IN PRACTICE?

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The vestibular system, or 'system of balance', is responsible for maintaining a normal orientation of the body, head and eyes in relation to gravitational forces and maintaining a normal position of the body and eyes in relation to motion or position of the head.[1] The vestibular system has a complicated anatomy and clinical signs can be caused by disorders outside or inside the central nervous system. These locations are also referred to as peripheral or central vestibular syndrome, respectively.[1] Veterinary surgeons confronted with an animal with vestibular dysfunction need to evaluate if patients with vestibular disease are more likely affected by peripheral or central vestibular syndrome.

ANATOMY OF THE VESTIBULAR SYSTEM[2]

The peripheral components of the vestibular system are located in the inner ear and consist of the receptors, ganglion, and the vestibular division of the vestibulocochlear nerve (Cranial nerve VIII). The central vestibular components are the vestibular nuclei in the brainstem, vestibular divisions in the brainstem, and the flocculonodular lobe of the cerebellum, fastigial nucleus of the cerebellum and the caudal cerebellar peduncle. More recently, it has been recognized that specific structures in the thalamus, which is located in the forebrain, also play a role in vestibular function.

Although not directly involved with vestibular function, parts of the facial nerve (cranial nerve VII) and sympathetic innervation to the eye run in close anatomical proximity to components of the peripheral vestibular system. More specifically, the facial nerve and sympathetic innervation to the eye course through the middle ear. It is therefore possible to see a combination vestibular signs, facial nerve paresis and Horner's syndrome in animals with disorders affecting the middle and inner ear.

CLINICAL SIGNS IN VESTIBULAR SYNDROME[1,2]

Dysfunction of the vestibular system is associated with a typical complex of clinical signs, involving postural, gait, and ocular abnormalities. _Head tilt_ is one of the easiest clinical signs to recognize and the ventrally deviated ear is directed towards the affected side. _Vestibular ataxia_ is characterized by a wide based stance and a tendency to fall, drift, or even roll towards the side of the lesion. Affected animals can also demonstrate circling towards the affected side with the circles being very tight around the axis. Ocular abnormalities can be more difficult to recognize and consist of pathological nystagmus and positional strabismus. _Nystagmus_, or the involuntary movement of eyes, is typically characterized by a jerk nystagmus, with the fast phase directed away from the lesion. The orientation of the nystagmus can be horizontal, rotary, or vertical. Nystagmus can be physiologic, which is evaluated during the vestibulo-ocular reflex, or pathological. Pathological nystagmus can be classified as spontaneous/ resting or positional nystagmus. Animals with vestibular disease can also demonstrate ipsilateral _positional strabismus_; extending the head upwards induces ventrolateral deviation of the eyeball with increased exposure of the dorsal sclera.

DIFFERENTIATION BETWEEN PERIPHERAL AND CENTRAL VESTIBULAR SYNDROME [3,4]

Because central vestibular syndrome is most commonly associated with disorders affecting the cerebellum or brainstem, affected animals can also demonstrate other brainstem or cerebellum signs. Presence of _proprioceptive deficits_ and _hemiparesis_ at the side of the lesion, _tetraparesis_, _decreased mentation_, and _multiple cranial nerve deficits_ are suggestive for central vestibular syndrome. Because the facial nerve (Cranial nerve VII) and the Sympathetic nerve are anatomically closely related to the inner ear, facial nerve paresis and Horner's syndrome can be seen in animals

with peripheral vestibular syndrome. Although debatable, _pure vertical nystagmus_ is also considered suggestive for a central vestibular syndrome. Nystagmus that _changes direction_ when position of the head is changed (for example from horizontal to rotatory after elevating the head) and _disconjugate nystagmus_ are also indications for central vestibular syndrome. Disconjugate nystagmus is characterized by both eyes displaying jerk nystagmus in a different direction. The rate of resting nystagmus has also been demonstrated to be significantly higher in dogs with peripheral vestibular syndrome.

Caution should however be exercised. Although the presence of the above discussed abnormalities is suggestive or diagnostic for a central vestibular syndrome, their absence does not exclude a central cause for vestibular dysfunction. **_A central vestibular localization can be ruled in, but not ruled out._**

PARADOXICAL VESTIBULAR SYNDROME

Although proprioceptive deficits occur usually at the same side as the head tilt, animals with central vestibular syndrome will occasionally demonstrate proprioceptive deficits contralateral to the side of the head tilt. This specific presentation is referred to as a paradoxical vestibular syndrome and is associated with a lesion affecting the caudal cerebellar peduncle.[5]

BILATERAL VESTIBULAR SYNDROME [1,2]

Bilateral vestibular syndrome is occasionally seen and is characterized by the absence of a head tilt and absence of any type of nystagmus. These animals will also not demonstrate physiologic nystagmus and will have a negative vestibulo-ocular reflex. Affected animals can crouch low over the floor, fall to both sides, and demonstrate wide bilateral excursions of the head. The most common causes of bilateral vestibular syndrome are bilateral middle/inner ear conditions.

COMMON CAUSES OF VESTIBULAR SYNDROME

In the author's institution, the **most common causes of vestibular syndrome in dogs** are[6]:

- Idiopathic vestibular syndrome – 34.2%
- Otitis media/interna – 23.7%
- Meningoencephalitis of unknown origin (MUO) – 15.4%
- Brain neoplasia – 11.4%
- Ischemic infarct – 11%
- Intracranial empyema (intracranial expansion of otitis interna) – 1.7%
- Metronidazole toxicity – 1.3%
- Middle ear neoplasia – 1.3%

Other potential causes for vestibular syndrome in dogs include hypothyroidism, congenital vestibular syndrome, trauma, ototoxicity, hydrocephalus, and infectious central nervous system disease.

In the author's institution, the **most common causes of vestibular syndrome in cats** are[7]:

- Otitis media/interna – 27.6%
- Idiopathic vestibular syndrome – 22.4%
- Intracranial neoplasia – 13.8%
- Middle ear polyp – 9.8%
- Feline Infectious peritonitis (FIP) virus – 7.5%
- Thiamine deficiency – 7.5%
- Intracranial empyema (intracranial expansion of otitis interna) – 6.3%
- Ischemic infarct – 2.3%

Other potential causes for vestibular syndrome in cats include congenital vestibular syndrome, trauma, ototoxicity, and other infectious central nervous system disease.

It is important to realize that these conditions and numbers come from a referral institution in the United Kingdom. It is likely that the distribution of specific disorders will vary between primary care and referral practice, different countries, and different geographic regions. Although it is not important to know the exact prevalence of a condition in your population, the above percentages were added to illustrate a useful statistic: the **8 most common conditions represent more than 95% of dogs and cats with vestibular syndrome**. In theory, you would therefore be able to help 95% of your patients if you would be able to diagnose and treat the 8 most common causes of vestibular syndrome.

CLINICAL REASONING IN ANIMALS WITH VESTIBULAR SYNDROME [6,7]

The following steps are important when applying clinical reasoning to recognise the most likely differential diagnoses:

1) **Do a neuro-exam**: identify that the animal is suffering from vestibular syndrome and identify if the problem is most likely localized to the central or peripheral vestibular components.
2) **Recognise easy to identify clinical characteristics and characterize the clinical presentation**: for vestibular syndrome, the most important clinical characteristics are signalment, onset and progression of clinical signs, presence of nystagmus, presence of positional strabismus, presence of facial nerve paresis, presence of Horner's syndrome, presence of proprioceptive deficits, presence of cranial nerve deficits, and most likely neuro-anatomical localisation (central or peripheral).
3) **Be aware of the most common causes of vestibular syndrome in dogs and cats**. See above.
4) **Identify which of those disorders can be associated with your key clinical characteristics.**
5) After you have identified the two or three most likely underlying conditions, discuss with the owners which **diagnostics, treatment options and outcome** can be considered for these specific conditions. Now you can decide if the animal needs to be referred or can be successfully treated in your practice.
6) **Reflection**. Evaluate if the patient is progressing as expected. If not, your differential diagnoses and clinical-decision-making should be re-evaluated. This step is especially important considering that a proportion of cases with presumptive peripheral vestibular syndrome will demonstrate a central lesion on advanced imaging.

References

1. Rossmeisl JH. Vestibular disease in dogs and cats. Vet Clin North Am Small Anim Pract. 2010;40:81-100.
2. Kent M, Platt SR, Schatzberg SJ. The neurology of balance: function and dysfunction of the vestibular system in dogs and cats. 2010;185:247-258.
3. Boudreau CE, Dominguez CE, Levine JM, et al. Reliability of interpretation of neurological examination findings for the localization of vestibular dysfunction in dogs. J Am Vet Med Assoc. 2018;252:830-838.
4. Bongartz U, Nessler J, Maiolini A, et al. Vestibular disease in dogs: association between neurological examination, MRI lesion localisation and outcome. J Small Anim Pract. 2020;61:57-63.
5. Vestibular System: Special proprioception. In: Veterinary Neuroanatomy and Clinical Neurology. Editors: de Lahunta A, Glass E, Kent M. 5th Edition. 2020. Pp 345-373.
6. Harrison E, Grapes NJ, Volk HA, De Decker S. Clinical reasoning in canine vestibular syndrome: which presenting factors are important? Vet Rec. 2021;188:e61.
7. Grapes NJ, Taylor-Brown FE, Volk HA, De Decker S. Clinical reasoning in feline vestibular syndrome: which presenting features are the most important? J Feline Med Surg. 2021;23:669-678.

EPILEPSY: WHAT, WHEN AND HOW

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WHAT IS AN EPILEPTIC SEIZURE?

A classic 'text-book' generalised epileptic seizure has the following characteristics[1]:

- Lateral recumbency and tonic-clonic movements ('jerking', 'paddling', 'running') of all limbs. The limbs and body are typically stiff.
- Loss of consciousness
- Occurs often at rest or during sleep.
- Lasts typically less than 2 to 3 minutes.
- Autonomic signs such as urination, defecation and salivation can be present.
- The character of the episodes is typically consistent.
- Post-ictal phase. When the actual epileptic seizure is finished, it might take a while before the animal regains its normal composure. For minutes or hours animals might demonstrate ataxia, abnormal behaviour, barking, aggression, transient blindness, or demonstrate abnormal hunger or thirst.

WHAT IS EPILEPSY?

Epilepsy is a disease of the brain characterized by an enduring predisposition to generate epileptic seizures.[1] Epilepsy can be divided into two aetiological categories: idiopathic and structural epilepsy.

Idiopathic epilepsy refers to a disorder characterised by recurrent epileptic seizures in which there is no identifiable brain abnormality. Epilepsy is the *'primary'* problem. Some breeds predisposed to idiopathic epilepsy include Beagle, Border Collie, Cocker Spaniel, German Shepherd dog, Labrador retriever, Vizsla, and many more. **Structural** epilepsy is defined as epilepsy caused by identifiable forebrain pathology.

The following clinical characteristics can be used to make a presumptive diagnosis of idiopathic epilepsy[1]:

- A breed in which there is a high prevalence of idiopathic epilepsy
- Age between 6 months and 6 years of age
- No other clinical signs than epileptic seizures
- Unremarkable general physical and neurological examinations
- No significant abnormalities on blood work and urinalysis

WHEN TO START TREATMENT AND WHAT TO EXPECT?[2,4]

Although treatment decisions are different for each individual patient, the following general recommendations have been suggested:

- An identifiable structural lesion or prior history of brain disease or injury (i.e. structural epilepsy)
- Status epilepticus or cluster seizures
- Two or more epileptic seizure events within a 6-month period
- Prolonged, severe, or an unusual postictal period

- The epileptic seizure frequency and/or duration and/or severity is increasing over 3 interictal periods

Treatment of epilepsy is complicated when your client has unrealistic expectations. There is no cure for idiopathic epilepsy and only a small percentage of animals will become seizure-free. It is therefore expected that treatment will be lifelong and that occasional seizures will be observed throughout the life of the pet. A realistic aim of treatment is to maintain an acceptable quality of life, consisting of a balance between decreased seizure frequency and avoidance of unacceptable AED side effects.

It should also be noted that 25-30% of cases will be refractory to medical management. The term *'refractory'* is used when a patient has poor seizure control despite therapeutic plasma drug concentrations of two or more adequate AEDs.[3]

WHICH TREATMENT IS RECOMMENDED?[2,4-6]

Although treatment of epilepsy can seem complicated, only a few anti-epileptic drugs (AEDs) are available. Having a good understanding about the indications, side effects and limitations will increase your confidence and success rates. From a practical point of view, AEDs can be divided into three categories:

1) **Very fast-acting, but very short-lasting effect**
   a. Benzodiazepines, such as diazepam and midazolam.
   b. These drugs work immediately and are used stop seizure activity in emergency situations. Their therapeutic effect last typically only a few minutes.

2) *Fast-acting and intermediate lasting effect*
   a. Levetiracetam
   b. Has a therapeutic effect within the first hour and is associated with minimal side effects. This is a very useful AED in emergency situations, but not effective as a maintenance drug.

3) *Slow-acting and long-lasting effect*
   a. These are the classic maintenance drugs. A delay in therapeutic effectivity is seen after administration, but the effect lasts longer.
   b. The most commonly used drugs are phenobarbitone, potassium bromide, Imepitoin (Pexion ©), and Zonisamide.

There are no evidence-based guidelines regarding which AED drug should be used first and your choice will be influenced by multiple factors[5], including efficacy, side effect profile, individual preference, and need of monitoring and costs. When you have made the decision to start treatment, you will typically select one of the following three drugs: phenobarbitone, potassium bromide, Imepitoin, or Zonisamide. Benzodiazepines and Levetiracetam are not useful as maintenance drug (i.e. daily, long-term administration) in dogs. Levetiracetam can however be considered as maintenance drug in cats.[6]

Phenobarbitone:
The first-choice AED for most veterinary surgeons. It has a proven efficacy and is relative safe when administered within the dose range. Most side effects are dose dependent and occur immediately after starting treatment or a dose increase: sedation, ataxia, polyphagia, polydipsia and polyuria. They typically improve or resolve over the first two weeks after starting treatment. Idiosyncratic drug reactions are very rare and include acute hepatotoxicity, haematological abnormalities and superficial necrolytic dermatitis. Changes in serum biochemistry profile variables are commonly seen of which an increase in hepatic enzymes is most common.

The recommended starting dose is 3 – 5mg/kg BID in dogs and 2 – 4 mg/kg BID in cats. There is individual variability in phenobarbitone absorption, excretion and elimination half-life. Absolute dosages (for example 3mg/kg/BID) are therefore not reliable to evaluate response to treatment.

Steady state concentrations are typically reached between 10 and 15 days. Therapeutic serum concentrations should be evaluated 2 weeks after treatment initiation or dose changes. Therapeutic serum concentrations are a key factor in evaluating response to treatment and should be used to guide dose changes or consideration of additional AEDs.

Phenobarbitone induces the hepatic enzyme cytochrome P-450. This has two important clinical consequences: 1) phenobarbitone is contra-indicated in animals with liver failure and 2) higher cytochrome P-450 promotes elimination of phenobarbitone.

Historically, there have been concerns about the potential of liver failure in animals receiving phenobarbitone. This is however rare, especially if the serum concentration is kept within its therapeutic range. For these reasons, it is important to continue monitoring the phenobarbitone serum concentration over time. Haematology, serum biochemistry and serum concentrations should be evaluated every 6 months after therapeutic serum concentrations have been reached. Pre -and postprandial bile acids should be evaluated if there are concerns about liver failure.

Potassium Bromide:
Often used as an add-on drug or if phenobarbitone is contra-indicated. Potassium Bromide is renally excreted and can be given to dogs with liver disease. Potassium bromide should not be given to cats due to a high incidence of severe and potentially irreversible respiratory complications. The initial dose is 20mg/kg BID. The elimination half-life is much longer than for phenobarbitone and steady-state serum concentrations are only reached after 80-120 days. Therapeutic serum concentrations are therefore only evaluated after 90 days.

Side effects include ataxia, pelvic limb stiffness, sedation, gastro-intestinal irritation. megaesophagus, pruritus and pancreatitis

Imepitoin:
Imepitoin or Pexion© is currently licensed in Europe and Australia. It is only registered for the management of single generalized epileptic seizures in dogs with idiopathic epilepsy. It is not registered for use in cats, treatment of cluster seizures, status epilepticus or treatment of structural epilepsy.

It has a similarly reported efficacy as phenobarbitone. Although most side effects are similar in nature as those for other AEDs (i.e. sedation, ataxia, polyphagia, polydipsia, and polyuria), they occur significantly less frequently compared to phenobarbitone. Imepitoin should not be given to dogs with liver, kidney or heart failure. Evaluation of serum concentrations is not necessary.

Levetiracetam and benzodiazepines:
Benzodiazepines, such as diazepam, should not be used as maintenance AED in dogs and cats. Dogs become rapidly tolerant to the anti-seizure effects of benzodiazepine and a high number of cats develop severe and even life-threating side effects (next to questionable efficacy).

Levetiracetam should not be used as a maintenance AED in dogs due to the development of tolerance after 4-6 months of continuous administration. Levetiracetam is however very useful in emergency situations and is an important AED to treat status epilepticus and cluster seizures. Levetiracetam has been recommended as maintenance AED in cats. A dose of 20mg/kg three times daily is recommended. Evaluation of serum concentrations is not necessary.

References

1. Berendt M, Farquhar RG, Mandigers PJ, et al. International veterinary epilepsy task force consensus report on epilepsy definition, classification and terminology in companion animals. BMC Vet Res. 2015;11:182.
2. Podell M, Volk HA, Berendt M, et al. 2015 ACVIM small animal consensus statement on seizure management in dogs. J Vet Intern Med. 2016;30:477-490.
3. Muñana KR. Management of refractory epilepsy. Top Companion Anim Med. 2013;28:67-71.

4. Bhatti SF, De Risio L, Muñana K, et al. International veterinary epilepsy task force consensus proposal: medical treatment of canine epilepsy in Europe. BMC Vet Res. 2015;11:176.
5. Charalambous M, Brodbelt D, Volk HA. Treatment in canine epilepsy – a systematic review. BMC Vet Res. 2014;10:257.
6. Charalambous M, Pakozdy A, Bhatti SFM, Volk HA. Systematic review of antiepileptic drugs' safety and effectiveness in feline epilepsy. BMC Vet Res. 2018;14:64.

EPILEPSY: WHY DON'T THEY RESPOND TO TREATMENT?

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The unpredictable and violent nature of epileptic seizures can cause severe emotional distress to owners of affected animals. Successful management requires an accurate assessment of the patient and commitment of the owner. A good relationship and mutual respect between the veterinarian and client are crucial for the optimal management of epilepsy. It is therefore important to feel confident about clinical decision making.

WHAT IF YOUR PATIENT DOESN'T RESPOND TO MEDICATION?

Although managing epilepsy patients can occasionally seem complex and difficult, it is important to go back to the basics when things don't go according to plan. This can be done by following the 'tripe D' mnemonic; Disease, Dose and Drug.

1. **DISEASE:**

   A common reason for unsuccessful therapy with anti-epileptic drugs (AEDs) is that the animal actually does not suffer from epileptic seizures. Several other 'paroxysmal' conditions can mimic seizures[1], which include syncope, REM-sleep disorders, narcolepsy/cataplexy and movement disorders. Movement disorders, including paroxysmal dyskinesias, are especially difficult to differentiate from seizures.[2] It is obvious that animals suffering from the above conditions will not respond positively to AEDs. This highlights the importance of obtaining a good description of the events. The following information should be collected when obtaining a clinical history of a patient with suspected epileptic seizures: nature and duration of the episode, level of consciousness during the episodes, time during the day when the episode occurs, presence of autonomic signs, and type of behaviour when the actual 'seizure' has ceased. Seizures typically last no longer than 1-2 minutes, occur during rest or sleep, the animal cannot be distracted during the episode, it can demonstrate decreased or loss of consciousness and autonomic signs (e.g. urination, defecation, hypersalivation), and an epileptic seizure is typically followed by a postictal phase in which the animal can demonstrate a variety of behaviours such as ataxia, paresis, barking, howling, attention-seeking, increased appetite, blindness and aggression. These characteristics can be used to differentiate epileptic seizures from other paroxysmal disorders.[3]

2. **DOSE:**

   Another common cause of unsuccessful treatment is an insufficient dose of AEDs. It is well-known that metabolism of common AEDs can differ considerably between individual patients. Different patients will therefore require a different, individualised, dose. Assessment of the correct dose of common AEDs, such as phenobarbitone, can therefore only be evaluated by obtaining therapeutic serum concentrations.[4] Two of the most common mistakes in the management of epilepsy are (1) failure to obtain therapeutic serum concentrations and (2) adding an additional AED before the first AED has been given maximum opportunity to be effective. In other words; a second AED is often added too soon without maximising the potential of the first AED. Although therapeutic serum concentration ranges vary between laboratories, they are often presented as a wide range. It is however important to adjust the dose until a serum concentration in the upper 75% of the therapeutic dose range is reached before considering the AED ineffective.[5] For example:

- The therapeutic range of phenobarbitone is often presented as 20 to 40 ug/mL
- We will consider phenobarbitone ineffective **ONLY** if a therapeutic serum concentration between 30 and 35 ug/mL has not resulted in satisfactory seizure control.
- If the serum concentration is below 30 ug/mL, it is advised to increase the dose of phenobarbitone with the following formula: *current dose X desired serum concentration/current serum concentration*
- If a serum concentration between 30 and 35 ug/mL has not resulted in satisfactory seizure control, it should be considered to add another AED

3. DRUG:

It should be considered to add a second AED when no satisfactory response is reached despite adequate therapeutic serum concentrations of the first AED. It is important to know the indications and limitations of the available AEDs. It can be considered both frustrating and comforting that only a few AEDs can be used as maintenance drug. The AEDs that can be used as maintenance drug include phenobarbitone, potassium bromide, Imepitoin (Pexion©) and zonisamide.[5,6]

Although Levetiracetam is a popular AED, which is useful in emergency situations, it is not effective as a maintenance AED in dogs.[7] Studies have demonstrated a decreased effectiveness when levetiracetam is administered for a prolonged period of time, which has been referred to as the 'honeymoon' phenomenon.[8] It should therefore not be considered as an add-on maintenance drug in dogs. The honeymoon phenomenon has not (yet) been reported in cats and levetiracetam could therefore be considered an alternative maintenance drug in this species.[9]

When a patient does not respond satisfactory to a well-established AED, it is less likely to respond to a second AED. When patients do not respond to a second AED, it becomes unlikely they will respond to any AED. Drug-resistant or refractory epilepsy is considered when an animal does not satisfactorily respond to two well-established AEDs with evidence of adequate therapeutic serum concentrations. In practice this can be translated as a dog that continues to demonstrate uncontrolled epileptic seizures despite a receiving correct doses of both phenobarbitone and potassium bromide.[10]

REFRACTORY EPILEPSY

Refractory epilepsy is characterised as a condition in which an animal with epilepsy fails to attain satisfactory seizure control or suffers intolerable side effects despite appropriate therapy with conventional AEDs.[10] It seems unlikely that a patient with refractory epilepsy will respond to any AED. There is therefore a large interest in development of non-medical management of refractory epilepsy. Non-medical management in humans includes epilepsy surgery, electrical brain stimulation, vagal nerve stimulation, and dietary modification.

Epilepsy surgery and electrical brain stimulation are in its infancy in veterinary medicine and should currently not be considered realistic options in dogs and cats. Although vagal nerve stimulation has been evaluated to a greater extent, dietary modification has so far shown most promise in dogs with refractory epilepsy. Several human studies have demonstrated positive effects of a ketogenic diet in children with epilepsy. Possibly due to species differences in metabolism, a 'classic' ketogenic diet, consisting of high fat, low protein and low carbohydrate has not demonstrated improved seizure control in dogs. More recent studies have demonstrated promising results of a medium-chain triglyceride (TAG) diet in dogs with refractory epilepsy.[11] It is however important to note that response to a medium-chain TAG diet is variable between individual dogs. While some dogs can have a drastic improvement in epileptic seizure control, no positive effects are observed in other dogs. This information is of great importance when discussing expectations with owners.

References

1. Packer RMA, Berendt M, Bhatti SF, et al. Inter-observer agreement of canine and feline paroxysmal event semiology and classification by veterinary neurology specialists and non-specialists. BMC Vet Res. 2015;11:39.
2. Lowrie M, Garosi L. Classification of involuntary movements in dogs: paroxysmal dyskinesias. Vet J. 2017;220:65-71.
3. Berendt M, Farquhar RG, Mandigers PJ, et al. International veterinary epilepsy task force consensus report on epilepsy definition, classification and terminology in companion animals. BMC Vet Res. 2015;11:182.
4. Podell M, Volk HA, Berendt M, et al. 2015 ACVIM small animal consensus statement on seizure management in dogs. J Vet Intern Med. 2016;30:477-490.
5. Bhatti SF, De Risio L, Muñana K, et al. International veterinary epilepsy task force consensus proposal: medical treatment of canine epilepsy in Europe. BMC Vet Res. 2015;11:176.
6. Charalambous M, Brodbelt D, Volk HA. Treatment in canine epilepsy – a systematic review. BMC Vet Res. 2014;10:257.
7. Fredsø N, Sabers A, Toft N, et al. A single-blinded phenobarbital-controlled trial of levetiracetam as mono-therapy in dogs with newly diagnosed epilepsy. Vet J. 2016;208:44-49.
8. Volk HA, Matiasek LA, Luján Feliu-Pascual A, et al. The efficacy and tolerability of levetiracetam in pharmacoresistant epileptic dogs. Vet J. 2008;176:310-319.
9. Barnes Heller H. Feline Epilepsy. Vet Clin North Am Small Anim Pract. 2018;48:31-43.
10. Muñana KR. Management of refractory epilepsy. Top Companion Anim Med. 2013;28:67-71.
11. Law TH, Davies ES, Pan Y, et al. A randomised trial of a medium-chain TAG diet as treatment for dogs with idiopathic epilepsy. Br J Nutr. 2015;114:1438-1447.

IMMUNE MEDIATED INFLAMMATORY CENTRAL NERVOUS SYSTEM DISEASE

MENINGOENCEPHALITIS OF UNNOWN ORIGIN (MUO) AND STEROID RESPONSIVE MENINGITIS ARTERITIS (SRMA)

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Inflammatory conditions are common causes of decreased mentation and abnormal behaviour in dogs and cats. Different terminology is used depending on which anatomical structures are affected[1]:

- **Encephalitis** = inflammatory condition affecting the brain parenchyma
- **Myelitis** = inflammatory condition affecting the spinal cord
- **Meningitis** = inflammatory condition affecting the meninges
- **Meningoencephalitis** = inflammatory condition affecting the meninges and underlying brain parenchyma
- **Encephalomyelitis** = inflammatory condition affecting the brain parenchyma and spinal cord
- **Encephalomyelomeningitis** = inflammatory condition affecting the brain parenchyma, spinal cord and meninges
- **Meningomyelitis** = inflammatory condition affecting the meninges and spinal cord parenchyma

A large variation of specific etiologies can cause inflammation of the central nervous system (CNS). These aetiologies can be divided into infectious and non-infectious disorders. Although the distribution of specific etiologies might differ between geographical locations, non-infectious, immune-mediated causes of CNS inflammation are in general far more common than infectious disorders. In the author's hospital, more than 85% of dogs with an inflammatory CNS disorder is diagnosed with a non-infectious condition.[2]

What is Meningoencephalitis of Unknown Origin (MUO)?[3,4]

Most non-infectious causes of CNS inflammation are idiopathic, immune-mediated conditions with a possible hereditary component. Breed specific causes of encephalitis have historically been considered, such as *'Pug encephalitis'* and *'Yorkie encephalitis'*. It has however become evident that multiple breeds can be affected by these 'breed specific' conditions. Different causes of non-infectious CNS inflammatory disorders are now classified based on their histopathological characteristics. The three most common causes of non-infectious inflammatory CNS disease are:

1. **Granulomatous meningoencephalitis (GME)** or granulomatous meningoencephalomyelitis (GMEM) if the spinal cord is also affected
2. **Necrotizing meningoencephalitis (NME)** – former *Pug encephalitis*
3. **Necrotizing leukoencephalitis (NLE)** – former *Yorkie encephalitis*

Making a definitive histopathological diagnosis requires examination of brain tissue, which can be obtained by brain biopsy or, more commonly, post-mortem examination. It is therefore evident that obtaining an antemortem final diagnosis of GME, NME or NLE is almost impossible in both general and specialist practice. The umbrella term ***meningoencephalitis of unknown origin (MUO)*** or ***meningoencephalitis of unknown aetiology (MUA)*** has therefore been introduced for dogs with

clinical characteristics and diagnostic findings suggestive for GME, NME or NLE. The following diagnostic criteria are considered for MUO[5]:

- Dogs older than 6 months of age
- Advanced imaging (MRI) suggestive for an inflammatory condition
- Cerebrospinal fluid analysis (CSF) reveals an increased total nucleated cell count, consisting for mor than 50% out of lymphocytes or monocytes (mononuclear cells) and an increased protein concentration.
- Exclusion of infectious disease commonly occurring in the geographical area

Although these diagnostic criteria are helpful for obtaining a diagnosis of MUO in specialist referral centres, they might not be very helpful for general practitioners.

The clinical presentation of dogs with MUO is variable. Young to middle-aged toy and terrier breeds, such as Maltese, West Highland white terrier, pug, Yorkshire terrier, Chihuahua, French bulldog, Pomeranian and Boston terrier are predisposed. Every breed can however be affected and 25% of dogs with MUO are large breed dogs.[6] Onset of clinical signs can be acute or more insidious progressive. Clinical signs are variable and can include one or a combination of decreased mentation, abnormal behaviour, epileptic seizures, blindness, central vestibular signs, ataxia, paresis, and spinal hyperesthesia. In contrast to popular belief, the general physical examination and blood work of affected dogs is typically normal.

The cornerstone of treatment is immunosuppressive drugs. Historically, this condition was treated solely with immunosuppressive doses of corticosteroids (prednisolone 2mg/kg BID for three days, followed by 2mg/kg SID, slowly tapered until a minimal effective dose has been identified). Treatment is lifelong in most cases and corticosteroid related side effects can significantly impact affected animals' quality of life. More recently, adjunctive immunomodulating drugs are used in combination with corticosteroids. This allows for more aggressive tapering and even cessation of corticosteroid therapy. The most commonly used immunomodulating drugs for this purpose are cytosine arabinoside and cyclosporine. Prognosis is variable and depends largely on the initial response to treatment. If dogs die because of MUO, this happens typically shortly after a diagnosis has been obtained. Up to 25% of dogs diagnosed with and treated for MUO dies in the first 7 days after reaching a diagnosis.[7] If a positive response to treatment is seen, a prolonged survival can be seen. There are indications that improved outcomes are obtained when an adjunctive immunosuppressive drug is introduced compared to sole corticosteroid therapy.[5] There are currently no indications that one type of adjunctive immunomodulating drug would be superior to another.

Steroid responsive meningitis arteritis (SRMA)

This is one of the most common causes of cervical hyperaesthesia in young dogs.[8] SRMA is a systemic immune-mediated vasculitis with predisposition for the vessels of the subarachnoid space. Affected animals are typically young (< 2 years of age) and have a characteristic clinical presentation consisting of severe cervical hyperesthesia, lethargy, pyrexia and a stiff gait. Neurological deficits, such as proprioceptive deficits and ataxia, are typically not present.[9] Although Beagles, Boxers, Jack Russel terriers, and Nova Scotia Duck tolling retrievers are predisposed, every dog breed can be affected. Blood work can demonstrate a leukocytosis and a diagnosis is confirmed by cerebrospinal fluid analysis. Cerebrospinal fluid analysis reveals an increased protein concentration and a highly elevated white blood cell count, which characteristically consists of a predominance of non-degenerate neutrophils. As suggested above, SRMA is associated with specific clinical characteristics. The three most reliable clinical variables to differentiate SRMA from other causes of cervical hyperesthesia are (1) younger age, (2) presence of pyrexia and (3) presence of abnormalities on blood work (i.e., leukocytosis on hematology). The presence of pyrexia with hematology abnormalities in a dog with cervical hyperesthesia has been associated with a specificity of 99.5% and a sensitivity of 55% for a diagnosis of SRMA.[8] Translated to clinical practice, this

means that the presence of pyrexia with hematology abnormalities make a diagnosis of SRMA very likely, while the absence of these findings cannot be used to exclude a diagnosis of SRMA.

Although relapses are possible, most dogs respond favorably to a prolonged period of corticosteroids, which is started at immunosuppressive doses.[9] Although different protocols have been proposed, the following can be considered:

- o Dexamethasone 0.4mg/kg/IV once a day until obvious improvement is seen (typically 1-3 days)
- o Prednisolone 1 mg/kg/PO twice a day for 2 weeks
- o Prednisolone 1mg/kg/PO once a day for 4-6 weeks
- o Prednisolone dose is continuously slowly tapered and stopped after 6 months

Corticosteroids side effects are unfortunately often observed, and this should be discussed with the owner.

References:

1. Tipold A, Stein VM. Inflammatory diseases of the spine in small animals. Vet Clin North Am Small Anim Pract. 2010;40:871-879.
2. Goncalves R, De Decker S, Walmsley G, et al. Inflammatory disease affecting the central nervous system in dogs: A retrospective study in England (2010-2019). Front Vet Sci. 2022;8:819945.
3. Cornelis I, Van Ham L, Gielen I, et al. Clinical presentation, diagnostic findings, prognostic factors, treatment and outcome in dogs with meningoencephalitis of unknown origin: a review. Vet J. 2019;244:37-44.
4. Jeffery N, Granger N. New insights into the treatment of meningoencephalitis of unknown origin since 2009: a review of 671 cases. Front Vet Sci. 2023;10:114798.
5. Granger N, Smith PM, Jeffery ND. Clinical findings and treatment of non-infectious meningoencephalitis in dogs: a systematic review of 457 published cases from 1962 to 2008. Vet J. 2010;184:290-297.
6. Cornelis I, Volk HA, De Decker S. Clinical presentation, diagnostic findings and long-term survival in large breed dogs with meningoencephalitis of unknown aetiology. Vet Rec. 2016;179:147.
7. Cornelis I, Volk HA, Van Ham L, De Decker S. Prognostic factors for 1-week survival in dogs diagnosed with meningoencephalitis of unknown aetiology. Vet J. 2016;214:91-95.
8. Grapes NJ, Packer RMA, De Decker S. Clinical reasoning in canine cervical hyperaesthesia: which presenting features are important? Vet Rec. 2020;187:448.
9. Tipold A, Schatzberg SJ. An update on steroid responsive meningitis-arteritis. J Small Anim Pract. 2010;51:150-154.

Oncology

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Dr. Antonio Giuliano graduated from the University of Messina in 2007. While working in general practice, he completed a master's degree in Small Animal Oncology from the University of Pisa, a post graduate certificate in cancer therapeutic at Barts Cancer Institute and the GpCert (SAM) in internal medicine. He completed a rotating internship in a busy referral practice in UK and an oncology internship and residency at the Queen Veterinary School Teaching Hospital (QVSH), at the University of Cambridge.

After successfully completing the residency, he worked for one year as oncology clinician and supervisor at the QVSH. In the 2019 he moved to Hong Kong (HK) working as oncologist at CityU VMC, the largest multidisciplinary referral Hospital in HK.

Dr Antonio Giuliano is a recognised European, RCVS and HK specialist in Companion Animals (Oncology). He published numerous articles in international peer reviewed journals and presented his research in many international conferences.

He has a broad interest in cancer research, with particular focus on finding new drugs/therapeutic approaches to improve survival time and quality of life of pets. He is also interested in preclinical and clinical investigations into the development of rapid tests to predict prognosis and/or early diagnosis of cancer.

HOW TO DIAGNOSE AND TREAT CANINE LYMPHOMA IN GENERAL PRACTICE

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Lymphoma is the most common hematopoietic tumour in dogs, and it is estimated that around 123 cases per 100000 dogs per year are affected in UK (Mellanby et al., 2002).

The most common anatomical form of lymphoma in dogs is multicentric, with generalised peripheral lymphadenopathy. Spleen, liver and abdominal lymph nodes are often involved. Diagnosis of lymphoma is straightforward, and a simple fine needle aspirate (FNA) is often diagnostic. However, some indolent types of lymphoma cannot be diagnosed by FNA and histopathology is required. Other tests like immunocytochemistry, flow cytometry or PARR can be used to confirm the diagnosis and can often be used to differentiate B from T cells lymphoma. Differentiating B from T cell lymphoma is important for prognosis and often to decide the type of treatment(Brown et al., 2018; Purzycka et al., 2020).

Dogs with multicentric lymphoma (especially B-cell) are mostly asymptomatic or paucisymptomatic, and staging is not always required before starting treatment. Thoracic radiographies and abdominal ultrasounds are used when staging is performed. Chemotherapy with a CHOP-type chemotherapy protocol is the most effective treatment for large cell lymphoma especially for B -cell lymphoma, while for T-cell lymphoma an alkylating-rich protocol (LOP/LOPP) could be more effective(Brown et al., 2018; Purzycka et al., 2020; Rebhun et al., 2011).

Most dogs treated with CHOP chemotherapy respond very well and dogs with B-cell lymphoma can live around 1 year with 20% alive at 2 years. Some dogs however even treated just with COP can have similar survival if rescued with doxorubicin at relapse(Davies et al., 2018). Large T-cell lymphoma has a poorer prognosis with survival of around 6-9 months.

There are no proven benefits of adding a maintenance chemotherapy treatment after completing the induction protocol. Once the induction chemotherapy protocol (CHOP/COP/LOPP) is completed the patient is regularly monitored. Unfortunately, the lymphoma will relapse, usually on average around 3 months after induction. Once relapse is confirmed, the original protocol is restarted. The induction protocol can be repeated until the lymphoma responds. Once this protocol is no longer effective a rescue protocol is started instead. There are many rescue protocols and the choice of one versus another will depend on various factors especially the first type of induction protocol used, available chemotherapy drugs and often the preference of the oncologist.

Other forms of lymphoma in dogs like gastrointestinal lymphoma are usually poorly responsive to chemotherapy and the prognosis is much poorer, a few weeks to 2-3 months(Rassnick et al., 2009). Indolent or low-grade lymphomas in dogs are treated by surgery (splenectomy for localised mantle cell lymphoma and marginal zone lymphoma of the spleen), while other types of generalised low-grade lymphoma like T-zone lymphoma are treated with oral chlorambucil and prednisolone and usually carry a very good prognosis.

References

Brown, P. M., Tzannes, S., Nguyen, S., White, J., & Langova, V. (2018). LOPP chemotherapy as a first-line treatment for dogs with T-cell lymphoma. *Veterinary and Comparative Oncology*, *16*(1). https://doi.org/10.1111/vco.12318

Davies, O., Szladovits, B., Polton, G., Garden, O. A., Leo, C., & Lara-Garcia, A. (2018). Prognostic significance of clinical presentation, induction and rescue treatment in 42 cases of canine centroblastic diffuse large B-cell multicentric lymphoma in the United Kingdom. *Veterinary and Comparative Oncology*, *16*(2). https://doi.org/10.1111/vco.12378

Mellanby, R. J., Herrtage, M. E., & Dobson, J. M. (2002). Treatment of canine lymphoma by veterinarians in first opinion practice in England. *Journal of Small Animal Practice*, *43*(5). https://doi.org/10.1111/j.1748-5827.2002.tb00056.x

Purzycka, K., Peters, L. M., Desmas, I., Davies, O., Chang, Y. M., & Lara-Garcia, A. (2020). Clinicopathological characteristics and prognostic factors for canine multicentric non-indolent T-cell lymphoma: 107 cases. *Veterinary and Comparative Oncology*, *18*(4). https://doi.org/10.1111/vco.12589

Rassnick, K. M., Moore, A. S., Collister, K. E., Northrup, N. C., Kristal, O., Chretin, J. D., & Bailey, D. B. (2009). Efficacy of combination chemotherapy for treatment of gastrointestinal lymphoma in dogs. *Journal of Veterinary Internal Medicine*, *23*(2). https://doi.org/10.1111/j.1939-1676.2008.0270.x

Rebhun, R. B., Kent, M. S., Borrofka, S. A. E. B., Frazier, S., Skorupski, K., & Rodriguez, C. O. (2011). CHOP chemotherapy for the treatment of canine multicentric T-cell lymphoma. *Veterinary and Comparative Oncology*, *9*(1). https://doi.org/10.1111/j.1476-5829.2010.00230.x

Diagnosis and treatment of feline lymphoma, challenges and rewards
Feline lymphoma, cats are not small dogs

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Lymphoma is the most common haematopoietic tumour and one of the most common neoplasia in cats(Louwerens et al., 2005). Lymphoma is classified depending on the retroviral status, anatomical form, histopathological grade and immunophenotype. The most common anatomical form in the "FeLV negative era" is the gastrointestinal type (both low and high grade), which often affects the small intestine, and/or stomach and/or mesenteric lymph nodes(Louwerens et al., 2005). In some countries where FeLV infection is still common, certain types of lymphoma, like multicentric and mediastinal forms are more common compared to countries with a low rate of infection, where these forms of lymphoma are relatively rare.

Compared to gastrointestinal lymphoma other types of lymphoma like the nasal cavities, kidneys, larynx, and mediastinum, are less common, while lung, skin, central nervous system (CNS), and eye are even rarer. Some presentations of lymphoma do not fit a specific anatomical classification because multiple locations are involved, these are often classified as mixed forms.
The treatment for lymphoma is chemotherapy. However certain types of localised lymphoma like nasal or CNS can be also treated with radiotherapy.

While low grades lymphomas are treated with low-intensity oral chemotherapy protocols, high grades are better treated with injectable chemotherapy protocols like COP or CHOP. Differently from dogs, there is no evidence in cats that CHOP is better than COP and the author has treated many cats successfully with a modified COP.

The prognosis of cats with lymphoma depends on various factors. One of the most important prognostic factors is the grade. Cats with low-grade lymphoma can live for 2-3 years or longer just on oral chlorambucil and prednisolone, while for large-cell/high-grade lymphoma, the prognosis is more difficult to predict. In cats differently from dogs, T and B-cell immunophenotype is not prognostic.

The most important prognostic indicator for large cell lymphoma is the response to treatment. Cats achieving a complete response can enjoy a good quality of life (considering all forms of lymphoma) for an average of 9–12 months, with some cases living longer than 2 years(Collette et al., 2016; Waite et al., 2013). Cats with progressive disease live only a few days to a couple of weeks, while cats achieving partial response live only 1-3 months (Collette et al., 2016; Waite et al., 2013)Another important prognostic factor is the type or location of the lymphoma. Cats with nasal tumours can live longer than 2 years, while cats with CNS lymphoma only a few days or weeks (Haney et al., 2009; Taylor et al., 2009). However, the location is often influenced by the response rate, for example, cats with nasal or mediastinal forms tend to live longer, but also achieve a high complete response rate compared to other forms. Some specific types of lymphoma, like large granular cell lymphoma, tend to also have a low response rate and poor survival(Finotello et al., 2018)

References

Collette, S. A., Allstadt, S. D., Chon, E. M., Vernau, W., Smith, A. N., Garrett, L. D., Choy, K., Rebhun, R. B., Rodriguez, C. O., & Skorupski, K. A. (2016). Treatment of feline intermediate- to high-grade lymphoma with a modified university of Wisconsin-Madison protocol: 119 cases (2004-2012). *Veterinary and Comparative Oncology, 14.* https://doi.org/10.1111/vco.12158
Finotello, R., Vasconi, M. E., Sabattini, S., Agnoli, C., Giacoboni, C., Annoni, M., Dentini, A., Bettini, G., Guazzi, P., Stefanello, D., Bottero, E., Mesto, P., Marinelli, R., De Feo, C., & Marconato, L. (2018). Feline large granular lymphocyte lymphoma: An Italian Society of Veterinary Oncology (SIONCOV) retrospective study. *Veterinary and Comparative Oncology, 16*(1). https://doi.org/10.1111/vco.12325

Haney, S. M., Beaver, L., Turrel, J., Clifford, C. A., Klein, M. K., Crawford, S., Poulson, J. M., & Azuma, C. (2009). Survival analysis of 97 cats with nasal lymphoma: A multi-institutional retrospective study (1986-2006). *Journal of Veterinary Internal Medicine*, *23*(2). https://doi.org/10.1111/j.1939-1676.2008.0243.x

Louwerens, M., London, C. A., Pedersen, N. C., & Lyons, L. A. (2005). Feline lymphoma in the post-feline leukemia virus era. *Journal of Veterinary Internal Medicine*, *19*(3). https://doi.org/10.1892/0891-6640(2005)19[329:FLITPL]2.0.CO;2

Taylor, S. S., Goodfellow, M. R., Browne, W. J., Walding, B., Murphy, S., Tzannes, S., Gerou-Ferriani, M., Schwartz, A., & Dobson, J. M. (2009). Feline extranodal lymphoma: Response to chemotherapy and survival in 110 cats. *Journal of Small Animal Practice*, *50*(11). https://doi.org/10.1111/j.1748-5827.2009.00813.x

Waite, A. H. K., Jackson, K., Gregor, T. P., & Krick, E. L. (2013). Lymphoma in cats treated with a weekly cyclophosphamide-, vincristine-, and prednisone-based protocol: 114 cases (1998-2008). *Journal of the American Veterinary Medical Association*, *242*(8). https://doi.org/10.2460/javma.242.8.1104

FELINE ORAL SQUAMOUS CELL CARCINOMA

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Feline oral SCC (FOSCC) is the most common malignant oral tumour in cats(Stebbins et al., 1989). The most common locations of oral SCC in cats are the sublingual region, maxilla, and mandible, less frequently, the lip and the tonsils can also be affected. The etiopathogenesis of feline SCC is unknown, but some factors have been implicated in the increased risk of FOSCC development. In human head and neck SCC, papillomavirus is considered an important risk factor as well as tobacco smoke and alcohol consumption. Cats living in households with smokers are considered more at risk of developing FOSCC compared to non-smoking households(Snyder et al., 2004). This is a possibility due to the deposition of chemicals from tobacco smoke on the fur in conjunction with the cat's grooming habit. Cats with a high intake of canned food in their diet and cats wearing flea collars have also been reported to be more at risk of developing FOSCC(Bertone et al., 2003; Snyder et al., 2004). The relationship between papillomavirus and FOSCC is not well established.

Cats with oral SCC often present with reduced appetite, drooling of saliva often tinged with blood, malodorous breath and/or a visible mass swelling in the mandible or maxilla. On oral examination, mass lesions in the sublingual area are typical for FOSCC, but lesions in the maxilla and mandible are not always so obvious and mainly ulcerative lesions can be mistaken for dental disease.

FOSCC is a locally aggressive tumour with a low metastatic rate, reported to be around 14-18% in the lymph nodes and around 12% in the lungs. Most patients are likely to die or be euthanised due to the primary tumour before developing metastasis(Hayes et al., 2007). Treatment of FOSCC is often not rewarding in particular because of the advanced stage of the disease at diagnosis. FOSCC is also not responsive to chemotherapy and has a poor long-term response to radiotherapy(Marconato et al., 2020; Mauldin et al., 1988). Recent publications, contrary to what was published before, suggest that aggressive oral surgeries (mandibulectomy/maxillectomy) are tolerated in cats. Surgical resection in selected cases could be an option, especially in the early stage of the disease and or in a favourable location, like the maxilla/mandible(Boston et al., 2020; Liptak et al., 2021). Hyper fractioned radiotherapy, brachytherapy and multimodal treatment with surgery, chemotherapy and radiotherapy in selected cases have been reported with some success, but the overall prognosis remains poor(Marconato et al., 2020). Palliative pain management and COX2 inhibitors plus/ minus toceranib are probably the treatment of choice for most cases(Wiles et al., 2017).

References

Bertone, E. R., Snyder, L. A., & Moore, A. S. (2003). Environmental and Lifestyle Risk Factors for Oral Squamous Cell Carcinoma in Domestic Cats. *Journal of Veterinary Internal Medicine*, *17*(4). https://doi.org/10.1892/0891-6640(2003)017<0557:EALRFF>2.3.CO;2

Boston, S. E., van Stee, L. L., Bacon, N. J., Szentimrey, D., Kirby, B. M., van Nimwegen, S., & Wavreille, V. A. (2020). Outcomes of eight cats with oral neoplasia treated with radical mandibulectomy. *Veterinary Surgery*, *49*(1). https://doi.org/10.1111/vsu.13341

Hayes, A. M., Adams, V. J., Scase, T. J., & Murphy, S. (2007). Survival of 54 cats with oral squamous cell carcinoma in United Kingdom general practice: Paper. *Journal of Small Animal Practice*, *48*(7). https://doi.org/10.1111/j.1748-5827.2007.00393.x

Liptak, J. M., Thatcher, G. P., Mestrinho, L. A., Séguin, B., Vernier, T., Martano, M., Husbands, B. D., Veytsman, S., Nimwegen, S. A., De Mello Souza, C. H., Mullins, R. A., Barry, S. L., & Selmic, L. E. (2021). Outcomes of cats treated with maxillectomy: 60 cases. A Veterinary Society of Surgical Oncology retrospective study. *Veterinary and Comparative Oncology*, *19*(4), 641–650. https://doi.org/10.1111/vco.12634

Marconato, L., Weyland, M., Tresch, N., Rossi, F., Leone, V., & Rohrer Bley, C. (2020). Toxicity and outcome in cats with oral squamous cell carcinoma after accelerated hypofractionated radiotherapy and concurrent systemic treatment. *Veterinary and Comparative Oncology*, *18*(3). https://doi.org/10.1111/vco.12557

Mauldin, G. N., Matus, R. E., Patnaik, A. K., Bond, B. R., & Mooney, S. C. (1988). Efficacy and Toxicity of Doxorubicin and Cyclophosphamide Used in the Treatment of Selected Malignant

Tumors in 23 Cats. *Journal of Veterinary Internal Medicine*, *2*(2). https://doi.org/10.1111/j.1939-1676.1988.tb02794.x

Snyder, L. A., Bertone, E. R., Jakowski, R. M., Dooner, M. S., Jennings-Ritchie, J., & Moore, A. S. (2004). p53 expression and environmental tobacco smoke exposure in feline oral squamous cell carcinoma. *Veterinary Pathology*, *41*(3). https://doi.org/10.1354/vp.41-3-209

Stebbins, K. E., Morse, C. C., & Goldschmidt, M. H. (1989). Feline Oral Neoplasia: A Ten-Year Survey. *Veterinary Pathology*, *26*(2). https://doi.org/10.1177/030098588902600204

Wiles, V., Hohenhaus, A., Lamb, K., Zaidi, B., Camps-Palau, M., & Leibman, N. (2017). Retrospective evaluation of toceranib phosphate (Palladia) in cats with oral squamous cell carcinoma. *Journal of Feline Medicine and Surgery*, *19*(2). https://doi.org/10.1177/1098612X15622237

FELINE CUTANEOUS SQUAMOUS CELL CARCINOMA

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Squamous cell carcinoma (SCC) is a common tumour of the skin. It is most commonly found in areas of the glabrous skin exposed to sunlight like the pinnae, nasal planum and eyelid. UV light exposure is the most important predisposing factor(Lana et al., 1997; Richard Dorn et al., 1971). However, papillomavirus infection could also be involved, especially in cats presenting multiple cutaneous lesions around the body(Munday et al., 2007).

Cutaneous SCC typically presents with small crusty erythematous skin lesions that progress slowly. At the early-stage cats develop UV-induced precancerous lesions called actinic dermatosis. These with time will transform into carcinoma in situ, which if not treated, will progress to advanced invasive carcinoma. The typical history, location and appearance of the lesions make a diagnosis of suspicion on clinical examination not challenging; however, a final diagnosis can only be made by biopsy and histopathology, while cytology examination of SCC is largely unrewarding. Cutaneous SCC is a local and invasive disease, but metastases are rare(Lana et al., 1997). Treatment depends on the tumour size and degree of local invasion (stage); advanced stages can be treated by surgery and/or electrochemotherapy/radiotherapy. Local control of superficial and less advanced tumours can be achieved with surgery, cryotherapy, photodynamic therapy (PD), brachytherapy with strontium-90, imiquimod cream and more rarely with local chemotherapy(Gill et al., 2008; Goodfellow et al., 2006; Jarrett et al., 2013; Peters-Kennedy et al., 2008; Prado et al., 2017; Russak et al., 2022; Stell et al., 2001).

Complete surgical excision of the cutaneous SCC is usually curative, but it is not unusual for the same cat to develop de novo lesions later in life. When the tumour is too advanced and cannot be treated by surgery, electrochemotherapy and radiotherapy are both reasonable and effective treatment options that often achieve good local control of the disease(Cunha et al., 2010; Gasymova et al., 2017; Simčič et al., 2021).

References

Cunha, S. C. S., Carvalho, L. A. V., Canary, P. C., Reisner, M., Corgozinho, K. B., Souza, H. J. M., & Ferreira, A. M. R. (2010). Radiation therapy for feline cutaneous squamous cell carcinoma using a hypofractionated protocol. *Journal of Feline Medicine and Surgery*, *12*(4). https://doi.org/10.1016/j.jfms.2009.10.005

Gasymova, E., Meier, V., Guscetti, F., Cancedda, S., Roos, M., & Rohrer Bley, C. (2017). Retrospective clinical study on outcome in cats with nasal planum squamous cell carcinoma treated with an accelerated radiation protocol. *BMC Veterinary Research*, *13*(1). https://doi.org/10.1186/s12917-017-1018-3

Gill, V. L., Bergman, P. J., Baer, K. E., Craft, D., & Leung, C. (2008). Use of imiquimod 5% cream (Aldara™) in cats with multicentric squamous cell carcinoma in situ: 12 cases (2002-2005). *Veterinary and Comparative Oncology*, *6*(1). https://doi.org/10.1111/j.1476-5829.2007.00144.x

Goodfellow, M., Hayes, A., Murphy, S., & Brearley, M. (2006). A retrospective study of 90Strontium plesiotherapy for feline squamous cell carcinoma of the nasal planum. *Journal of Feline Medicine and Surgery*, *8*(3). https://doi.org/10.1016/j.jfms.2005.12.003

Jarrett, R. H., Norman, E. J., Gibson, I. R., & Jarrett, P. (2013). Curettage and diathermy: A treatment for feline nasal planum actinic dysplasia and superficial squamous cell carcinoma. *Journal of Small Animal Practice*, *54*(2). https://doi.org/10.1111/jsap.12025

Lana, S. E., Ogilvie, G. K., Withrow, S. J., Straw, R. C., & Rogers, K. S. (1997). Feline Cutaneous Squamous Cell Carcinoma of the Nasal Planum and the Pinnae: 61 Cases. *Journal of the American Animal Hospital Association*, *33*(4). https://doi.org/10.5326/15473317-33-4-329

Munday, J. S., Kiupel, M., French, A. F., Howe, L., & Squires, R. A. (2007). Detection of papillomaviral sequences in feline Bowenoid in situ carcinoma using consensus primers. *Veterinary Dermatology*, *18*(4). https://doi.org/10.1111/j.1365-3164.2007.00600.x

Peters-Kennedy, J., Scott, D. W., & Miller, W. H. (2008). Apparent clinical resolution of pinnal actinic keratoses and squamous cell carcinoma in a cat using topical imiquimod 5% cream. *Journal of Feline Medicine and Surgery*, *10*(6). https://doi.org/10.1016/j.jfms.2008.02.002

Prado, L. O. C., Rossetto, V. J. V., Carvalho, L. M. C. R., Ferreira, A. P., Matsubara, L. M., Rodrigues, J. C. Z., & Brandão, C. V. S. (2017). Evaluation of the cryosurgery for treatment of squamous cell carcinoma in cats. *Arquivo Brasileiro de Medicina Veterinaria e Zootecnia*, *69*(4). https://doi.org/10.1590/1678-4162-9060

Richard Dorn, C., Taylor, D. O. N., & Schneider, R. (1971). Sunlight exposure and risk of developing cutaneous and oral squamous cell carcinomas in white cats. *Journal of the National Cancer Institute*, *46*(5). https://doi.org/10.1093/jnci/46.5.1073

Russak, O. M., Verganti, S., & Berlato, D. (2022). Strontium 90 plesiotherapy for the treatment of eyelid squamous cell carcinoma in eight cats. *Journal of Feline Medicine and Surgery*, *24*(6). https://doi.org/10.1177/1098612X211038141

Simčič, P., Pierini, A., Lubas, G., Lowe, R., Granziera, V., Tornago, R., Valentini, F., Alterio, G., Cochi, M., Rangel, M. M. M., de Oliveira, K. D., Freytag, J. O., Quadros, P. G., Sponza, E., Gattino, F., Impellizeri, J. A., & Torrigiani, F. (2021). A retrospective multicentric study of electrochemotherapy in the treatment of feline nasal planum squamous cell carcinoma. *Veterinary Sciences*, *8*(3). https://doi.org/10.3390/vetsci8030053

Stell, A. J., Dobson, J. M., & Langmack, K. (2001). Photodynamic therapy of feline superficial squamous cell carcinoma using topical 5-aminolaevulinic acid. *Journal of Small Animal Practice*, *42*(4). https://doi.org/10.1111/j.1748-5827.2001.tb01796.x

MAST CELL TUMOURS IN DOGS, THE GREAT IMITATOR

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Mast cell tumour (MCT) is one of the most common types of cancer in dogs(Dobson et al., 2002). It can have variable clinical appearance and presentation. MCT can look like a skin tag, a papule, a small nodule or a large mass. MCT can resemble a fluid-filled cyst or a soft and movable subcutaneous mass like a lipoma.

Diagnosis of MCT is really important to plan further treatment and it can be easily achieved by FNA. However, achieving a diagnosis of MCT is not sufficient, because the prognosis and treatment will depend on the histological grade (Kiupel et al., 2011).

Predicting the biological behaviour of MCT is really important, but it can be challenging. Histopathology grading and mitotic index are probably the most important way to predict the biological behaviour of MCT, but it is not always enough (Kiupel et al., 2011; Romansik et al., 2007). Some immunohistochemistry stains or molecular features can be requested to have more comprehensive prognostic information in ambiguous cases(Thamm et al., 2019).

The clinical appearance and stage of the MCT are also important for predicting prognosis and treatment planning(Stefanello et al., 2015).

The need to perform staging in a dog with MCT depends on a case-by-case, but the majority of dogs with MCT do not need to be staged.

MCTs usually have predictable biological behaviour and metastatic pattern, usually infiltrating the regional lymph nodes first, followed by the liver and spleen. When needed, a sufficient baseline staging can be easily performed by FNA of the regional lymph node, abdominal ultrasound and FNA of the liver and spleen or just the spleen(Brown et al., 2022; Pecceu et al., 2018).

CT scan is often not necessary, unless for surgical planning of large masses. Both ultrasound and CT scan of the liver and spleen can appear completely normal despite significant MCT infiltration. Cytology of apparently normal-looking spleen and liver is often necessary to confirm or rule out organ involvement(Pecceu et al., 2018). Thoracic radiography is rarely included in the staging of MCT, as this tumour very rarely metastasis to the lungs. However, ruling out comorbidities in the lung/heart in an old dog before going for extensive surgery is often a good idea.

For high-grade/high risks MCT adjuvant treatment, local or systemic or both are often necessary. Various local treatments can be used for incompletely resected MCTs, like scar resection, radiotherapy, electrochemotherapy or even just monitoring.

There are a few chemotherapy treatments for MCTs; vinblastine and prednisolone are probably still the most effective treatment (in particular in microscopic diseases). Other available chemotherapies like lomustine and chlorambucil, or various combinations can also be used. Tyrosine kinase inhibitors (TKI) are effective in the treatment of MCT and have been extensively studied(Weishaar et al., 2018). Both TKIs, masitinib and toceranib have similar response rates, but slightly different safety profiles.

In summary, Most MCTs will be treated and often cured just by surgical resection. Establishing which case will need staging/chemotherapy/other adjuvant treatment will depend on the accurate evaluation of multiple factors like the history, clinical appearance, grading, staging, and sometimes molecular markers or histopathology review/second opinion.

References

Brown, M., Hokamp, J., Selmic, L. E., & Kovac, R. (2022). Utility of Spleen and Liver Cytology in Staging of Canine Mast Cell Tumors. *Journal of the American Animal Hospital Association*, *58*(4). https://doi.org/10.5326/JAAHA-MS-7006

Dobson, J. M., Samuel, S., Milstein, H., Rogers, K., & Wood, J. L. N. (2002). Canine neoplasia in the UK: Estimates of incidence rates from a population of insured dogs. *Journal of Small Animal Practice*, *43*(6). https://doi.org/10.1111/j.1748-5827.2002.tb00066.x

Kiupel, M., Webster, J. D., Bailey, K. L., Best, S., DeLay, J., Detrisac, C. J., Fitzgerald, S. D., Gamble, D., Ginn, P. E., Goldschmidt, M. H., Hendrick, M. J., Howerth, E. W., Janovitz, E. B., Langohr, I., Lenz, S. D., Lipscomb, T. P., Miller, M. A., Misdorp, W., Moroff, S., … Miller, R. (2011). Proposal of a 2-tier histologic grading system for canine cutaneous mast cell tumors to more accurately predict biological behavior. *Veterinary Pathology*, *48*(1). https://doi.org/10.1177/0300985810386469

Pecceu, E., Serra, J. C., Piccinelli, C., Handel, I., Milne, E., & Lawrence, J. (2018). Poor performance of routine abdominal ultrasound in the detection of visceral metastasis in a uniform population of dogs with high-risk mast cell tumours. In *BSAVA Congress Proceedings 2016*. https://doi.org/10.22233/9781910443446.60.8

Romansik, E. M., Reilly, C. M., Kass, P. H., Moore, P. F., & London, C. A. (2007). Mitotic index is predictive for survival for canine cutaneous mast cell tumors. In *Veterinary Pathology* (Vol. 44, Issue 3). https://doi.org/10.1354/vp.44-3-335

Stefanello, D., Buracco, P., Sabattini, S., Finotello, R., Giudice, C., Grieco, V., Iussich, S., Tursi, M., Scase, T., Di Palma, S., Bettini, G., Ferrari, R., Martano, M., Gattino, F., Marrington, M., Mazzola, M., Elisabetta Vasconi, M., Annoni, M., & Marconato, L. (2015). Comparison of 2- and 3-category histologic grading systems for predicting the presence of metastasis at the time of initial evaluation in dogs with cutaneous mast cell tumors: 386 cases (2009–2014). *Journal of the American Veterinary Medical Association*, *246*(7), 765–769. https://doi.org/10.2460/javma.246.7.765

Thamm, D. H., Avery, A. C., Berlato, D., Bulman-Fleming, J., Clifford, C. A., Hershey, A. E., Intile, J. L., Jones, P. D., Kamstock, D. A., Liptak, J. M., Pavuk, A., Peauroi, J., Powell, R., Rissetto, K., Valli, V. E. O., & Webster, J. D. (2019). Prognostic and predictive significance of KIT protein expression and c-kit gene mutation in canine cutaneous mast cell tumours: A consensus of the Oncology-Pathology Working Group. In *Veterinary and Comparative Oncology* (Vol. 17, Issue 4). https://doi.org/10.1111/vco.12518

Weishaar, K. M., Ehrhart, E. J., Avery, A. C., Charles, J. B., Elmslie, R. E., Vail, D. M., London, C. A., Clifford, C. A., Eickhoff, J. C., & Thamm, D. H. (2018). c-Kit Mutation and Localization Status as Response Predictors in Mast Cell Tumors in Dogs Treated with Prednisone and Toceranib or Vinblastine. *Journal of Veterinary Internal Medicine*, *32*(1). https://doi.org/10.1111/jvim.14889

NASAL TUMOURS IN DOGS AND CATS, WHEN RADIOTHERAPY IS NOT AVAILABLE

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Nasal tumours are relatively common tumours in dogs and cats. Nasal tumours are the most common cause of chronic nasal disease and discharge in both dogs and cats (Demko & Cohn, 2007; Madewell et al., 1976; Mortier & Blackwood, 2020). In dogs, nasal adenocarcinoma is the most common tumour type followed by chondrosarcoma(Mortier & Blackwood, 2020). In cats, nasal lymphoma and carcinoma are reported as equally prevalent in some studies, while in others (as in the author's experience) nasal lymphoma is more prevalent than adenocarcinoma (Demko & Cohn, 2007; Henderson et al., 2004).

In dogs and in cats, tumours of the nasal cavities present with sneezing and chronic nasal discharge. The clinical signs progress over several weeks or a few months. Often the nasal discharge from watery becomes mucopurulent or frank epistaxis, respiratory noise and reverse sneezing are also common clinical signs.

Diagnosis is better achieved by a CT scan of the head and multiple biopsies of the mass. A biopsy can be taken blindly without rhinoscopy but guided by the interpretation of the CT scan images. The most effective treatment of nasal carcinoma in both dogs and cats is radiotherapy (Giuliano & Dobson, 2020; Mortier & Blackwood, 2020. Lymphoma in cats can be successfully treated with chemotherapy and there is no proof that radiotherapy is more effective than chemotherapy, but the combination could be superior in certain cases (Haney et al., 2009). However, radiotherapy is not available in every country or not affordable for every owner.

In cases where radiotherapy is not available, carcinoma of the nasal cavity in dogs can be treated with chemotherapy and some recent publications found certain chemotherapy regimens to be reasonably effective(Giuliano & Almendros, 2022; Woodruff et al., 2019).

Toceranib has also been investigated for nasal carcinoma and even in advanced stages toceranib could achieve a reasonably good outcome(Ehling et al., 2022; Merino-Gutierrez et al., 2021).

Cats with nasal lymphoma treated with a simple modified COP can achieve very long survival (2-3 years or more), while cats with carcinoma rarely respond and the prognosis without radiotherapy remains quite poor. Contrary to dogs, toceranib has not been investigated in cats with nasal carcinoma, but in the author's experience response is unlikely.

References

Demko, J. L., & Cohn, L. A. (2007). Chronic nasal discharge in cats: 75 Cases (1993-2004). *Journal of the American Veterinary Medical Association*, *230*(7). https://doi.org/10.2460/javma.230.7.1032

Ehling, T. J., Klein, M. K., Smith, L., Prescott, D., Haney, S., Looper, J., LaDue, T., Brawner, W., Fidel, J., Shiomitsu, K., Green, E., Saba, C., Turek, M., & Farrelly, J. (2022). A prospective, multi-centre, Veterinary Radiation Therapy Oncology Group study reveals potential efficacy of toceranib phosphate (Palladia) as a primary or adjuvant agent in the treatment of canine nasal carcinoma. *Veterinary and Comparative Oncology*, *20*(1). https://doi.org/10.1111/vco.12776

Giuliano, A., & Almendros, A. (2022). Retrospective Evaluation of a Combination of Carboplatin and Bleomycin for the Treatment of Canine Carcinomas. *Animals*, *12*(18). https://doi.org/10.3390/ani12182340

Giuliano, A., & Dobson, J. (2020). Clinical response and survival time of cats with carcinoma of the nasal cavity treated with palliative coarse fractionated radiotherapy. *Journal of Feline Medicine and Surgery*, *22*(10). https://doi.org/10.1177/1098612X19893445

Haney, S. M., Beaver, L., Turrel, J., Clifford, C. A., Klein, M. K., Crawford, S., Poulson, J. M., & Azuma, C. (2009). Survival analysis of 97 cats with nasal lymphoma: A multi-institutional retrospective study (1986-2006). *Journal of Veterinary Internal Medicine*, *23*(2). https://doi.org/10.1111/j.1939-1676.2008.0243.x

Henderson, S. M., Bradley, K., Day, M. J., Tasker, S., Caney, S. M. A., Hotston Moore, A., & Gruffydd-Jones, T. J. (2004). Investigation of nasal disease in the cat - A retrospective study of 77 cases. *Journal of Feline Medicine and Surgery*, *6*(4). https://doi.org/10.1016/j.jfms.2003.08.005

Madewell, B. R., Priester, W. A., Gillette, E. L., & Snyder, S. P. (1976). Neoplasms of the nasal passages and paranasal sinuses in domesticated animals as reported by 13 veterinary colleges. *American Journal of Veterinary Research*, *37*(7).

Merino-Gutierrez, V., Borrego, J. F., Puig, J., Hernández, A., & Clemente-Vicario, F. (2021). Treatment of advanced-stage canine nasal carcinomas with toceranib phosphate: 23 cases (2015–2020). *Journal of Small Animal Practice*, *62*(10). https://doi.org/10.1111/jsap.13387

Mortier, J. R., & Blackwood, L. (2020). Treatment of nasal tumours in dogs: a review. In *Journal of Small Animal Practice* (Vol. 61, Issue 7). https://doi.org/10.1111/jsap.13173

Woodruff, M. J., Heading, K. L., & Bennett, P. (2019). Canine intranasal tumours treated with alternating carboplatin and doxorubin in conjunction with oral piroxicam: 29 cases. *Veterinary and Comparative Oncology*, *17*(1). https://doi.org/10.1111/vco.12443

LUNG CANCERS IN DOGS, CHALLENGES, AND REWARDS

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The lung is the most common metastatic site for many primary tumours. Primary tumours affecting the lungs are not common in dogs(Lee et al., 2020; Ogilvie, Haschek, et al., 1989). The most common primary lung cancer in dogs is adenocarcinoma(Ogilvie, Haschek, et al., 1989). Another less common primary lung tumour is histiocytic sarcoma more commonly found in Welsh Corgi and Miniature Schnauzers(Kagawa et al., 2016; Purzycka et al., 2020). Primary lung cancer can present with a chronic cough lasting for a few weeks or a couple of months or can be even diagnosed incidentally on thoracic radiographies during investigations for unrelated problems. Dogs occasionally present with mild tachypnoea or dyspnoea, however, rarely are severely unwell and dyspnoeic due to pleural effusion or widespread metastases(Ogilvie, Haschek, et al., 1989).

The prognosis for lung cancer varies on the type of cancer; primary versus metastatic, carcinoma versus histiocytic sarcoma or others. For the most common lung carcinoma, specific prognostic factors are well known of which the most important are the stage, tumour volume and invasion, histological grade, differentiation and type of carcinoma (squamous cell carcinoma versus papillary carcinoma), treatment type (surgically resectable versus not, complete resection versus incomplete)(McNiel et al., 1997; Mehlhaff et al., 1984; Ogilvie, Weigel, et al., 1989).

The most effective treatment for localised lung carcinoma is surgical resection, however, this is not always possible. Chemotherapy has limited evidence of efficacy but can be used in selected cases in the adjuvant treatment of incomplete resected tumours or completely resected with multiple negative prognostic factors. The most effective treatment for localised histiocytic sarcoma is surgery followed by lomustine chemotherapy achieving a median survival time of around 15 months (Murray et al., 2022). In cases where surgery is not possible, due to the presence of multiple lesions or large/multiple lymph node metastases, chemotherapy with lomustine can achieve a high response rate despite survival remaining poor (3-4 months)(Marlowe et al., 2018). In the author's experience treatment of pulmonary advanced and unresectable histiocytic sarcoma with lomustine alternated to doxorubicin achieve much better outcomes than previously reported with only lomustine.

References

Kagawa, Y., Nakano, Y., Kobayashi, T., Asano, K., & Takagi, S. (2016). Localized pulmonary histiocytic sarcomas in Pembroke Welsh Corgi. In *Journal of Veterinary Medical Science* (Vol. 77, Issue 12). https://doi.org/10.1292/jvms.15-0284

Lee, B. M., Clarke, D., Watson, M., & Laver, T. (2020). Retrospective evaluation of a modified human lung cancer stage classification in dogs with surgically excised primary pulmonary carcinomas. *Veterinary and Comparative Oncology*, *18*(4). https://doi.org/10.1111/vco.12582

Marlowe, K. W., Robat, C. S., Clarke, D. M., Taylor, A., Touret, M., Husbands, B. D., & Vail, D. M. (2018). Primary pulmonary histiocytic sarcoma in dogs: A retrospective analysis of 37 cases (2000-2015). *Veterinary and Comparative Oncology*, *16*(4). https://doi.org/10.1111/vco.12437

McNiel, E. A., Ogilvie, G. K., Powers, B. E., Hutchison, J. M., Salman, M. D., & Withrow, S. J. (1997). Evaluation of prognostic factors for dogs with primary lung tumors: 67 cases (1985-1992). In *Journal of the American Veterinary Medical Association* (Vol. 211, Issue 11).

Mehlhaff, C. J., Leifer, C. E., Patnaik, A. K., & Schwarz, P. D. (1984). Surgical treatment of primary pulmonary neoplasia in 15 dogs. *Journal of the American Animal Hospital Association*, *20*(5).

Murray, C. A., Willcox, J. L., De Mello Souza, C. H., Husbands, B., Cook, M. R., Clifford, C., Leeper, H., Pellin, M., Richardson, D., Herrera, C. L., Krick, E., McMillan, S., Al-Nadaf, S., & Skorupski, K. A. (2022). Outcome in dogs with curative-intent treatment of localized primary pulmonary histiocytic sarcoma. *Veterinary and Comparative Oncology*, *20*(2). https://doi.org/10.1111/vco.12791

Ogilvie, G. K., Haschek, W. M., Withrow, S. J., Richardson, R. C., Harvey, H. J., Henderson, R. A., Fowler, J. D., Norris, A. M., Tomlinson, J., & McCaw, D. (1989). Classification of primary lung

tumors in dogs: 210 cases (1975-1985). *Journal of the American Veterinary Medical Association*, *195*(1).

Ogilvie, G. K., Weigel, R. M., Haschek, W. M., Withrow, S. J., Richardson, R. C., Harvey, H. J., Henderson, R. A., Fowler, J. D., Norris, A. M., & Tomlinson, J. (1989). Prognostic factors for tumor remission and survival in dogs after surgery for primary lung tumor: 76 cases (1975-1985). *Journal of the American Veterinary Medical Association*, *195*(1).

Purzycka, K., Peters, L. M., Elliott, J., Lamb, C. R., Priestnall, S. L., Hardas, A., Johnston, C. A., & Rodriguez-Piza, I. (2020). Histiocytic sarcoma in miniature schnauzers: 30 cases. *Journal of Small Animal Practice*, *61*(6). https://doi.org/10.1111/jsap.13139

FELINE INJECTABLE SITE SARCOMA

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Feline injectable site sarcoma (FISS) is a neoplastic condition affecting the subcutaneous and occasionally intramuscular tissues (Hendrick & Brooks, 1994). FISS is a relatively rare tumour with an incidence of 1-4 in 10,000 vaccinated cats in the USA and 1/16,000-50,000 in the UK(Coyne et al., 1997; Dean et al., 2013). The local chronic inflammation, initiated at the injection site, stimulates the inflammatory cells to produce numerous growth factors and cytokines that promote the neoplastic transformation of the mesenchymal cells. The tumour usually arises in the most common area of subcutaneous injection like the interscapular region or thoracolumbar area.

FISS are locally invasive tumours with a low metastatic rate (around 10-28%). The metastasis usually develops at a later stage with the lungs being the most common site(Hershey et al., 2000). Diagnosis of FISS can be achieved by cytology, but a more secure diagnosis is obtained by histopathology.
Staging will require advanced imaging, with a CT scan or MRI being the most sensitive technique for surgical planning.

The most effective treatment for FISS is a wide/compartmental surgical resection performed by an experienced skilled surgeon (Bray & Polton, 2016; Hershey et al., 2000; Rossi et al., 2019). Surgery can be curative at the first attempt, but second/third surgical resection following tumour recurrence is usually only palliative as the recurrence rate is very high. Even with the best effort and radical surgery, around 15-30% of completely resected tumours will recur locally(Hershey et al., 2000; Romanelli et al., 2008).

A multimodal treatment approach including surgery, radiotherapy, chemotherapy, and immunotherapy is likely to achieve the best outcome(Bray & Polton, 2016; Rossi et al., 2019). FISS can be prevented, and prevention is the best treatment!
Avoid any intramuscular injections and when possible, also subcutaneous injections (particularly long-acting ones). Avoid the interscapular/dorsal region.
Vaccination should be given as frequently as necessary.
Early diagnosis is the key to successful treatment. Remember the 3-2-1 rule for FISS: mass is still present three months after vaccination, it is larger than two centimetres in diameter or it is increasing in size one month after vaccination(Hartmann et al., 2015).

References
Bray, J., & Polton, G. (2016). Neoadjuvant and adjuvant chemotherapy combined with anatomical resection of feline injection-site sarcoma: results in 21 cats. *Veterinary and Comparative Oncology*, *14*(2), 147–160. https://doi.org/10.1111/vco.12083
Coyne, M. J., Postorino Reeves, N. C., & Rosen, D. K. (1997). Estimated prevalence of injection-site sarcomas in cats during 1992. *Journal of the American Veterinary Medical Association*, *210*(2).
Dean, R. S., Pfeiffer, D. U., & Adams, V. J. (2013). The incidence of feline injection site sarcomas in the United Kingdom. *BMC Veterinary Research*, *9*. https://doi.org/10.1186/1746-6148-9-17
Hartmann, K., Day, M. J., Thiry, E., Lloret, A., Frymus, T., Addie, D., Boucraut-Baralon, C., Egberink, H., Gruffydd-Jones, T., Horzinek, M. C., Hosie, M. J., Lutz, H., Marsilio, F., Pennisi, M. G., Radford, A. D., Truyen, U., & Möstl, K. (2015). Feline injection-site sarcoma: ABCD guidelines on prevention and management. *Journal of Feline Medicine and Surgery*, *17*(7). https://doi.org/10.1177/1098612X15588451
Hendrick, M. J., & Brooks, J. J. (1994). Postvaccinal Sarcomas in the Cat: Histology and Immunohistochemistry. *Veterinary Pathology*, *31*(1). https://doi.org/10.1177/030098589403100121
Hershey, A. E., Sorenmo, K. U., Hendrick, M. J., Shofer, F. S., & Vail, D. M. (2000). Prognosis for presumed feline vaccine-associated sarcoma after excision: 61 Cases (1986-1996). *Journal*

of the American Veterinary Medical Association, *216*(1). https://doi.org/10.2460/javma.2000.216.58

Romanelli, G., Marconato, L., Olivero, D., Massari, F., & Zini, E. (2008). Analysis of prognostic factors associated with injection-site sarcomas in cats: 57 cases (2001-2007). *Journal of the American Veterinary Medical Association*, *232*(8). https://doi.org/10.2460/javma.232.8.1193

Rossi, F., Marconato, L., Sabattini, S., Cancedda, S., Laganga, P., Leone, V. F., & Rohrer Bley, C. (2019). Comparison of definitive-intent finely fractionated and palliative-intent coarsely fractionated radiotherapy as adjuvant treatment of feline microscopic injection-site sarcoma. *Journal of Feline Medicine and Surgery*, *21*(2). https://doi.org/10.1177/1098612X18758883

Gillian Dank (Israel)

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Gillian Dank, DVM, is a board certified veterinary oncologist and senior lecturer at the Koret School of Veterinary Medicine, Robert H. Smith Faculty of Agriculture, Food and Environment of the Hebrew University of Jerusalem. She earned her Doctor of Veterinary Medicine from the Koret School in 1998 and completed her residency in oncology at the University of California, Davis in 2002.

Dr. Dank is a Diplomate of the American College and European College of Veterinary Internal Medicine – Oncology, with research interests in clinical small animal oncology, the study of Procalcitonin C in canines, and the effects of passive smoking on pets.

Dr. Dank established the Oncology Department at the Veterinary Teaching Hospital, where she pursues research and lectures in basic and clinical oncology to veterinary students during their clinical and preclinical training. The Koret School of Veterinary Medicine was founded in 1985, and is Israel's only veterinary school.

DIAGNOSING LUMPS IN THE CLINIC: DIY TIPS
(AND A PEEK AT THE FUTURE)

Gillian Dank, DVM, D-ACVIM, D-ECVIM-Ca

Lumps

Many of the dogs that you see on a daily basis present to you because of " lumps and bumps". These lumps and bumps can vary widely in the size and severity.

So what kinds of cases do we all see in the clinics?

1. Dogs with very astute owners we can see masses that they found yesterday and are a few mm and already causing them stress
2. Dogs with very large masses they have been there for weeks to months

The first thing one should do is a complete history. The critical questions that we need to ask are: How long has the mass been there? When did you first notice it? How much has it changed since you first saw it? Has the consistency changed? Is it more firm? Warm? Painful?Has the size changed? Does your dog know it is there? Does the mass bother your dog? Itch? Cause lameness or pain? Previous masses in the history that were surgically removed? All of these questions are critical for us to have the full picture.

Critical points for a dog with a mass on physical exam include measuring (in cm) all of the masses that you find and the location, the location (dermal or SC, where on the body), is there hair on the mass, is it ulcerated, firm or soft, well circumscribed or not, ulcerated or not. In addition, it is important to describe any enlarged lymph nodes.

We then have a problem list and a list of differential diagnosis based on the problem list. The problem list is the mass- which may include any or all of the following:

1. Cysts- both sebaceous and fluid filled
2. Abcess
3. Scar tissue
4. Cancer- which can either be benign or malignant

The next step is to diagnose the tumor and NOT to watch it grow. Diagnosis can be either an aspirate or biopsy. The advantages of an aspirate are that it is relatively quick, relatively easy to do, low risk, inexpensive and it provides in house screening. The limitations are the ability to get a diagnostic sample. (60-80% depending on the publication). In addition, there may be cases with false positives due to inflammation. Biopsies have the advantage of seeing the architecture of the tissue. However, they are more invasive and expensive. They also require general anesthesia.

Critical Questions that can help you decide on whether

Factors that can affect your ability to diagnose-

1. The location of the mass- Is it easy to get do? Will the animal require sedation?
2. The owners -how much will the test cost
3. What are the results of the test going to change anything??

There are two ways to perform fine needle aspirates: the needle jab and with aspiration. After the aspiration we apply them to the glass slides, pull apart and try to have a good monolayer of cells; air dry; stain. Using thin plastic to for a top layer can help get better slides. It is rare to see complications, but they may include seeding of tumor along biopsy track, hemorrhage, infection, and pneumothorax. In is a very good idea to stain one slide BEFORE you send it to the lab to make sure you are submitting a cellular sample. If it is not cellular, try to resample. If you only red blood cells- resample. If you only see inflammation and you really think it is a tumor- resample. If the cells are all ruptured- the lab won't get an answer either. If there is a lot of inflammation- the inflammation can change the epithelial and mesenchymal cells to look atypical= false positive.

Indications for malignancy include anisocytosis, anisokaryosis, high N/C ratio, nucleoli mitotic figures, and multinucleated cells.

In cases if inflammation we will see neutrophils, macrophages, eosinophils, lymphocytes, plasma cells, mast cells. We may also see etiologic agents including bacteria and fungi. If there is a mass with no indication of inflammation it is most likely neoplasia, which can be either benign or malignant. There are three typed of cancers based on cytology:

- Epithelial tumors of the glandular or parenchymal tissues that are called Adenoma (benign) , carcinoma, or adenocarcinoma (malignant) . They have a round to oval nucleus with clusters or sheets of cells that are round to polygonal. The cytoplasmatic borders are often indistinct because of cell-to-cell adhesions. They exfoliate well on FNAs.
- Mesenchymal tumors of the connective tissue that are sarcomas. The nucleus – oval or elliptical and the cells usually exfoliate individually. The cell shape is oval, stellate, or fusiform. The cytoplasmic borders are indistinct. The benign tumors are = -oma for example- Lipoma. The malignant are sarcoma, for example- fibrosarcoma. The sarcomas can be split into two groups: Typical Sarcomas=Soft tissue sarcomas that share a similar biological behavior, including that they are slow growing, have Octopus or tree roots and the majority of these tumors only require local control. The most important prognostic indicator is grade. Atypical Sarcomas include osteosarcoma and hemangiosarcoma, and they are both locally aggressive AND systemically aggressive and require staging BEFORE surgery.
- Round cell tumors have a round to indented nucleus, individual cells, roundish in shape. The cytoplasmic borders are distinct and they exfoliate well. The five round cell tumors include lymphoma (systemic disease with systemic treatment), mast cell tumor (most are surgical and require local control) , TVT(most are cured with vincristine), Histiocytic tumors and Plasma cell tumors.

Malignant melanoma can look like round cells, carcinomas and sarcomas.

In conclusion- Be proactive, don't wait and see. Perform in house cytology as it can help you increase chance of diagnosis because you can make sure you are sending good samples. Measure and Map all of the tumors that you see, and remember that most tumors are cured with surgery alone(but that surgery plan depends on the tumor type!! Therefore- newer tools may help us make better decisions.

TUMORS IN THE PERINEAL AREA

Gillian Dank, DVM, D-ACVIM, D-ECVIM-Ca

The perineal area contains several glands and structures.
The definition of perianal is circumanal- located in the dermis in a circular fashion around the anus and also scattered in areas on the prepuce, tail, pelvic limbs and trunk.
The tumors in this area include:

1. The perianal glands, also referred to as hepatoid glands because the cells resemble hepatocytes
   a. Perianal sebaceous adenoma
   b. Perianal sebaceous adenocarcinoma
2. Anal Sacs- blind cutaneous diverticula at 4 and 8 o'clock
   a. Apocrine gland anal sac adenocarcinoma
   b. Additional tumors from the anal sac
      i. SCC
      ii. Melanoma
3. Other cutaneous or SC tumors in the perineal area-
   MCT, STS, SCC, HMS, lymphoma, melanoma, leiomyoma, TVT

Anal sac adenocarcinoma (AGASAC) is an uncommon tumor in the dog and comprises approximately 17% of perianal malignancies; however, it is one of the most common causes of paraneoplastic hypercalcemia.
Clinical signs in affected dogs most commonly are associated with mechanical obstruction caused by the primary tumor or enlarged regional metastatic lymph nodes and the effects of paraneoplastic hypercalcemia when present.
Surgical excision of the primary tumor **and** metastasectomy of affected locoregional lymph nodes is the preferred initial treatment option for most dogs, although radiation therapy and adjuvant chemotherapy are commonly incorporated into multi-modality treatment plans.
Prolonged survival times are possible, especially for dogs with smaller primary tumors and for dogs that undergo further treatments for recurrent disease.
In this lecture, we will discuss the clinical signs, diagnosis, staging, treatment, and prognosis of AGASAC in the dog

Ophthalmology

James Oliver (UK)
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(Ophthalmology)

James graduated from the University of Bristol with distinction in 2002. He spent 5 years in general practice where he developed his passion for veterinary ophthalmology. He achieved European Specialist status in 2011 and has worked as a Specialist in several referral hospitals in the UK and currently heads up a team of nine ophthalmologists at Dick White Referrals. James has extensive experience in research, is widely published in the scientific literature and has completed a PhD in the genetics of canine glaucoma.

His main research interest is the genetics of inherited eye diseases which is focussed on developing DNA tests to eliminate painful and blinding eye conditions of dogs and cats. James has also written a book on feline ophthalmology and has made contributions to other textbooks on various aspects of veterinary ophthalmology. He is actively involved in the teaching and training of vets in their pursuit of improved understanding and post graduate qualifications in this field. James is past Chair of the European College of Veterinary Ophthalmologists' Education and Residency Committee.

Feeling the pressure: definitions & causes of glaucoma

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The term *glaucoma* encompasses an array of different ocular diseases which are united in the presence of pathologically elevated intraocular pressure (IOP) which results in retinal ganglion cell (RGC) death and visual deficits. Normotensive glaucoma, in which progressive RGC death continues without detectable elevations in IOP, has been documented in humans but not yet in animals. Thus, IOP is a consistent risk factor for glaucoma. The pathophysiology behind IOP elevations and elevated IOP is damaging for several reasons. Firstly, it causes direct damage to the optic nerve (which is made up of RGC axons) which clinically is manifested as optic nerve head cupping. Elevations in IOP also lead to reduced perfusion of the optic nerve head and ischaemia, loss of RGC axonal transport of trophic factors, amino acid excitotoxicity, gliosis and mitochondrial destabilisation. Thus, glaucoma can be considered, not only to be a neuropathy, but also a vasculopathy and gliopathy. Maintenance of IOP is a delicate balance between aqueous humour (AH) production by the ciliary body and drainage via the conventional (trabecular meshwork) and non-conventional (uveoscleral) pathways. Therefore, theoretically, elevation in IOP may occur if there is either an increase in the rate of AH production or a reduction in the rate of AH drainage. However, in practice, only interruptions in AH flow and drainage have been documented to cause IOP elevations. Identifying the locations of these interruptions by asking yourself the question 'where is the block?' is key to therapeutic success and will be illustrated using various case examples.

Traditionally, glaucoma is classified as being either primary or secondary. In primary glaucoma, there are pre-existing anatomical abnormalities in the AH outflow pathways which may either be congenital or acquired, or a combination of the two. Primary glaucomas are generally further subdivided into two main forms: primary open angle glaucoma (POAG) and primary closed angle glaucoma (PCAG) based on the gonioscopic appearance of the iridocorneal angle (ICA). A further type of primary glaucoma which is also occasionally documented in dogs and cats is primary congenital glaucoma. Secondary glaucoma occurs when there is an identifiable pre-existing intraocular disease process which, in turn, leads to an interruption in AH flow and drainage. Examples of secondary glaucoma include anterior uveitis, lens luxation, intraocular haemorrhage and neoplasia.

Feeling the pressure: clinical signs & diagnostic techniques in glaucoma

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The signs of glaucoma vary according to the onset of disease (acute vs chronic), degree of IOP elevation, cause (primary vs secondary) and location of the interruption to AH flow and drainage. Enlargement of the globe (buphthalmos or hydrophthalmos) tends to occur when there is a gradual increase in IOP in conjunction with a relatively elastic sclera and cornea as occurs with congenital glaucoma and POAG. As a result, the sclera becomes thinner and staphylomas may develop. Elevations in IOP cause damage to the corneal endothelial cells and Descemet's membrane which can cause corneal oedema and Haabs striae. Mydriasis is common to most forms of glaucoma as a result of damage to the optic nerve (lack of sensory input) and damage to the iris sphincter muscle (reduction in ability of pupil to constrict). When anterior uveitis is present, however, mydriasis may not be a feature. Unsurprisingly, as the traditional definition of glaucoma include RGC death, visual deficits form arguably the most important clinical sign associated with disease.

The three mainstays in glaucoma diagnosis in animals are tonometry, gonioscopy and ophthalmoscopy and I will discuss all these in turn. Of these, I will pay particular attention to gonioscopy as this technique is usually less familiar to clinicians and has formed a large part of my research. Furthermore, gonioscopy forms an important part of Hereditary Eye Disease screening including the ECVO HED Scheme. Other, arguably more sophisticated techniques, are gaining more interest in researching veterinary ophthalmologists and include ultrasound biomicroscopy, high resolution ultrasound and optical coherence tomography and will also be discussed briefly.

Releasing the pressure: glaucoma treatment with case examples

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Treatment of glaucoma in dogs and cats has come on in leaps and bounds over the last two decades. However, veterinarians are still heavily reliant on using therapeutics developed for the counterpart disease in human patients which may not be as efficacious in veterinary species. No therapeutics have been specifically developed with canine and feline glaucoma in mind. Furthermore, surgical treatments of glaucoma are quite extensive and successful in human patients but much more limited and less successful in canines. This is due in part to delays in presentation as well as differences in the underlying pathological mechanisms and, indeed, ocular anatomical species differences. I will spend the majority of time discussing topical medical therapy for glaucoma in dogs and cats and a relatively more brief amount of time on surgical treatments of glaucoma and namely endocyclophotocoagulation (ECP) and gonioimplantation.

Ocular hypotensive agents
Hyperosmotic agents
These include mannitol and glycerol but only mannitol is used with any significant frequency in veterinary medicine. Hyperosmotic agents increase the osmotic pressure of the plasma to a level greater than that of the aqueous and vitreous humours. The resultant osmotic gradient leads to a decrease in aqueous humour ultrafiltration and a loss of water from the vitreous. The loss of vitreous volume also results in posterior movement of the iris-lens diaphragm which leads to opening of the iridocorneal angle and enhancement of aqueous humour outflow. In veterinary ophthalmology, the only indication for these drugs is in acute glaucoma. **Mannitol** is a high molecular weight sugar available for IV administration as a 20% solution. A dose of 1-2g/kg is injected over 20-30 minutes in association with 4-6 hours of water deprivation. IOP reduction occurs after 15 minutes and the effect may last for around 6 hours. The use of mannitol in veterinary ophthalmology has become less common since the availability of topical prostaglandin analogues which have potent IOP-lowering effects.

Adrenergic agents
Both β-blockers and α_2-agonists can have IOP lowering effects but only β-blockers are used with any real frequency to reduce IOP in dogs and cats.
α_2-agonists
Apraclonidine (Iopidine™) is very occasionally used to help reduce IOP in dogs when all other conventional medical therapy has been exhausted. Bradycardia may occur in some individuals and so manual occlusion of the proximal nasolacrimal apparatus is advised during and for at least one minute following application should be considered. Pulse/heart rate should be monitored for 30 minutes following first usage and, occasionally, reversal of the drug with a systemic anti-adrenergic (atipamezole) is required. Apraclonidine should not be used in cats owing to the frequency of side effects (bradycardia and vomiting) associated with its administration.
β-blockers
The exact IOP-lowering mechanism of action of β-blockers is unknown but three possibilities have been suggested:
1. Blockade of the β-receptors of the ciliary body epithelium results in reduced activation of adenylate cyclase which leads to a reduction in cAMP formation and ultimately in AH formation

2. Inhibition of Na+/K+-ATPase activity leading to a reduction in AH formation
3. They may exert a vasoactive effect and increase AH outflow

Systemic side effects of β-blockers are significant and relate to effects on the cardiovascular and pulmonary systems. These drugs should not be used in patients with heart block, bradycardia, heart failure, asthma or chronic bronchitis. They should be used with caution in cats and small dogs.

Timolol. Timolol is a non-selective β-blocker and is available as 0.25% and 0.5% ophthalmic solutions (Timoptol™). It is also available as a 0.5% solution in combination with 1% brinzolamide (Azarga™), 2% dorzolamide (Cosopt™) and 0.004% travoprost (DuoTrav™). These combinations allow the potential for additive IOP-lowering effects. Combined dorzolamide/timolol appears more effective at reducing IOP in glaucomatous dogs than either drug used alone. 0.5% timolol reduces IOP by around 15% in normal dogs and around 20% in normal cats in association with a reduction in pupil size in both species. This drug is most effective when used every 6-8 hours but the risk of side effects in smaller patients is significant.

Levobunolol. Levobunolol is also a non-selective β-blocker and appears to have similar efficacy to timolol and is available as a 0.5% ophthalmic solution (Betagan™).

Betaxolol. Betaxolol is a β_1-blocker and its specificity theoretically results it a reduction in undesirable pulmonary side effects. It has been used in dogs to delay onset of primary glaucoma as a 0.5% solution given twice daily.

Cholinergic agonists

These parasympathomimetics work either by stimulating cholinergic receptors at the post-synaptic junction by mimicking ACh (direct-acting) or inhibit the breakdown of ACh by acetylcholinesterase at the post-synaptic junction (indirect-acting).

Pilocarpine. Pilocarpine is a direct-acting cholinergic agonist. It is available as an ophthalmic solution in a number of concentrations (0.5%-8%). Pilocarpine is rarely used as a standard treatment for glaucoma in cats and dogs. It can cause significant ocular irritation and undesirable systemic side effects such as vomiting and diarrhoea. It also causes pronounced miosis and should not be used in patients with secondary glaucoma resulting from inflammation or anterior lens luxation. The main therapeutic use of this drug in veterinary ophthalmology is in the treatment of neurogenic KCS. Pilocarpine stimulates tear secretion by mimicking ACh at the effector lacrimal cell therefore is useful when functional lacrimal tissue exists in the face of parasympathetic denervation. For KCS, it is usually administered orally at a dose of 1 drop of 1% pilocarpine per 10kg bodyweight given twice daily in the food. The dose can be increased very gradually until tear production improves but should be decreased or stopped if there are signs of toxicity (e.g. urinary incontinence, diarrhoea, emesis). Some ophthalmologists advocate the use of topical pilocarpine (e.g. 0.1% in hypromellose qid) to treat neurogenic KCS but its benefit has not been proven.

Carbachol. Carbachol is a direct-acting cholinergic agonist and is available as 0.75%-3% ophthalmic solutions but its main use in dogs relates to its intracameral injection at the conclusion of phacoemulsification cataract surgery. Injection of 0.5ml of 0.01% carbachol (Biochol™) into the anterior chamber at the conclusion of cataract surgery is associated with a reduction in the occurrence and degree of postoperative ocular hypertension.

Carbonic anhydrase inhibitors (CAIs)

Carbonic anhydrases (CAs) are found throughout the body with seven iso-enzymes existing. CAII is the predominant form within human ciliary processes being found within the cytosol. Membrane-bound CAIV is also found within the mammalian eye. CAs catalyse conversion of carbon dioxide and water to bicarbonate and hydrogen ions. This process occurs within the ciliary process and the resultant bicarbonate ions are transported with sodium ions into the posterior chamber. Water follows the osmotic gradient created resulting in the formation of aqueous humour. Use of carbonic anhydrase inhibitors is thus associated with a reduction in aqueous humour formation and thus IOP. Although systemic formulations of CAIs exist (e.g.

acetazolamide and methazolamide), they are rarely used in veterinary ophthalmology owing to their systemic side effects which include metabolic acidosis (through urinary excretion of bicarbonate), gastrointestinal irritation, blood dyscrasias (chronic use), fatigue and anorexia. The most commonly used topical ophthalmic CAIs in veterinary ophthalmology are dorzolamide and brinzolamide.

Dorzolamide. Dorzolamide is available as a 2% ophthalmic solution on its own (Truspot™) and in combination with 0.5% timolol (Cosopt™). It has a pH of 5.6 and can be irritating. It has good corneal penetration owing to its alternating diphasic forms (allowing for both lipid and water solubility). 2% dorzolamide reduces IOP of normal canine eyes by up to 20% starting 30 minutes after application and lasting for 6 hours. It is usually administered every 6-8 hours. 2% dorzolamide also significantly reduces IOP in normal cats and those with congenital glaucoma.

Brinzolamide. Brinzolamide is available as a 1% solution on its own (Azopt™) or in combination with 0.5% timolol (Azarga™). The pH of 1% brinzolamide solution is 7.5 and thus tends to be less irritating than dorzolamide. It appears to be more effective at lowering IOP in man as a result enhanced affinity for CAII. In dogs, brinzolamide has a similar level of efficacy to dorzolamide but, in cats, it appears to be less effective at reducing IOP.

Prostaglandin analogues

As discussed previously, prostaglandins (PGs) are mediators of inflammation. The chemically modified PG, $PGF_{2\alpha}$ has been developed as an ocular hypotensive agent. Various prodrug formulations of $PGF_{2\alpha}$ have been designed to provide enhanced lipid solubility and corneal penetration. The prodrug is hydrolysed to the active form (17-phenyl-$PGF_{2\alpha}$ for most drugs) as it passes through the corneal epithelium by resident corneal esterases. Reduction in IOP is mediated by PG interaction with prostanoid FP receptors. In primates, these receptors are present within the ciliary and iris sphincter muscles and within the trabecular meshwork. PG analogues are generally thought to be ineffective in reducing IOP in cats owing to the absence of prostanoid FP receptors in the feline ciliary muscle and outflow pathways although a recent study has shown efficacy of topical latanoprost in cats with primary congenital glaucoma. Long-term use of PG analogues is thought to increase uveoscleral outflow by remodelling of the ciliary muscle extracellular matrix by activation of matrix metalloproteinases which degrade collagen. There may be a similar long-term effect on the trabecular meshwork resulting in an increase in conventional outflow. Side effects in man include iris darkening, increased eyelid pigmentation and conjunctival hyperaemia. All PG analogues have the potential to incite or exacerbate anterior uveitis and these drugs are contraindicated. These drugs cause significant miosis (in dogs and cats) and their use is contraindicated in the presence of anterior lens luxation.

Latanoprost. Latanoprost is available as a 0.005% solution (Xalatan™). It is a potent ocular hypotensive in dogs reducing IOP by around 40% in normal eyes. The main side effects are miosis and conjunctival hyperaemia. Latanprost is usually administered every 8-12 hours.
Travoprost. Travoprost is available as a 0.004% solution (Travatan™) and is also available in combination with 0.5% timolol (DuoTrav™). It has very similar efficacy and side effects as latanoprost.

Drug	Dosage	Main indications	Side effects	Contraindications
Hyperosmotics: Mannitol (10% and 20%)	Dogs: 1-2g/kg IV over 20-30 min (10-20ml/kg of a 10% solution)	Acute glaucoma in dogs	Fluid and electrolyte disturbance Acute renal failure	Congestive heart failure Pulmonary oedema Anuric renal failure

PG analogues: Latanoprost (0.005%) Travoprost (0.004%)	Dogs: 1 drop in eye q8-24h	Acute primary glaucoma and chronic glaucoma in dogs	Conjunctival hyperaemia Miosis Blood-aqueous barrier disruption	Uveitis Anterior lens luxation Ineffective in most cats
CAIs: Brinzolamide (1%) Dorzolamide (2%)	Dogs and cats: 1 drop in eye q8-12h	All types of glaucoma in dogs and cats Brinzolamide ineffective in normal cats but effective in glaucomatous cats	Local irritation may be greater with dorzolamide (pH 5.6) than brinzolamide (pH 7.5)	Severe hepatic or renal insufficiency
B-blockers: Timolol (0.25% and 0.5%	Dogs: 1 drop in eye q8-12h Cats: 1 drop in eye q12h	All types of glaucoma in dogs and cats	Miosis Conjunctival hyperaemia Local irritation Bradycardia Hypotension	Uveitis Anterior lens luxation Heart failure Asthma

Table 4. Anti-glaucoma drugs commonly used in cats and dogs (Oliver and Smith 2014)

Prevention is better than cure: selective breeding and DNA testing to reduce glaucoma prevalence

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Owing to the breed predispositions of the primary glaucomas, an inherited basis is implied. In all forms of canine POAG reported, inheritance follows an autosomal recessive pattern and breed-specific mutations in *ADAMTS10* and *ADAMTS17* genes have been documented which allow for eradication of the diseases by DNA testing and selective breeding. Inheritance of PCAG appears to be complex in most breeds. This means that multiple genetic mutations, and perhaps environmental factors, may interplay to bring about disease. Identification of the genetic causes of PCAG is therefore more difficult and disease eradication, in most breeds, is based on selective breeding based on serial gonioscopic examinations in predisposed breeds. An exception to this is the Border Collie, in which a mutation in *OLFML3* has been strongly associated with both pectinate ligament abnormality and PCAG in two separate studies and a DNA test can be used to reduced disease prevalence.

Letting the cat out of the bag: demystifying feline eye diseases & Hidden in plain sight: systemic diseases masquerading as eye problems in the cat

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I will spend the first of the feline ophthalmology talks discussing those ocular diseases which are reasonably unique to cats and the second on ocular manifestations of systemic diseases in the cat. Veterinary ophthalmology textbooks have traditionally, and understandably, focussed their attention on diseases and treatment of diseases of the canine eye with little space or details devoted to that of the cat. In our textbook, Feline Ophthalmology – The Manual, we attempted to right this wrong. Congenital, inherited, infectious and inflammatory pathologies of the feline eye and ocular manifestations of feline systemic disease must be understood as they pertain specifically to the feline eye and cannot simply be extrapolated from the dog. In the first talk, those fairly specific feline ocular disease will be covered in logical tissue based sequence (adnexa, ocular surface, uvea, fundus etc.) and will include eyelid agenesis, squamous cell carcinoma, FHV-1 associated ocular disease, corneal sequestration, eosinophilic keratitis, acute bullous keratopathy, idiopathic anterior uveitis, diffuse iris melanoma, intraocular sarcoma and progressive retinal atrophy. The talk will be largely image-based to familiarise you with how they clinically present because once these diseases have been seen, they are rarely forgotten which will improve disease recognition in primary care practice. In the ocular manifestations of systemic disease talk, I will go through a number of conditions which commonly are referred as ophthalmological problems but subsequent investigation reveals an underlying causative systemic disease process. This talk will be illustrated with a number of cases to demonstrate how such cases may be a approached in the specialist setting. As time is limited, I have cherry picked a few of my favourite diseases and presenting conditions and these will include epiphora and uveitis (infectious and neoplastic). A significant proportion of those cats that present with blindness are subsequently found to have a systemic problem. I will cover systemic hypertension, examples of some toxic and dietary retinal degenerations as well thromboembolic chorioretinal necrosis and examples of CNS blindness.

How to 'see your way through': an approach to blindness in cats and dogs

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We will start by going through the pertinent parts of the ophthalmic examination when confronted with a dog or cat presenting with visual deficits. In particular, I will spend some time on the neuro-ophthalmic examination to include its components, practical use along with interpretation especially with respect to lesion localisation. In some cases, examination alone, is sufficient to obtain an aetiological diagnosis. However, with some retinal and all central nervous system (CNS) causes of blindness, further investigations are required often which require referral to a specialist with appropriate instrumentation. I will therefore discuss the principles of electroretinography (ERG) and magnetic resonance imaging (MRI). I will then summarise the main causes of blindness before presenting several case examples of dogs and cats which presented with visual deficits and how investigations into the causes were performed along with treatment and patient outcomes.

Orthopedics

Mike Farrell (United Kingdom)

BVetMed CertVA CertSAS Dip ECVS, EBVS and RCVS Specialist in Small Animal Surgery
(Orthopedics)

Mike Farrell graduated from the Royal Veterinary College in 1997 and completed internships at Bristol and Edinburgh Universities. He's worked in the UK and Australia as a general practitioner and in the USA and Switzerland as a veterinary anaesthetist.

Mike completed a surgery residency at Glasgow University in 2006 and gained his European Diploma in Small Animal Surgery in 2007. He's an EBVS and RCVS board certified specialist in small animal surgery. Mike's open access educational YouTube channel, www.youtube.com/vetlessons, helps veterinary practitioners and animal lovers make difficult choices for their pets.

THE PERFECT CONSULT: SHARED DECISION-MAKING

Mike Farrell BVetMed CertVA CertSAS DipECVS MRCVS

In this lecture, we'll discuss the decision-making models used in human and veterinary healthcare. Find up to date resources here.

THE PERFECT CONSULT: UNDERSTANDING RISK

Mike Farrell BVetMed CertVA CertSAS DipECVS MRCVS

In this lecture, we will talk about the best ways to tell caregivers about the pros and cons of different treatments. Find up to date resources [here](#).
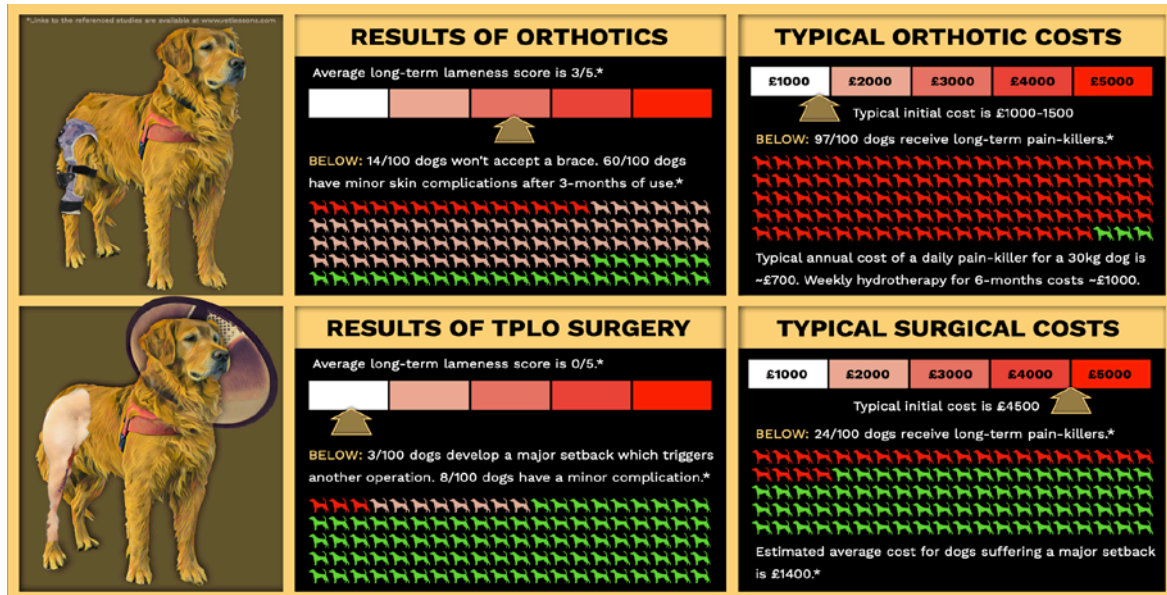
THE PERFECT CONSULT: ORTHOPAEDIC EXAM

Mike Farrell BVetMed CertVA CertSAS DipECVS MRCVS

In this lecture, I'll teach you how to perform and interpret a specialist orthopaedic exam. Find narrated videos here.

THE RISKS AND BENEFITS OF NEUTERING

Mike Farrell BVetMed CertVA CertSAS DipECVS MRCVS

Here are the 5 key questions I'll answer:

1. What's the impact of neutering dogs on lifespan?
2. Are neutered dogs more or less likely to develop cancer?
3. Does neutering increase the risk of joint disease?
4. Are neutered females likely to develop incontinence?
5. Does castration improve undesirable behaviours?

Find the lecture course here.

FIGHTING THE CANINE OBESITY EPIDEMIC

Mike Farrell BVetMed CertVA CertSAS DipECVS MRCVS

The obesity epidemic is harming our pets just as much as it's harming us. In other words, too many pet dogs are overweight, which puts them at an increased risk of developing cancer, osteoarthritis, and several other serious diseases. Find up to date resources [here](.).

LOWERING RISK IN TRAUMA SURGERY

Mike Farrell BVetMed CertVA CertSAS DipECVS MRCVS

In this lecture, I'll teach you how to lower the risk of complications during and after companion animal trauma surgery. Find up to date resources here.

THE TRUTH ABOUT ELBOW DYSPLASIA

Mike Farrell BVetMed CertVA CertSAS DipECVS MRCVS

The truth about elbow dysplasia is currently buried under a mountain of myths, misinformation and half-truths. In this lecture, I'll discuss what specialists do and don't know about this important condition. Find up to date resources here.

TPLO VERSUS TTA

Mike Farrell BVetMed CertVA CertSAS DipECVS MRCVS

In this lecture, I'll discuss the history of canine ACL surgery, and review the published evidence comparing two of the most popular treatment options. Find up to date resources [here](#).

SURGICAL OPTIONS FOR HIP DYSPLASIA

Mike Farrell BVetMed CertVA CertSAS DipECVS MRCVS

In this lecture, I'll discuss the non-surgical and surgical options for the commonest canine orthopaedic condition, hip dysplasia. Find up to date resources [here](#).

Reproduction

Xavier Lévy (France)

DVM, PhD, Dipl. ECAR
(Reproduction)

Dr Levy started his specialisation by an intership in dog and cat internal medicine and surgery in Alfort Vetschool in 2003. Then, he did his residency in reproduction and in parallel be involved as a clinician in urology-nephrology in the medicine department of Alfort vetschool until 2007.

In 2006, he became the head of CERCA (Center of Research and Clinics in Small Animal Reproduction, ENVA). In 2007, he became ECAR diplomate.

He was in the Board of European Society for Small Animal Reproduction (EVSSAR) from 2010 to 2016.

Dr Levy is Past-president of the French Veterinary Society of Small Animal Reproduction, Breeding and Genetics from 2012 to 2018 (GERES, AFVAC).

Since 2019, Dr Levy is elected as vice-president of European and International affairs of French Veterinary Society (AFVAC). Dr Levy is the French representative of FAFVAC, FECAVA and WSAVA associations.

Since 2004, Dr Levy is involved in a breeding program in wildlife for cheetah in South Africa started by the CRESAM society. He contributed actively to develop the first technique of non-invasive intra uterine insemination for wild felids: cheetah, leopard, tigers and lions. Since 2011, he is co-head of the scientific committee of CRESAM society. Dr Levy is also involved in clinical research as schedule C-section, prostatitis diagnosis, BPH blood markers (ODELIS CPSE® test), paediatric surgery and breeding soundness. Since 2008, Dr Levy is co-heading the Private Centre of Small Animal Reproduction and Paediatrics (CRECS) and since 2023, he is also the director of the Reproduction development for FOVEA company.

Dr Levy is still very involved in vetenarian education through a website (www.vetreproduction.com), teaching in European vet schools, and regular lectures/workshops in France, Europe and overseas.

INTERPRETATION OF HORMONE ANALYSIS IN PRACTICE (PROGESTERONE, ETC.)

Xavier Lévy, DVM, ECAR dipl.
CRECS – contact@clinvetdugers.fr

The method of analysis: a crucial factor

The interpretation of progesterone concentration is related to the method of evaluation. Semi-quantitative ELISA kits are commercially available for use in the clinic, and allow estimating progesterone in canine serum. Nevertheless, some semi-quantitative assay (K9 Proges-check, Premate test and Minireader®) may lead to mistake of ovulation date determination by false-positive and false-negative results (limitations to the sensitivity of ELISA testing) or gap quickly between the observed colours and the interpretation which is made (Target Canine Ovulation without, no internal control). In our experience, semi-quantitative tests might be used: in case of repeated mating but should be avoid for chilled/frozen/poor sperm quality AI; to determine the P4 drop a time of parturition. Quantitative tests with accurate measurements of progesterone concentrations (P4) are nowadays available in many veterinary diagnostic laboratories and in-clinic laboratories (electrochemiluminescence technology). The quantitative assays have the advantage to be more precise and to allow the veterinarian to limit to best the number of visits realized to determine the timing of ovulation. Nevertheless, the application of a quantitative assay supposes to master the automat-slope of P4 around ovulation, diestrus and before parturition. It is important to know the slope for each automat use in your practice (see below).

How to interpret progesterone during heat follow-up

Interpretation must be based mainly on the rise of the P4 (slope of the curve) and not only on the values obtained. Mainly because of individual variations of P4 at time of ovulation, and because of automats intra-assay and inter-assay variations (significant with all automats during estrus = low progesterone variations). In bitches, there is a luteinization of the follicles in the days preceding ovulation (onset of the LH surge/peak). This leads to a gradual increase from basal to non-basal P4. Then after a period of 2 to 4 days, the values increase very significantly (x3 to x4) after ovulation is completed. Thus, the higher is the slope of the progesterone concentration curve, the better is the interpretation. Because of diurnal variation of P4, it is also recommended to collect the blood sample at the same time of the day (particularly for pregnancy follow-up, see below) Therefore, in our practice, a sloping curve is more reliable than a flattened curve where low result variations express large physiological differences (and day of ovulation and ideal mating-dates) (see graphic 2). Delay between LH surge/peak and ovulation is around 2-4 days, ovulation and ideal insemination day 2-4 days. In addition, 2/3 of bitches are ovulating around 10 to 15 days of heat. Therefore, a first blood sample should be performed at 5 to 8 days of heat, then every 3 to 4 days if basal value, and every other day at time of LH surge. 3 to 4 samples are necessary in average to determine the best days of insemination/mating.

NB: a rise of P4 doesn't discard an ovarian cyst that may lead to infertility. An ultrasonography and/or estradiol serum concentration must be performed in case of follicular cyst hypothesis (infertility, prolonged estrus, etc.). A clinical case will detail estradiol interpretation during estrus. Estradiol should be basal at time of ovulation (< 60 pmol.l). Analysis must be run only in vetlab: a plasmatic interference may lead to false-positive results in dog species, vetlab take it into account at time of analysis.

	Basal value (no significant concentration or variation)	LH surge/peak ng/ml *	Ovulation ng/ml	24 hours after ovulation ng/ml
AIA 360™ Tosoh© Elecsys™ Roche©	< 2	2 – 4	5 - 10	10 - 20
Speadreader™ Virbac® Minireader™ Minitube©	< 2	2 - 5	4 - 10	
Minividas™ Biomérieux©	< 3	3 - 6	10 - 15	18 – 25

Figure 1: interpretation of progesterone concentration during estrus in the bicth
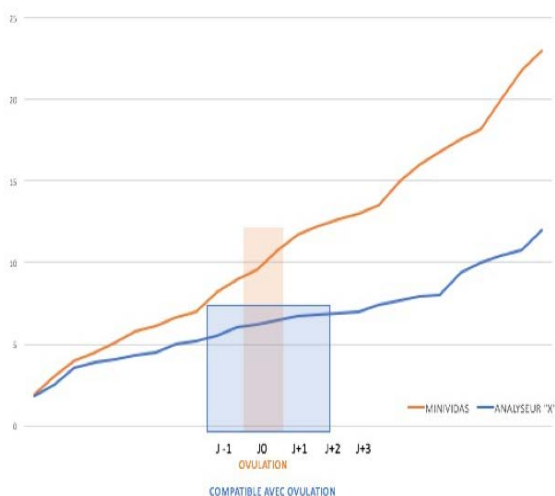**1 ng/mL= 1 pg/µL=3.18 nmol/l*

Figure 2: Influence of the automat for the interpretation and the precision of ovulation determination

How to interpret progesterone during pregnancy

After ovulation, corpora lutea develop on the ovaries within the ruptured follicular cavities, resulting in a cell population capable of synthesizing and secreting progesterone during pregnancy. The maximum progesterone synthesis from the corpora lutea is usually achieved 10 to 20 days after ovulation, At this time, P4 concentration varies widely among bitches. Anyway, during this period (10- 25 days post-ovulation) P4 must be from 25 ng/ml to more than 80 ng/ml. Important points for interpretation are: there is a diurnal variation more than 20%, morning concentration is higher than evening concentration, blood sample should be performed at the same time of the day during a follow-up; a value lower than 20 ng/ml maybe associated with lower fertility and higher risk of luteal insufficiency and abortion; a decline of P4 in the first 30 days of pregnancy is not normal; P4 must be measured by the same automat for a follow-up (only AIA, Elecsys and Minividas can be used up to date). After 30 days' post-ovulation, serum concentrations of progesterone begin a gradual decline that continues for 5 to 6 weeks. The progesterone profile is similar for pregnant, non-mated, and hysterectomized bitches during estrus. Progesterone should remain over 15 ng/ml the first 45 days of pregnancy, and over 10 ng/ml the first 55 days of pregnancy.

The luteal phase ends abruptly in the pregnant bitch (approximately 60 to 62 days after ovulation) as part of the onset of parturition, while it slowly wanes in the non-pregnant bitch, often lasting 10 to 30 days longer than observed in pregnant bitch. The abrupt drop of P4 in the 24 hours before parturition is systematic: < 2 ng/ml (AIA, Elecsys, Speadreader), < 3-4 ng/ml (Minividas). When P4 > 5 ng/ml (AIA, Elecsys, Speadreader) or > 10 ng/ml (Minividas) a bitch will never whelp in the next 24 hours (important for planed c-section). Sawtooth values are frequent in the days before parturition between 5 and 15 ng / ml.
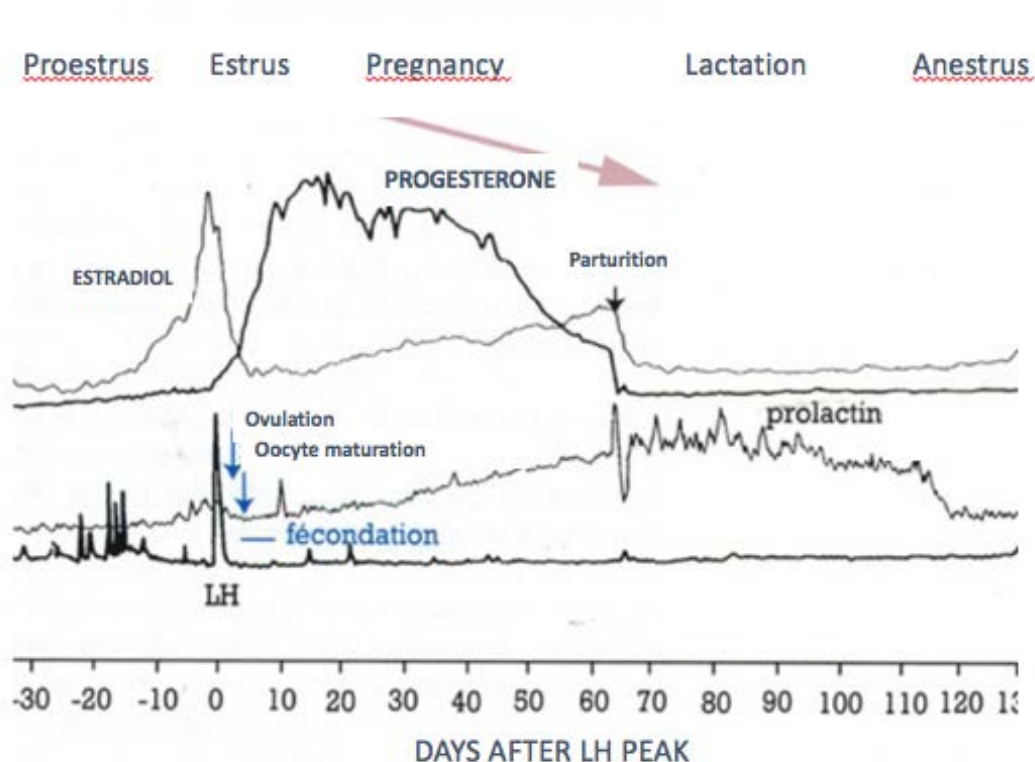
Figure 3: Hormonal profiles during estrus cycle in a pregnant bitch

Our presentation will cover the interpretation of other reproductive hormone assays (LH, AMH, testosterone and estradiol).

Semi quantitative test for LH allow to objective an ovariant remnant syndrome and confirm a neutered status of a dog or cat (male as female). Quantitative AMH test may also lead to the same information.

Oestradiol 17B measurement may me useful in case of an ovarian cyst or a feminization syndrome in a male with testicular tumor.

Testosterone measurement is most of the time useless. We will report normal concentration in an entire male.

GESTATION DIAGNOSIS AND MONITORING IN PRACTICE

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CRECS (Isle jourdain, France). www.vetreproduction.com

The bitch has a short gestation period of two months. The apparent gestation period is 57 to 70 days if we take the day of mating as the reference point.

The **"real" gestation period is 60 to 62 days**, i.e. from the day of mating if the bitch is mated at the optimum time for fertilization.

Fertilization between ovocyte and sperm takes place in the oviduct (end of the uterus) and the embryos enter the uterine horns on around day 11 . The embryos then bathe in "uterine milk" until they are attached to the wall of the uterus, via the placenta, at around 16ème days: implantation.

The embryos then gradually develop in the amniotic sac, connected to the mother by the umbilical cord.

Fetal growth is greatest in the last third of gestation, between 45 and 60 days.

Progesterone, secreted by the corpora lutea in the ovaries, maintains gestation. Other hormones are produced by the placenta, including relaxin, which is essential for the relaxation of peripubic tissue prior to parturition.

The skeleton begins to ossify at around 42 days gestation, with clear ossification from day 50.

Why carry out a pregnancy diagnosis?

- Knowing early on whether a bitch is pregnant or not. The diagnosis of an "empty" bitch is different if she aborts early or if she is not pregnant.

- Estimates the number of puppies to be born. Allows you to adapt the diet at the end of gestation, to assess the risk of difficult whelping (large number of puppies or, conversely, risk of single-puppy syndrome). Finally, it helps the owner to book puppies.

- Evaluate the puppies' growth, the presence of resorption (early abortion) or a development anomaly (disproportion between the embryonic ampullae).

Diagnostic methods

Exterior modification of the bitch

▶ Enlargement of the abdomen from the 4th week onwards

▶ It is accompanied by abdominal ptosis in the second month, in the case of a large litter.

▶ Mammary tissue development: from 25 to 30 days
The mammary tissu is hard, turgid and congested. The mammary cord is clearly visible. This sign is not very reliable because it is also present in non-pregnant bitches (pseudopregnancy).

▶ Scanty serous and/or whitish vulval discharge may appear around 25-30 days: this is rare but does not indicate the existence of pyometra, and when it does, is almost pathognomonic of gestation. Be careful not to confuse this with pyometra.

Palpation

▶ Palpation should be carried out as gently as possible, as it can lead to abortion if it is done too frequently and too gently.

▶ The embryos form a series of oval blisters in the gravid uterus, the most caudal of which can be palpated through the abdominal wall from around the 21st day.

▶ After 35 days, the foetal blisters can no longer be detected by palpation as they increase in size, then merge and can no longer be distinguished. They cannot be distinguished from stools in the colon.

▶ From 45 days onwards, palpation of the bony relief once again reveals the foetuses.

Auscultation

▶ At the end of gestation, foetuses have a heart rate of 220 to 240 beats per minute, before which it is difficult to detect them.

▶ Auscultation is particularly useful at the time of parturition, during a post-term for example, to determine whether the foetuses are still alive (see specific sheet in "medical techniques").

▶ Foetal hearts are often difficult to hear in large bitches.
Note: Doppler equipment (small boxes) is available to detect the presence of heartbeats. The main error is the confusion between a foetal heartbeat and the noise produced by the bitch's aorta.

Abdominal ultrasound
Ultrasound is the gold standard, it allows an:
▶ Early diagnosis (> 17-21 days)
▶ Estimation of vitality and early diagnosis of an abortion: observation of the heartbeat, identification of embryonic resorptions and placental disenfranchisement.
▶ Assess the embryo ampulla, endometrial and placental thickness and possibly measure uterine and umbilical IR if placental insufficiency/placentitis is suspected.
▶ Estimating the number of puppies
▶ Assessment of puppy growth
▶ Date term to +-1 day in the absence of accurate ovulation monitoring;
It is recommended that the test is carried out between 21 and 25 days after ovulation or 20 to 23 days after mating.
If no heat monitoring has been carried out, it is preferable to wait until 25 days post-sire, in case the bitch was bred too early.

Relaxin hormone assay :
In the bitch, relaxin is the most specific gestation hormone yet found. In fact, it is only secreted in pregnant bitches.
It is initially secreted by the placenta, from 3 weeks of gestation, and enables the smooth muscle fibres of the uterus to relax. The intensity of the signal is independent of litter size.
There are two blood tests for measuring relaxin.
These tests can be used from the 3rd week of gestation, but if the test is carried out too early, there is a risk of a false negative. It is therefore advisable to wait 25 days before carrying out the test. If the result is negative, it is advisable to repeat the test a week later.
The test can be used to determine whether a bitch is pregnant, but does not provide any information about a possible abortion (the test will remain positive) or the number of puppies.
Progesterone levels are always high, so it is not possible to tell whether the bitch is pregnant or not.
Abdominal X-ray
X-rays are a late examination which is not useful for diagnosing pregnancy, but which does allow the number of puppies to be determined accurately.
On the other hand, contrary to popular belief, X-rays cannot tell you whether a puppy will be able to pass through the birth canal, except in the case of a monstrous foetus (major growth anomaly).
▶ From 45 days:
There is mineralisation of the foetal skeleton, which then becomes visible on the X-ray.
In practice, X-rays are taken **in the last week of gestation** so that the skeletons are clearly ossified.

Note:
X-rays and ultrasounds are not harmful to embryos or foetuses.

Gestation monitoring
There are many diseases that can affect the bitch and her foetus during pregnancy.

Some breeds, mainly dwarfs, are prone to metabolic imbalances in the last two weeks of gestation, which can lead to severe wasting or worse.
However, diseases are rare and do not justify systematic monitoring of pregnant bitches.
Checks are generally recommended following a previous pregnancy that went badly, or if the vet and/or owner are concerned.
Monitoring must be tailored to the diseases at risk or suspected. The most common diseases are:
Gestational diabetes mellitus (hyperglycaemia)
Gestational diabetes mellitus in dogs is a rare condition, unlike in women, in whom this endocrinopathy affects 2 to 12% of pregnancies.
The signs are an increased intake of fluids, more frequent urination and depression.
Treatment consists of trying to regulate blood sugar levels using insulin therapy (which is difficult

because pregnancy hormones interact with treatment) or abortion.

<u>Late gestation toxaemia and hypoglycaemia</u> Especially small breeds with many foetuses. Depression, leading to coma and death of the bitch
Diagnosis is made by a blood test combined with a urine analysis. Treatment is possible if the disease is detected early.

<u>Late gestation eclampsia: abnormal fall in calcium levels</u> Calcium imbalance at the end of gestation and during lactation Risk factors:
- Small bitch
- Heavy lactation: more frequent illness during lactation
- Calcium supplementation at the end of gestation in a healthy bitch
Caution: by over-supplementing, you run the risk of generating the very thing you are trying to prevent.
Symptoms:
- Unusual restlessness, anxiety, moaning,
- Increased salivation,
- Rigidity of gait, loss of balance and pain when walking.
- High temperature
- Rapid breathing Diagnosis: blood analysis
Treatment: oral or intravenous supplementation (under cardiac control) depending on the case.
A regular check, once a week for the last 15 days (or more if necessary) on bitches at risk means that treatment can be given before the disease manifests itself "dramatically".

<u>Luteal insufficiency</u> (hypoprogesteronemia)
Some bitches may experience a premature fall in progesterone, the hormone that maintains pregnancy, during gestation.
This disease is very often over-diagnosed, and it is normal to see a gradual decline from the third week of gestation.
If luteal insufficiency is suspected, progesterone levels should be monitored for the first 40 to 50 days of gestation.

<u>Endometritis and gestational placentitis</u>
There is increasing evidence that inflammation is a frequent cause of pregnancy resorption and termination. It may be worth measuring CReactive Protein from the 15th day of gestation (embryonic implantation phase in the bitch) and, depending on the result, considering treatment.
Inflammation can also lead to a defect in the vascularisation of the placenta. Treatments are also possible and will be described in detail.

CSECTION AND NEONATAL RESUSCITATION

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Caesarean section involves extracting the foetus by abdominal route after performing a hysterotomy. The surgical procedure is quick and technically simple, but requires the female to be suitably anaesthetised (narcosis and muscle relaxation). The aim of Caesarean section is to deliver live foetuses, without increasing their suffering (in the event of dystocia), with primary sucking and breathing reflexes. However, anaesthesia must also take into account the physiological fragility of the parturient female (ASA III according to the American Society of Anaesthesiology) and enable her to care for her babies quickly. This is why analgesia and fluid therapy are the keys to a successful caesarean section.

1. Understanding the specific characteristics of pregnant and nursing females

The high level of progesterone during gestation has a sedative effect on the central nervous system and increases the permeability of the blood-brain barrier. The massive release of endorphins and oxytocin during parturition significantly lowers the pain threshold. As a result, the need for anaesthetic agents is significantly reduced.

Systemic vascular resistance decreases under the effect of progesterone, making the bitch more susceptible to hypotension. Oxygen requirements increase by 20% at the end of gestation, while the female shows a decrease in total lung volume and functional residual capacity. Gastric emptying decreases, while oesophageal sphincter tone decreases, stomach pressure increases, as does gastric acidity (reduced renal elimination of gastrin).

Thus, during anaesthesia, the pregnant female presents a greater risk of regurgitation and inhalation of food particles, as well as a risk of hypoventilation and hypoxia, hypotension and tissue hypoperfusion. Hypovolaemia and hypoxia must therefore be controlled throughout the procedure (from preparation to recovery) by means of appropriate positioning of the female, appropriate perfusion flow, control of stress and pain, and maintenance of a short duration of narcosis (see below).

On the foetal side, the placental barrier mainly allows the passage of lipophilic substances that are weakly or non-ionised, weakly bound to proteins and/or have a low molecular weight (<500 dalton). This is the case for the majority of anaesthetic agents used, which have high diffusion constants (K).

The blood-brain barrier of the foetus is more permeable to drugs than that of adults. In addition, liver and kidney functions are immature, resulting in slower metabolism and excretion, and therefore prolonged depression of the nervous system. On the other hand, by diluting the umbilical venous blood that contains the anaesthetics before reaching the vital organs (brain and heart), the foetal circulation plays a protective role (around 80% of the blood in the umbilical vein goes directly to the foetal liver where the drugs will be metabolised or stored). As a result, the anaesthetic agent is less concentrated in the blood of the foetus than in that of the mother.

2. Preparing for surgery: reducing stress and hypoxia

The surgical procedure involves shearing and then cleaning/disinfecting the surgical area. This preparation time should be carried out in a calm environment, and if possible in the presence of the owner, to reduce the female's stress.

The table can be tilted by 10 to 15°C (head upwards) to limit uterine compression on the diaphragm, and the bitch positioned in partial lateral decubitus to reduce compression of the vena cava and renal arteries.

In order to reduce the effects of vasodilatation during the subsequent induction phase, fluid therapy is introduced using a solution of Ringer Lactate at a flow rate limited to 5 to 10 ml/kg/min. During the preparation phase (about five minutes), the bitch can be oxygenated with a mask to saturate the pulmonary alveoli with oxygen and limit maternal and foetal hypoxia during the induction phase. This stage is often difficult, as the female becomes excited in the presence of the mask. If it causes too much stress for the female, it is advisable to abandon this stage.

The operator prepares himself and sets up his surgical equipment on his mute assistant to reduce the time needed between induction and extraction of the first foetus; while the neonatal resuscitation equipment is set up (incubator, baby fly, dry linen, clamp and umbilical cord thread, etc.).

If restraint is not possible (female nerves), a low-dose, short-acting, antagonisable "tranquillising" agent can be used (Medetomidine, 5 to 10 µg/kg IM; Midazolam, 0.1 mg/kg IM).

3 Induction and maintenance of anaesthesia prior to fetal extraction

Induction is characterised by rapid loss of consciousness followed by progression to a level of surgical narcosis. Maintaining haemodynamic stability and ventilation is an integral part of the initial phase of anaesthesia. The physiological particularities of the pregnant bitch mean that the doses to be administered must be reduced in order to obtain good induction and maintenance of anaesthesia, but also that the bitch must be rapidly oxygenated by means of rapid intubation and respiratory assistance (ballooning or respirator).

The choice of anaesthetic agents used for induction is crucial. They must be fast-acting, of short duration and be rapidly eliminated by the mother and infants. Propofol and alfaxalone are the molecules of choice for Caesarean induction. The latter also has the advantage of inducing a more marked loss of the swallowing reflex, facilitating "atraumatic" intubation, and can be administered intramuscularly in untouchable cats. The doses required to obtain sufficient narcosis are generally 3 mg/kg and 4 mg/kg for alfaxalone and propofol respectively. During intravenous injection, it is essential to administer anaesthetics slowly (over 40 seconds) in order to use only the minimum dose necessary to induce narcosis (titration) and to limit induction apnoeas. However, care must be taken to ensure rapid intubation in order to limit the risk of regurgitation and a "false route". In women, compression of the cricoid region is sometimes applied to increase pressure on the PCOS, but its effectiveness is controversial.

In a female cat that is difficult to contain for catheter insertion, it is also possible to perform a mask induction (Isoflurane/O2). According to the author, this method is very effective in nervous cats. It is imperative to be aware of the risks of airway obstruction, regurgitation, vomiting and possible laryngospasm during this technique. You must be able to insert a venous line very quickly. In general, peripheral vasodilation occurs rapidly, making catheter placement easier.

Once narcosis has been achieved and intubation performed, the surgeon can proceed to anaesthetise the abdominal wall by ultrasound-guided infiltration using a TAP block. It is also possible, although less effective, to infiltrate the linea alba with Lidocaine (not exceeding 6 mg/kg) or Bupivacaine.

Before extraction of the foetuses, narcosis is maintained by the lowest possible dose of anaesthetic agent. In the case of a mixture of O2 /Iso- or Sevoflurane, the fraction of anaesthetic agent is limited to 2% (if possible). In the absence of gaseous anaesthesia, boluses of anaesthetic agents should be kept to a minimum. In this context, alfaxan is preferred to propofol: no cumulative effect, reduced hypotension and vasoplegia.

4. Maintaining anaesthesia after fetal extraction

Once all the foetuses have been extracted, i.e. 10 to 15 minutes after induction, it is often necessary to adjust the anaesthetic dose in order to prevent awakening, as most of the alfaxalone or propofol has already been metabolised by the female. The volatile anaesthetic fraction can be increased if necessary or, in the absence of gas, an additional bolus of anaesthetic can be administered.

It is essential at this stage to ensure that the uterus is spontaneously contractile and that there is no significant uterine haemorrhage. An injection of oxytocin *in utero* is possible to encourage uterine contractions and provoke local vasoconstriction. In the most serious cases, an ovariohysterectomy may be necessary.

The infusion, at a rate of 10 to 20 ml/kg/min, is maintained until the female is fully awake. The female generally regains ambulatory capacity 20 to 40 minutes after the end of the procedure. Recovery is quicker with volatile anaesthesia than with injectable anaesthesia.

The bitch or cat should not be extubated until the swallowing reflex has clearly returned. In brachycephalic breeds, it is advisable to wait until the female is chewing the endotracheal tube.

5. Intra- and post-operative pain management

The pain caused by intubation, muscular and visceral incisions (post-operative uterine contractions) is a factor in intra- and post-operative morbidity, reduced milk production, rejection of infants and even cannibalism (particularly in the feline species). Propofol, alfaxalone and isoflurane have no analgesic properties. Induction with alfaxalone reduces laryngeal spasm and consequently the painful reaction to intubation (which may lead to hypertension and reflex tachycardia). Nevertheless, a lidocaine spray (gel) applied to the larynx is recommended prior to intubation.

Infiltration of the linea alba with lidocaine limits peri-operative pain (also infiltration of the ovarian pedicles in the case of ovh), as well as local inflammation. This not only reduces the need for anaesthetic agents, but also promotes quality recovery (important for rapid adoption of newborns). Buprenorphine, a mu receptor partial agonist, is the morphine of choice for managing analgesia in caesarean sections. Its action is more powerful and prolonged than that of morphine (>8 hours), without the latter's sedative and digestive side-effects. Buprenorphine takes 30 to 45 minutes to take effect. It is recommended to administer it by IV (or IM) before shearing the female. Administration may be repeated, depending on the intensity of the pain observed in the mother, 8 to 24 hours after the caesarean section, but this is rarely necessary. Although the compound crosses the placental barrier and diffuses in low concentrations into milk, no adverse effects have been described in human or veterinary gynaecology or paediatrics (personal data). Mothers undergoing withdrawal (on Subutex®[H]) are treated throughout their pregnancy with no adverse effects on the unborn child.

Methadone and other analgesics can also be used, and these will be described during the presentation.

Some authors recommend the administration of NSAIDs at the end of surgery (and possibly in the days that follow) in order to reduce pain and facilitate milk supply and adoption. NSAIDs concentrate very low levels in milk (< 5%), so the risk of nephrotoxicity seems limited.

6. The operation

We recommend making a moderate ante-pubic opening (at around 5-10 cm) so as to be located directly opposite the body of the uterus and the cornuate bifurcation.

Incise the uterine wall between two foetuses then enlarge slightly with the scissors so as not to incise the foetus. For brachycephalic breeds, we recommend that you avoid extracting the uterus too quickly, and that you gradually remove the puppies and then the uterus.

The amniotic sac should be ruptured immediately in front of the head, and the placenta kept attached to the cord for a few minutes. The foetus is given head down to an assistant as soon as possible, and the placenta is kept with the foetus in order to encourage a return of blood to the newborn via the umbilical cord.

Placentas must be carefully extracted to prevent metrorrhagia.

Once all the fetuses have come out, we check that there is no excessive bleeding and assess uterine tone after injecting 2 to 5 iu of oxytocin intra-luminally. The uterus is then closed in 2 planes using a simple overjet and then a burying overjet. The burying suture reduces local uterine complications.

It is possible to sterilise the mother during the caesarean section. Of course, care must be taken with ligatures, and the two uterine vessels must be ligated separately before a mass ligation is carried out.

The abdominal wall is closed using an intra-dermal suture.

In the event of major uterine bleeding, various strategies are possible and will be described in detail.

7. Neonatal resuscitation

An infant puppy or kitten is a very immature animal. It is unable to maintain its temperature and blood sugar levels. They are prone to dehydration (large body surface area/volume, permeable skin) and may have blocked airways, leading to fatal hypoxia in just a few minutes. Difficult delivery can lead to foetal distress, requiring neonatal resuscitation, which can often save the animal if carried out early and methodically.

- Ensuring oxygenation of the infant
  - Clear the airways.

Place the animal prone in the palm of your hand. Position the head in semi-extension, tilted downwards.

Aspirate pharyngeal and nasal mucus gently (low vacuum < 10 mmHg) using a baby fly, suction bulb or small-diameter suction tube.

In the event of false swallowing of amniotic fluid, an aspirator on a low-vacuum probe can be used to catheterise the trachea down to the stem bronchi.

- o Oxygenation

In the absence of spontaneous breathing and/or cyanotic mucous membranes. Place the animal on oxygen using a paediatric mask. It is also possible to bag the animal using an "ambubag": one squeeze every 8 to 10 seconds.

- o CStimulate breathing

Only if the airways are clear and oxygenation is guaranteed.

Vigorous rubbing of the sides activates mechanoreceptors that stimulate the baby's natural breathing.

An acupuncture point described in all mammals can be used in the event of dieback after a few minutes (without anaesthetic cause): point GV 26 (philtrum).

The use of Doxipram in sub-lingual or injectable form is mentioned, but should only be reserved for animals on oxygen.

- Maintaining body temperature without dehydration
  - o Dry the animal by rubbing it with clean, non-abrasive cloths.
  - o After a few minutes, place the baby in a warm environment (28 to 32°C). Paediatric incubators are particularly suitable (Vétario®), but a cage equipped with an infra-red lamp or hot water bottles are effective alternatives.
  - o Maintain sufficient humidity between 60 and 70%: incubator, sponge soaked in water, etc. Increase to 85% for premature babies over 48 hours old.
- Cutting the umbilical cord

Cutting the cord is not the first thing to be done, if possible, but care must be taken not to encourage a hernia by allowing the placenta to hang during the initial phases of resuscitation. In non-aseptic conditions, tie the cord about 2 cm from the umbilicus using a wire. Cut the cord with scissors beyond the ligature. Dab with a chlorine or iodine solution.

- Feed

Energy and fluid intake are essential in the first 2 hours to combat hypoglycaemia and dehydration. It is possible to put the newborn puppies on the teats on the operating table before she wakes up. Otherwise, it is necessary to wait until the bitch is sufficiently awake to put her newborn puppies on the teats.

Bottle-feeding or tube-feeding is possible if no colostrum is available at the time of the caesarean section.

NEONATAL DISEASE: FROM DIAGNOSIS TO TREATMENT

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When a neonate shows clinical signs of wasting, a clinical assessment of the puppy should first be carried out in order to adapt the emergency therapeutic management. Complementary examinations can then be carried out to establish an aetiological diagnosis (where possible) and thus formulate a prognosis and targeted treatment.

1. Carrying out a clinical examination of the newborn baby

The clinical examination of the neonate requires knowledge of the specific features and methods for assessing the various organ functions depending on the age of the baby (first 4 weeks of life): respiratory rate, heart rate, body temperature, digestive motility, hydration status, etc.

1.1. Assessment of cardiorespiratory function

Respiratory distress is common in neonates, especially if the mother does not take care of the baby at birth: presence of fluid in the airways or failure of the pulmonary alveoli to expand: inspiration of meconium, failure of a premature puppy to synthesise surfactant, congenital damage leading to persistent pulmonary hypertension, etc.

The newborn cannot fight hypoxia effectively (rapid muscular fatigue due to respiratory effort, low pulmonary compliance, more difficult pulmonary gas exchange). Blood circulation is altered: cutaneous, hepatic, renal, intestinal, intraosseous and pulmonary perfusions are reduced (in favour of those of the central nervous system and the heart), causing ischaemia, hypoxia and significant cellular damage (data from human medicine). Myocardial and cerebral blood flow may be altered over time: increases in intracranial pressure or the development of intracranial oedema may occur, as may bradycardia or asystole due to myocardial hypoxia. The **respiratory rate of newborn babies varies from 10-18 movements per minute (mpm)** (during the first 2 days) **to 15-32 mpm** (1 week).

The clinical examination must assess :

•   the colour of the mucous membranes, which will be cyanotic in the event of tissue hypoxia

•   the presence of mucus in the mouth, nostrils and lungs. In the event of inhalation of fluids or (broncho)pneumonia, the infant becomes discordant and inspiratory (and expiratory) crepitus is clearly perceptible (sometimes even without a stethoscope).

•   heart rate. **Bradycardia is observed during hypoxia in the first days of life**. Physiological mechanism for conserving available oxygen.

1.2. The temperature

Newborn babies are immature in terms of their ability to regulate body temperature.

The normal temperature is 35.5 ± 0.8°C in an animal born at term during the first week of life and reaches adult temperature at around 4 weeks of age (increase of 0.5 to 1°C per week). All authors agree that, unlike adults, newborn babies are **immature homeotherms**. It rapidly loses heat through conduction, convection, radiation and evaporation, and must therefore have an external source of heat (mother's udder, rest of litter, heating system).

The puppy shows remarkable resistance to hypothermia, enabling it to survive for some time.

Hypothermia increases metabolic requirements. It can reduce the neonate's response to other resuscitation measures and their effectiveness.

•   Mild hypothermia.

There is an increase in activity and the exhalation is vocalised with a high-pitched note on each exhalation.

Respiratory rate increases and heart rate decreases: **200-250 bpm at 35-37°C and 40-50 bpm at 30°C.**

The skin is cold to the touch but the mucous membranes remain pink. Simply place the puppy on a hot water bottle and the crying will stop.

- Moderate hypothermia

When the core temperature falls **below 31°C**, the puppy gradually becomes numb. Muscle tone is weak and sucking attempts are unsuccessful.

- Deep hypothermia

Below 25°C, the puppy remains immobile in a lateral decubitus position. This state is reached in 4 to 5 hours at an ambient temperature of 10°C. Breathing becomes imperceptible and reflexes non-existent. The mucous membranes are bronze in colour.

Ureus, reduced intestinal absorption and increased susceptibility to infection may also be observed. If deep hypothermia persists, the animal may eventually die.

A previously healthy newborn puppy can survive up to 12 hours in deep hypothermia.

1.3. State of hydration

Water requirements are higher than for adults: **10 to 20 ml/100 g**.

The degree of dehydration is assessed by: weight loss, dryness of the mucous membranes and urine density.

- The urine density of a newborn puppy is around **1.006**. A newborn puppy is considered to be **dehydrated if its specific gravity is greater than 1.017**.
- The persistence of the **skin fold is not always a reliable criterion** (at least in the first few days of life and for moderate dehydration) due to the lack of elasticity of skin tissue in neonates.
- The weight should double in 10 days (5 to 10% of its weight per day) and then the daily gain should be 2 to 7 g/kg of expected adult weight.

1.4. Digestive function

In newborn wasting syndrome linked to septic shock or hypothermia, digestive function slows down and then stops, leading rapidly to the animal's death.

It is therefore important to assess an infant's ability to absorb fluids orally.

- The presence of a **sucking reflex** is an interesting prognostic criterion. A strong reflex indicates that the animal's vitality has been preserved and that it is perfectly possible to feed it (bottle feeding, suckling, probing). Conversely, loss of the sucking reflex is often associated with lethargy and a loss of gastric emptying capacity. In these cases, resuscitation is required before the baby can be fed again.
- Abdominal distension associated with constant moaning is often a sign of digestive pain, or colic.
- The presence of a swollen, reddish-purple anus is suggestive of enterocolitis.
- The nature of the stool will be assessed by emptying with a thermometer: granulation showing a lack of milk digestion, diarrhoea, etc.

1.5. Neurological examination

The examination is brief in infants. The eyes open around 12 to 14 days of age and vision does not become operative until 21 to 28 days. The **blink at the threat is only present from 2 to 3 months of age.**

Pain is perceptible from birth, but the **withdrawal reflex only develops after 7 to 20 days (very variable).**

Only the so-called archaic reflexes are present in the first 15 days of life: digging, sucking and perineal.

2. Additional examinations

Complementary examinations are often essential to assess the severity of the disease and, in some cases, to determine the cause of the decline. Urine examination, included in the clinical examination (see above), should be complemented by ultrasound.

Unlike X-rays in young animals, ultrasound is the examination of choice for assessing the abdomen, heart, thorax (< 8 weeks) and brain. The absence of fatty tissue and the small volume of the animal make it easier to visualise all the organs. The fact that the fontanelles are not fused allows easy access to the cranial contents (to check for hydrocephalus, for example).

2.1. Ultrasound
In the case of wasting syndrome in neonates (frustrated syndromes), ultrasound examination can sometimes reveal organic lesions.

Priority should be given to looking for: intussusception/invasions, inflammation of the abdominal organs, liver, kidney or lung abscesses (in the case of septicaemia), porto- systemic shunt, signs of renal dysplasia, ectopic ureter, persistence of the urachus canal, and cardiac malformation.

It should be noted that certain pathological images in adults may be physiological in neonates:

- presence of a discrete (anechogenic) intra-abdominal effusion.
- Large liver
- Very slightly dilated pyelic cavities
- Mesenteric lymph nodes developed and clearly visible.

2.2. Biochemistry and Haematology
In order to interpret the results of blood tests, it is essential to be familiar with the physiological characteristics of newborn babies.

3. Emergency management of neonates with wasting disease
3.1. Body temperature control.
Newborn babies should be kept at between 36 and 37.5°C.
In cases of severe hypothermia (< 31°C), a gradual increase (1°C/h) is recommended. This gradual increase is not easy to achieve in practice (paediatric incubator, peritoneal rinsing, etc.).

3.2. Checking hydration (and nutritional) status

If a sucking reflex is present, hydration, milk or mixed feeding is recommended by mouth. Oesophageal probing is often necessary. Start with a low volume (2% of live weight) then gradually increase the volume depending on the puppy's clinical condition. The frequency should be adapted to the situation (every 2 to 6 hours).
In the event of more marked dehydration (or the absence of a sucking reflex), a parenteral infusion is required. Various routes are possible: SC (1ml/30g of puppy every 8 hours, without diarrhoea), IV (bolus 3-4ml/100g/15min then maintenance: 15-20ml/100g/d), intra-rectal, intra-peritoneal. Intraosseous administration is possible but is rarely used in our practice these days.

3.3. Maintaining blood sugar and electrolyte balance
Different protocols are used in practice: sugar water (Glc 50%) or honey* (2 ml/100g every
2 hours until feeding is possible on the oral mucosa), support solution (Hydraboost®) by IR, IV/IO route: 0.5 -1 g/kg Glc 5-10% or 2-4 ml Glc 10% if severe hypoglycaemia or major clinical   signs (dehydration, tachypnoea, bradycardia, absence of sucking reflex, convulsions, coma). It is recommended that Glc 30 or 50% should never be administered SC, as this could lead to phlebitis or skin necrosis.

3.4. Pain management
Analgesic management must be adapted to the intensity of the pain and its origin. Opiates can be used (buprenorphine, for example), as can colicky pain (Estocelan®, Spasfon®, Debridat®, etc.).

3.5. Controlling sepsis
In the event of proven sepsis or high risk of sepsis (prolonged cessation of transit and/or prolonged hypothermia), antibiotic therapy is recommended. Parenteral antibiotics are preferred, while oral amoxicillin should be avoided (to limit intestinal dysbiosis). A faecal flora transplant in cases of persistent enteritis or antibiotic therapy is currently being studied, but the results are very promising (personal data).
In cases of pneumonia or bronchopneumonia, aerosol therapy combined with oxygen therapy is recommended.

Slide 1

Infections causes of resorption/abortion in dogs

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Slide 2

How do
infectious diseases
cause resorption/abortion?

2

Slide 3

Uterine infection may induce

- Lymphogenic infiltration of the uterine wall
- Hostile environment for the eggs
  (Linde-Forsberg and Bölske 1995)
- Early embryonnic death (Freshman 1991)
- Interference with the development of the zygote
  (Van Duijkeren 1992)
- Inflammatory process ➔ endometritis
  (Van Duijkeren 1992)
- Placentitis or placental infection
  (Anvik 1991)

3

Isadora, Cane corso, 3 yo

- Two repeated abortion and metritis

- Vaginal cytology
  → Anestrus and vaginitis

- US: no abnormality

- 3 consecutive treatments:
  → Oral: Clavulanic ac./clamox 8 and 20 days
  → Local therapy: Clavulanic ac./clamox ; cefquinome; AISD, Saline solution rincage, Gynaecologic betadine rincage, etc.
  → Oral probiotic therapy

- Vaginal bacteriology
  → by vaginal swab *(without speculum)*
  → *E.coli* isolated in pure culture sensitive to most antibiotics

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4

What to do ?

What do you think ?

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5

Clinical examination !

- Vulvar entropion, leading to:
  → Peri-vulvar dermatitis
  → Vestibulitis
  → Vaginitis
  → Endometritis

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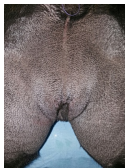**What is your diagnosis ?**

- Vulvar entropion, leading to:
  → Peri-vulvar dermatitis
  → Vestibulitis
  → Vaginitis
  → Endometritis

7

Think secondary contamination and not only primary infection!
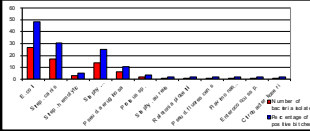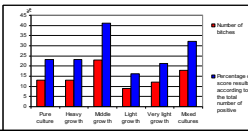
8

Genital collection for bacteriology: Pro and cons

- Hypothesis:
  → Mixed-population in normal vagina
  → Infertile bitches have more commonly a pure-culture *(Van Duijkeren 1992)*
- BUT *(Groppetti et al 2012-34* bitches):
  → 79.1% pure culture
  → 73.5% pure culture and 23.5% mixed cultures
  → No correlation with: resorption, abortion and normal pregnancy

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How to collect ? A crucial point !

10

Bacteriology before mating: pro and cons

- Over-diagnosis of infection and over-treatment
  - Bacterial resistance

- When to collect ?
  - Only if clinical signs (Groppetti et al.2012)
    - Vulvar discharge, endoscopy abnormality,

- Treat only : > 10^4 CFU/sample

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Role of (non hemotropic) mycoplasmosis

Resorption and Abortion

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Slide 13

- Small genomes
  → restricts metabolic capacity
  → depend on nourishment from a rich environment: mucosal membranes of the respiratory and urogenital tracts

- Absence of protective cell wall
  → Fragile outside the host
  → Resistance to lysozyme and cell wall–inhibiting antibacterials
    ▸ penicillin, cephalosporin, vancomycin, and bacitracin
- Ureaplasmas require urea for fermentation
  → adaptive preference for the genitourinary mucosae

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Slide 14

Many species in dogs and cats

TABLE 32-1

Species of *Mycoplasma*, *Acholeplasma*, and *Ureaplasma* Isolated from Dogs and Cats

Situation	Dogs	Cats
Genital tract	A. laidlawii, M. bovigenitalium, M. canis, M. cynos, M. edwardii, M. feliminutum, M. gateae, M. maculosum, M. molare, M. opalescens, M. spumans, Ureaplasma canigenitalum, Unclassified Mycoplasma sp. HRC 689, Mycoplasma spp. [62,89]	M. felis, M. gateae, Ureaplasma spp.[1]
Urine	M. canis, M. spumans, M. cynos[88,60]	NR

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Slide 15

Mycoplasms and ureaplasms...

… Are commonly isolated in the vagina of healthy dogs
(Linde Forsberg and Bölske 1995)

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Etiology

- Bitch:
  - → *Mycoplasma canis*
  - → *Ureaplasma urealyticum*

- Contamination especially sexual

- Low resistance to the surroundings

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Signs of potential impact

- **Ureaplasma impact** *(Doig et al. 1981)*
  - →Isolation higher in the vagina of infertile bitches: 75% vs 40% (p>0.1)
  - →Isolation higher in the prepuce of infertile male dogs: 69% vs 0% (p<0.05)

- **Mycoplasmes impact** *(Zoldag et al. 1992):*

  Mycoplasmes isolated in 106 / 145 bitches:
  - ▸ 80.5 % bitches with reproductive trouble
  - ▸ 51.3% normal bitches

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Relation Mycoplasms/Infertility
(Fontbonne, Martin, Buff and Le Grand)

- 40 kennel bitches:
  - →group A (n=20): no trouble of reproduction
  - →group B (n=20): trouble of reproduction

- Mycoplasms isolation :
  - →group A 45% of bitches
  - → group B: 80% of bitches

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Pathogeny

- Meaning threshold pathogenicity *(Mimouni 1999)* :

  → Under 10^4 CFU / ml: no problem
  → Between 10^4 et 10^6 : Troubles may appear
  → Meaning threshold pathogenicity : 10^6 CFU / ml ?

- **Association with other germs ?**

19

Clinical signs in bitches

- Reccurent vaginitis
- infertility
- Resorption and reduce prolificity
- Abortion
- premature parturition

20

Diagnosis

- Bacteriology:
  → Fast sending of sample
  → Specialised laboratory
  → Specific transport medium

- Semi-quantitative PCR

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Influence in female cat infertility?

- Uro-genital tract
  - → High Urine osmolarity in cats
    - ‣ Mycoplasma cannot survive / Ureaplasma may survive
  - → Restricted estrus discharge → reduced nurishment
  - → Need more study
    - ‣ Normal quantification ? (as dogs > 10^5)

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(Endo)-metritis and vaginitis

ANTIBIOTHERAPY

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Some considerations

- The therapeutic decision is still very empirical
  - → because little is known about the influence of antibiotics on the vaginal flora
- Other inter-current diseases that may promote vaginitis or make healing more difficult should be excluded
  - → General pyodermatitis
  - → Chronical diarrhea
  - → Urinary incontinence
  - → Anatomical abnormalities: vulvar hypoplasia, etc.

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Antibiotherapy: some considerations

- In case of chronic vaginitis or second-line treatment
  → Antibiogram
  → Antibiotherapy is maybe not the solution
    ▸ Bacterial translocation ?

Ex:
Bitch with infertility
History of beta-lactamines
repeated treatments.

25

Antibiotherapy: molecules selections

- There are very few publication about antibiotic tissue diffusion … in carnivores / farm animals / woman / mare
  → Only recommendations and no scientific consensus
- First-line antibiotics:
  → broad-spectrum + good mucosal penetration + available
  → amoxicillin-clavulanate
  → Cephalosporin (cefalexine)
  → Trimethoprim-sulfonamide
  → Fluoroquinolones: critical use!

Gasser TC et al. Quinolone penetration into canine vaginal and urethral secretions. Scand J Urol Nephrol Suppl. 1987;104:101-5.. Bretzlaff, et a.. 1983. Distribution of oxytetracycline in genital tract tissues of postpartum cows given the drug by intravenous and intrauterine routes. Am. J. Vet. Res. 44:764–769. Ström B et al. Effects of ampicillin and trimethoprim-sulfamethoxazole on the vaginal bacterial flora of bitches. Am J Vet Res. 1993 Jun;54(6):891-6.

- Mycoplasma: no antibiogram available + over-diagnosed!
  → josacine®[H], tylosin (Tylan® inj.),
  → spectinomycin (Lyncospectin® inj.),
  → fluoroquinolones (Marbocyl®, Baytril®, etc.)

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Antibiotherapy: duration of treatment

- Unjustified or prolonged administration (> 20 days)
  → Promote emergence of pathogenic vaginal flora
    ▸ Mycoplasmas, *E. coli, Enterococcus, multi-resistant drug Staphylococcus.*
- Most of authors recommend:
  → acute vaginitis: < 7 to 10 days
  → chronic recurrent vaginitis: 30 days maximum

- In human medicine, no long-term improvement between 7 *vs* 14 days
  → But estrus cycle is different, vagina shorter and environmental contamination reduce

Menard JP Antibacterial treatment of bacterial vaginosis: current and emerging therapies. International Journal of Women's Health 2011:3 295–305

27

Genital tract and flora imbalance

Probiotics and prebiotics

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Probiotics: Antimicrobial Effects

- Modify microflora to suppress pathogens
- Secrete antibacterial substances
  → to both gram-positive and gram-negative bacteria.
  → through reduction of luminal pH
    ▸ production of volatile short-chain fatty acids (acetates, propionates and butyrates).
    ▸ production of lactic acid (*Bifidobacterium, Lactobacillus, etc.*),
- Compete with pathogens to prevent their adhesion to the epithelium cells.
- Compete for nutrients necessary for pathogen survive. Antitoxin effect

Howard JC, et al. Identification of collagen-binding proteins in Lactobacillus spp. with surface-enhanced laser desorption/ionization-time of light proteinchip technology. Appl Environ Microbiol. 2000;66:4396–4400.

Sheil B et al.. Probiotic effects on inflammatory bowel disease. J Nutr. 2007;137:819S–824S.

Fenimore A et al. Evaluation of Metronidazole With and Without Enterococcus Faecium SF68 in Shelter Dogs With Diarrhea. Top Companion Anim Med. 2017 Sep;32(3):100-103

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Interest of probiotics in reproductive system of the bitch ?

- 30 days oral *Lactobacillus sp*.
  → may lower the concentration of potentially pathgenic bacteria (*Staphylocoques, Proteus and Enterobacterias*)
  Sanchez et al 2011
- 30 days oral *Lactobacillus sp. + Bifidobacterium sp.+ Bacillus sp.*
  → No significant change in the vaginal flora
  Hutchins et al. 2013
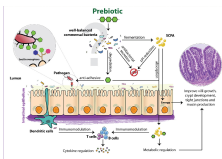- *Lactobacillus fermentum* found in the vagina after one month of oral treatment
  Sanchez 2015 (PhD-Barcelona)
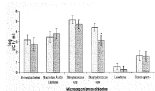
→ Other studies on probiotics (nature, methods of use) need to be conducted

30

Prebiotics ?

- « Non viable » selective fermented food
  - → stimulate the growth and activity of one or a limited number of microbes
  - → Fructo-oligosaccharides (FOS), Mannan-oligosaccharides (MOS), Inulin, Lactulose, Xylo-oligosaccharides (XOS).
- Combining of both prebiotic and probiotic are known as symbiotic (in the digestive system)

FAO. FAO technical meeting on prebiotics, available at http://www.fao.org/ag/agn/files/prebiotics_tech_meeting report.pdf, 2007
Walton GE, Swann JR, Gibson GR. Prebiotics. The prokaryotes Springer Berlin Heidelberg.2013; 18:25-43

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Vaginitis - Endometritis

Local treatments : see previous lecture

32

RAW MEAT CONTAMINATION

LEADING TO ABORTION, etc.

33

Seems to be an increased problem

- *Salmanolla thyphimurium* and *S. panama*
  - → Boxer kennel, abortion and raw chicken diet (Redwood 1983)
  - → Role of undiscriminate use of antibiotics ?
    - ◗ « 1 million less organisms to create a disease » *(Jones 1987)*

  Greene CE, Infectious diseases of the dog and cat, 3rd ed., 2006
  Axnér E, BSAVA, 2nd ed., 2010

34

Seems to be an increased problem

- *Campylobacter jejuni, etc.*
  - → Diarrhoea especially among young puppies(< 6 month)
  - → Possible abortion of pregnant bitches
  - → Childen owner diarrhea !
  - → Prevalence in fecal swabs : 26.2% (95/362)
  - → Diagnosis
    - ◗ culture from the liver/stomach content/swab of the cervical area
      (Johnston et al. 2001)
    - ◗ special culture media

  Greene CE, Infectious diseases of the dog and cat, 3rd ed., 2006
  Axnér E, BSAVA, 2nd ed., 2010

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Pyometra leading to abortion

Frequently diagnosed in breeding female

36

Why is Pyometra important?

- Bernese Mountain Dog - 66%
- Great Dane - 62%
- Rottweiler - 58%
- Irish Wolfhound - 58%
- Staffordshire Bullterrier - 54%
- Leonberger - 52%
- Bullterrier - 52%
- Keeshound- 52%
- Bouvier des Flandres - 50%
- Newfoundland – 50%
  (Jitpean et al. 2012)

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Pyometra

- Pathogenesis: role of bacterial infection
  - A secondary step ?
    - Marked suppression of the immune system activity / lymphopenia, induced by progesterone *(Faldyna et al. 2001)*
      - periods of highest sensitivity to infection: days 11-20 and 21-30 after the LH peak ?

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Etio-pathogenesis of pyometra

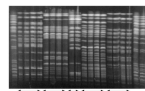- Pathogenesis: role of bacterial infection
  - A secondary step ?
    - *E. coli* most commonly found (70% of the cases):
    - Role of endotoxins : < 10% of the cases
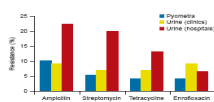   - Many strains: cytotoxin necrotising factors, often haemolytic *(Dhaliwal et al. 1998)*
    - Controversial interest of a bacterial culture

The Veterinary Record, August 13, 2

Hagman and Greko 2005

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Etio-pathogenesis

- Other bacterial infection ?
  - *15% Staphylococcus and Streptococcus*
    - *± Klebsiella, Proteus, Pseudomonas...*
  - Anaerobic bacteria: 15% of the cases ?
    - *Bacteroïdes sp., Peptostreptococcus sp., Clostridium perfringens, Fusobacterium necrophorum*
  - Mycoplasms ?: found in 16% of pyometra *(Mattson et al. 1989)*

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Pyometra at the gene-level
analysis of RNA in the uterine tissue by gene-array

- Up-regulation of >800 genes

  - IGF binding protein 1
  - Prostaglandin synthase
  - Matrix metalloproteases (MMPs)
  - Interleukines (IL-8, IL-6, IL-1b, IL-18)
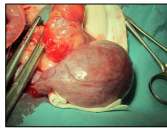
(Hagman et al, 2009, Affymetrix GeneChip® expression arrays (Canine Genome 2.0 Array)

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Other studies showing up-regulation of genes associated with inflammation in pyometra uteri

- Cytokines: IL-1β, TNF-α, IFN-γ, IL-17, IL-8

  (Bartoskova et al. 2012; Karlsson et al, 2012)

- *Toll-like receptor 2 and 4, PG-synthesis genes*

  (Chotimanukul et al 2011; Silva et al. 2010)

- *Matrix metalloproteinases 2,7,9*

  (Chu et al. 2002)

> Products from up-regulated genes:
> Diagnostic or prognostic markers?

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Pyometra clinical signs in infertile female

- In breeding females
  - → Partial pyometra may be observed during gestation follow-up
  - → No "overt" signs
  - → Segmental pyometra is occasionally encountered

- Vulvar discharge in diestrus/early anestrus

- Infertility soundness

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Pyometra: diagnosis

- Use of compression radiography ? *(Armbrust et al. 2000)*

Without compression **With compression**

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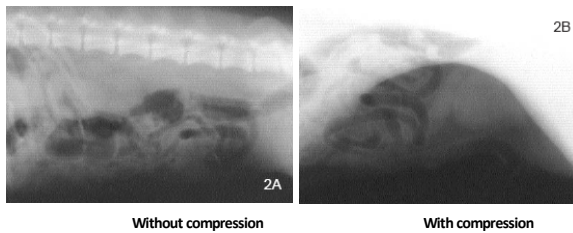
44

Pyometra: diagnosis

- Ultrasonography

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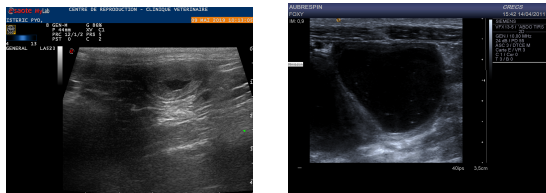
45

Blood chemistry

- **Leucocytosis and granulocytosis (30 000 à 100 000/mm³) and monocytosis :**
  - → Arneth curve « left shift » > 70% bitches
  - → Slight increase when open cervix
  - → Neutropenia at time of endotoxemia
  - → WBC in the normal range in 25 % of bitches

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Other biochemistry parameters

- ↗ **Alcaline phosphatase : 50-70% bitches**
- Hypergammaglobulinemia (30% - mainly close cervix), hypoalbuminemia (20%)
- ↗ urea (< 30%), creatinemia
- Metabolic acidosis
- PGFM increases (*Hagman et al, 2006*)
- **C reactive protein > 35 mg/l (N < 15 mg/l)** *(Fransson et al 2003)*
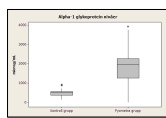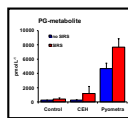
47

Prognostic indicator in practice

- **CRP,** Serum amyloid A, Haptoglobin, *(Fransson et al, 2004; Dabrowskij et al. 2015)*

Table 2
Median (interquartile range) levels of IGF-1 and CRP in healthy bitches (n = 11) and bitches with pyometra (n = 16) before, and 3 and 10 days after ovariohysterectomy.

| Group	Analyte	BS	3d	10d
Healthy	IGF-1, ng/mL	126.0 (58.0–240)	102.0 (85.0–182.0)	128.0 (47.6–192.0)
	CRP, mg/L	5.0 (5.0–7.7)*	30.4 (14.2–58.3)	9.3 (7.7–35.4)
Pyometra	IGF-1, ng/mL	140.5 (88.5–252.8)	101.6 (73.8–177.8)	186.0 (94.6–344.3)*
	CRP, mg/L	114.6 (95.3–131.6)***	90.1 (58.4–113.1)	23.3 (9.9–77.0)**

*P less than 0.05 versus 3d within the group.
**P less than 0.05 versus BS and 3d within the group.
***P less than 0.001 versus healthy dogs.
Abbreviations: BS, before surgery; CRP, C-reactive protein; IGF-1, insulin-like growth factor l; 3d, 3 days after surgery; 10d, 10 days after surgery.

676 R. Dąbrowski et al. / Theriogenology 83 (2015) 674–677

48

How to treat?

General strategy

49

Antagonize the effect of progesterone
endogenous (if < 3 months post-heat) or progestins

Aglepristone - Cabergoline

- Objectives:
  - → to stop uterine stimulation and glandular production
  - → to promote the local immune response (progesterone inhibits the action of leukocytes in particular),
  - → to allow rapid relaxation (<24h) of the cervix to facilitate spontaneous emptying of the uterine pus (especially during closed cervix).
- Side effects:
  - → shortening of the inter-estrus interval. Next heat often close to 1 to 2 months

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Antagonize the effect of progesterone (+ ATB)
endogenous (if < 3 months post-heat) or progestins

- Aglepristone alone(Alizine®)
  - → Success at one month
    - ▶ 40 – 90 % closed-cervix
    - ▶ 80 – 100 % opened-cervix
  - → Recurrence
    - ▶ 10 to 20%
  - → Fertility recovery
    - ▶ 60 to 100%
- Cabergoline + cloprostenol
  - → Success rate at one month
    - ▶ 60 to 80%
  - → Recurrence
    - ▶ 20%
  - → Fertility recovery
    - ▶ 50 – 60%

Hagman R. Pyometra in small animals. Vet Clin Small Anim 48 (2018) 639–661

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Aglepristone + PGF2α (+ ATB)

→ Aglepristone (Alizine®)
  ▸ Until Progesterone < 1-2 ng/ml or total recovery
→ Cloprostenol (Estrumate®) *vs* Dynolytic
  ▸ Estrumate: 1 to 2,5 μg/kg SC D 3 – 4 - 5
  ▸ Dynolytic: 100-250 μg/kg 2-3times a day. more side-effects

Table 1. Recorded parameters, expressed as mean ± SD values, in the 4 study groups and in the overall population enrolled in the present study

Parameter	Small dogs	Medium dogs	Large dogs	Giant dogs	Overall
Age (yr)	5.15 ± 1.80*	5.41 ± 1.96*	5.10 ± 1.45*	4.89 ± 1.84*	5.14 ± 1.75
Aglepristone administrations	4.79 ± 1.36*	4.84 ± 0.96*	4.69 ± 1.38*	4.69 ± 1.02*	4.75 ± 1.18
Success rate	33/33 (100)*	44/44 (100)*	52/52 (100)*	45/45 (100)*	174/174 (100)
Relapse rate	4/33 (12)*	2/44 (5)*	5/52 (10)*	4/45 (9)*	15/174 (9)
Interval diagnosis to relapse (days)	416 ± 265.07*	635 ± 629.33*	329 ± 131.74*	258.50 ± 94.28*	409.63 ± 354.90
Pregnancy rate	23/25 (90.00)*	32/35 (91.43)*	38/41 (92.68)*	36/39 (90.31)*	129/140 (92.14)
Litters after treatment	1.52 ± 0.51*	1.30 ± 0.64*	1.29 ± 0.46*	1.77 ± 0.81*	1.47 ± 0.65
Interval diagnosis to 1st litter (days)	163.32 ± 51.47*	210.58 ± 88.50*,†	192.92 ± 83.63*,†	225.77 ± 90.97†	198.05 ± 94.27
Interval diagnosis to last litter (days)	398.25 ± 125.35*	373.25 ± 102.66*	415.88 ± 117.20*	487.11 ± 148.70*	418.62 ± 129.03
Litter size	3.87 ± 1.14*	4.52 ± 1.68*,†	5.26 ± 1.54†	6.86 ± 1.69‡	5.13 ± 1.89
ΔLS	−0.72 ± 0.91*	−0.86 ± 1.79*	−0.64 ± 1.76*	0.47 ± 1.18*	−0.40 ± 1.62

Data are shown as mean ± SD or number (%).
SD, standard deviation.
*,†,‡Different superscripts denote statistically significant differences among columns, at *p* < 0.05.

Melandri M., Fertility outcome after medically treated pyometra in dogs. J Vet Sci. 2019 Jul;20(4):e39
Fieni F. Medical treatments for pyometra in dogs Reprod Dom Anim 49 (Suppl. 2), 28–32 (2014)

52

Cabergoline *vs* Aglepristone + ATB

- Cabergoline 5μg/kg/d orally
- Cloprostenol 1μg/kg/d to 5 μg/kg every 3 days SC
- ATB: see later
  → > 80% treated by Day 14 (19/22 bitches; 24/29 bitches)
  → 7/11 pregnancies
  → Recurrence < 20%
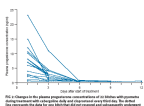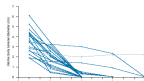
Englang GC. Treatment of spontaneous pyometra in 22 bitches with a combination of cabergoline and cloprostenol. Vet Rec. 2007 Mar 3;160(9):293-6.

Corrada Y et al. Combination dopamine agonist and prostaglandin agonist treatment of cystic endometrial hyperplasia-pyometra complex in the bitch. Theriogenology. 2006 Oct;66(6-7):1557-9.

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Antibiotherapy

- <u>ALWAYS</u> use concomitant broad spectrum antibiotherapy
  → Risk of: septicemia, kidney failure, disseminated intravascular coagulation

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Which antibiotic? Duration ?

- Few studies about antibiotic diffusion in the endometrium
  - → None in pathological conditions
- Adapt to the case:
  - → In the absence of any impact on the general and biological condition
    - ◗ Amoxicilin – clavulanic ac. 8 days
  - → In other cases (more severe):
    - ◗ Clav. Amox. + Fluoroquinolones ?., 8 to 14 days
      - • widens the antibiotic activity spectrum
      - • fluoroQ concentrate very well in the canine myometrium, with uterine fluid concentrations exceeding plasmatic ones

Sheer M. Concentrations of active ingredient in the serum and in tissues a er oral and parenteral administration of BAYTRIL. Vet Med Rev 1987;2:104-118

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PGE in case of close and open-cervix

- PGE2: Dinoprostone <u>gel</u>
  - → 0.5 mg, peri-cervical with a probe, 4x/d

- PGE1: Misoprostol <u>tablets</u>
  - → 400 μg, peri-cervical with a probe, 4x/d or

- Can be performed from the first therapeutic day
  - → Few side effects.
  - → No risk of uterine rupture.

Agaoglu AR et al. Clinical evaluation of different applications of misoprostol and aglepristone for induction of abortion in bitches. Theriogenology 81 (2014) 947–951

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Sensuelle, 2 yo, french bulldog

- 38 days post-AI
  - → "Closed-cervix" pyometra ?
- No clinical sign
  - → No leukocytosis, CRP high
- Do not answer to medical treatment
  - → Aglepristone, 10 mg/kg SC, 24 hours apart
  - → PGF2a, low dose
  - → Systemic antibiotic
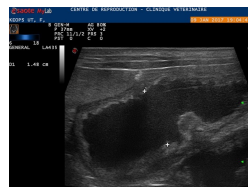
WHAT DO YOU SUGGEST ?

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Slide 58:

- Transcervial irrigation
  → With saline solution

- Catheter remains 12 hours

- PGE2 (Misoprostol®) locally

- Dinolytic 250 microg/kg, 3 times a day

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Slide 59:

Follow-up

- A week later
  → Strong improvement

- 4 months later
  → Pregnant !

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Slide 60:

Uterine rinsing and drainage by TCI
Uterine local treatment in case of sticky discharge

- N-acetylcysteine
  → disrupts disulphide bonds between mucin polymers, = reducing the viscosity of mucus
  → antioxidant (and possibly some antimicrobial) properties

- 0.6% solution of N-acetylcysteine (ACE) intra-uterine

→ unpublished data in carnivores

LeBlanc MM. Advances in the Diagnosis and Treatment of Chronic Infectious and Post–Mating-Induced Endometritis in the Mare. Reprod Dom Anim 45 (Suppl. 2), 21–27 (2010)

60

Pyometra and gestation still in progress

- In case of segmental pyometra
  - → Maintenance of pregnancy may be try In case of good health status
  - → Antibiotherapy and endometritis protocol
  - → Unilateral hysterectomy is possible
    - ▶ Single unpublished cases are reported

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Particular pathogens

Leading to resorption and abortion, etc.

fovéa **CRECS**

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Herpesvirus

CHV-1

fovéa **CRECS**

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CHV

- Presumed to be enzootic in the dog population
- Fertility disorders and neonatal mortality
- Real clinical impact unknown:
  → of the virus itself
  → of serological status of the kennel

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HISTORY   ETIOLOGY

- 1964: United-States
  (Carmichael)
- 1967: France

- Wrapped virus, slightly resistant in the environment
- Infective reduced at elevated temperature

Reduces 10000 after 5 hours at 37 degrees

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PATHOGENY

- Transmission:
  → Trans-placental way
  → Venereal way
  → Oro-nasale way

- Contaminating materials:
  → Oronasal or pharynx secretions
  → « Physiological » genital secretions (sperm, blood during heats, lochies)
  → Pathological secretions

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In adult bitches

- Genital signs:
  - → In the pregnant bitch:
    - ⦁ Infertility / abortion
    - ⦁ Improvement after one or two clinical outbreaks
  - → Locally ? :
    - ⦁ Vesicules on preputial or vestibular mucosae
    - ⦁ May disappear and reappear after a « sress »
- Possible associated symptoms:
  - → Respiratory problems:
    - ⦁ Adults with immunodepression: rhinitis, pharyngitis
    - ⦁ Secondary agent of the « kennel cough »
  - → Occular problems:
    - Conjonctivitis...
  - → Digestive problems ?

fovéa   *CRECS*

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Elements suggesting a role of CHV on canine infertility

- First clinical suspicion *(Poste and King 1971)*
  - → small group of breeding Alsatians (German Shepherds)
  - → after infection:
    - ⦁ number of pregnancies/matings was halved
    - ⦁ number of puppies per litter was reduced (9 ➡ 5-7)
    - ⦁ two bitches aborted

fovéa   *CRECS*
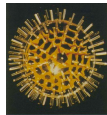
71

Elements suggesting a role of CHV on canine infertility

- Effects of vaccination upon pregnancy in an infected kennel *(Poulet et al. 2000)*
  - → fertility in 7 infected kennels
    - ⦁ non vaccinated group: n= 28
      - •pregnancy rate = 67.9 % average prolificity = 3.86 pups/litter
    - ⦁ vaccinated group: n= 61
      - •pregnancy rate = 82.0 % average prolificity = 5.06 pups/litter

fovéa   *CRECS*

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Serological findings

Ronsse et al (2004) :
- no significant difference in serological status could be observed with or without reproductive problems:
  - tendency of association between abortion and seropositivity
- no dogs below 6 months of age were seropositive:
  - → no interest to test the neonates !
- no significantly higher titers in prooestrus or oestrus:
  - but significantly lower titers in early dioestrus

Guigal et al. (2002):
- one labrador breeding kennel:
  - 24 dogs
  - 100% seropositives with high antibody titers
  - no reproductive problems

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Serology or PCR ?

Serology *Ronsse et al. 2005*
- 27 infected bitches
- 4 bitches with reproductive disorders:
  - decline of titers on oestrus and early dioestrus
  - it cannot be excided that uterine infection may occur without viremia
- In many breeding colonies, the entire dog population is infected
  - sometimes dogs remain seropositive for months
- Need for repeated serological testing
  - or antibody titers cinetic evolution (seroconversion) in case of clinical troubles

PCR
- Do different strains exist ?
- A negative PCR doesn't mean no contamination !
  - the use of PCR at matings seems a rather useless tool
- Which samples to use ?

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TREATMENT

Medical :
- Antivirals (vidarabine, acyclovir):
  - Human: Interest in local forms
  - Dog: ?
- Serotherapy of puppies by intra-peritoneal way

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Prevention

- Sanitarily:
  - → Physical agents:
    - ▶ heat, UV
  - → Hygiene: classical desinfectants
- Artificial insemination ?
- Vaccination: *Eurican Herpes®*
  - → Inactivated homologous vaccine
  - → Two injections (around heats and before parturition)
  - → Protection against neonatal mortality

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Canine distemper virus

Kralowka et al. 1977
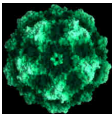
77

Canine minute virus (CPV1)

- Parvovirus type 1
- This disease may have a high prevalence inside dog kennels:
  - → seroprevalence:
    - ▶ USA: > 50%
    - ▶ Japon: 15,4 %

78

Canine minute virus (CPV1)

- Experimentally: resorption in 3/8 pregnant bitches
  (Carmichael et al. 1991)
  → One clinical case described in Germany *(Tryuen et al. 1996)*

- Role in stillbirth: anasarca ?

79

Canine minute virus (CPV1)

- USA: many authors check this disease systematically in case of reproductive problems :

« Canine minute virus and Canine Herpes Virus are major pathogens for canine foetuses and newborn pups » (Mochizuki 2002)

80

Canine minute virus (CPV1)

- Diagnosis: difficult
  → histology: intranuclear inclusions
  → Serology ?
  → PCR

- Prevention:
  → hygiene, desinfection, quarantaine
  → No protection with CPV2 vaccine

81

Canine Brucellosis

82

Canine Brucellosis
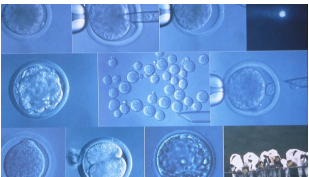
- Infectious and contagious diseases giving:
  → abortions
  → Infertility (male et female)

- There is several Brucellosis:
  → *Cattle / sheep / pig (Brucella abortus/melitensis/suis)*
  → Specific of dog *(Brucella canis)* canine Brucellose
- Dog Brucellosis are minor zoonoses

83

Animal brucellosis

- Cattle and sheep brucellosis can contaminate dogs :
  ▸ Absorption of contaminated milk products, aborted foetuses, or placenta of fetal annexes

84

Canine brucellosis

● <u>Canine brucellosis s.s.:</u> contamination:

→ Conjonctival, genital and oronasal mucosal
  ▸ mating, flairages, post-partum +++

→ Bodily secretions (saliva, urine ...) little
  contaminating

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85

Canine brucellosis

● Characteristics of the infection :

→ Time between infection and bacteremia: 21 days
→ bacteremia during several weeks to several month
→ Persistence of bacteria in some organs (genital tract, joints ...)
→ Vaginal fluid and milk hightly contaminated :
  ▸ ==> Isolation of dogs who come to abortion

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86

Canine Brucellosis: *is it frequent ?*

● Incidence varies in the world:
  → countries with high prevalence:
    ▸ Argentina, Mexico, Peru …
  → countries with an enzootic situation:
    ▸ USA: 1-10 % of kennels are infected
● Situation in Europe:
  → isolated cases reported in Germany, Italy, Tchecoslovakia (*Berthelot and Garin 1993)*
  → 3 cases isolated in France *(Fontbonne and Garin 1996)*

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87

Canine brucellosis in Spain
(Mateu de Antonio et al. 1998)

- **-** Seroprévalence: 4-5%

- séroprévalence higher in breeding dogs than in particular dogs
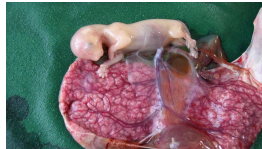
88

Clinical signs

● General symptoms:

→ pyrexia rarely present *(Wanke 2004)*
→ general deterioriation of condition
→ intolerance to exercise

● Other possible symptoms:
→ Lymphadenitis
→ Retropharyngeal and inguinal nodes
→ Follicular hyperplasia of the spleen
→ Discospondylitis
→ Polygranulous dermatidis
→ Meningo encephalomyelitis
→ Endocarditis

89

Genital signs

● In the bitch:
→ Late abortion (30-57 days)
  ◗ Higher frequency between d45 and d55 (Carmichael 1968)
  ◗ Aborted puppies appear highly autolysed
→ If puppies are born alive: often generalised lymphadenitis at puberty
→ Conception failure: due to embryonic resorption
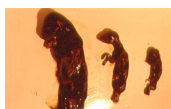
90

Serology

- beef / sheep and dog brucellosis : No cross reaction
  - ➜ ask 2 differents tests

- Canin brucellosis :
  - ➜ General considerations:
    - Seropositivity not before 8 to 12 weeks after contamination
  - ➜ Benefits – disadvantages :
    - *Allow to assert a non-contamination (seronegativity)*
    - Existence of many false positives (cross reaction with Moraxella sp., Pseudomonas sp. ...)

91

Bacterial culture

- Blood culture :
  - Technical difficulties
  - Long waiting times for diagnostic
- Vaginal culture:
  - Strong presence of bacteria, but for a limited time
  - Precautions for transport
- Other sources of brucelles:
  - semen, milk, avortons,enveloppes fœtales
  - rarely urine

92

PCR on aborted fetus, genital biopsy

93

Treatement

- Frequent failures :
  - Resurgence after treatment
  - No interest to follow seronegativation of dogs to evaluate the healing

94

Prevention

- → No vaccination
- → Safe breeding kennel :
  - New comers : serological screening
- → test male reproductors every 6 month
- → test all male dog or bitch who have a reproductive disorder
- → Reached kennel (or suspected ?)
  - Eliminer séropositif animals and do several control during several month.

95

Neospora caninum

A parasite

96

Neosporosis

- Disease related to a microscopic parasite
  - → :Neospora caninum
- No. 1 cause of abortion in cows in Europe
- Contamination of the dog by
  - → transplacental route
  - → ingestion of raw meat or placenta?
- Known symptoms in dogs
  - → mainly neurological disorders
- Role on reproduction?
  - → Neospora can enter the placenta in bitches (Dubey and Lindsay 1989).
  - → Several experimental studies indicate that the disease may induce pregnancy termination in bitches (Dubey and Lindsay 1996).

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Others causes of abortion

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98

Are there new specific bacterial diseases acting on infertility ?

- Bibliography is pointing out the potential role of:

  - → *Listeria monocytogenes* (Sturgess 1989)
  - → *Leptospira interrogans* (serovar: bratislava)
    (Bolin 1996)

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99
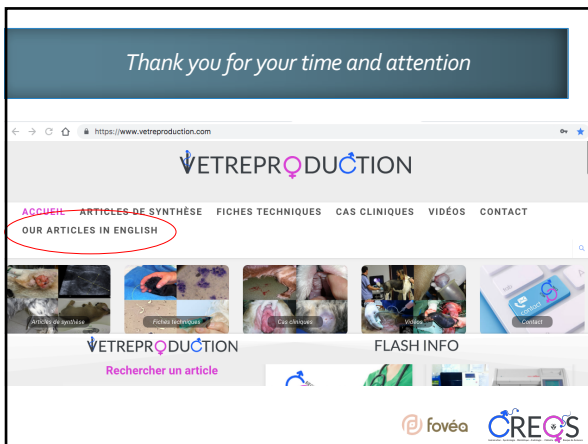
100

IN DOGS

- Serologic surveys have detected antibodies to chlamydiae in up to 50% of healthy dogs
- *Cp. psittaci* was detected using PCR in dogs with recurrent keratoconjunctivitis, respiratory distress, and multiple stillborn puppies from a German dog-breeding facility.
- In another house- hold, three humans and three dogs developed infection attributed to psittacosis from a cockatiel.33 Although the bird was euthanized, the a ected people and dogs had clinical recovery with treatment.

101

Non infections causes of resorption/abortion in dogs

Xavier LEVY, *DVM, ECAR dipl.*

Centre de Reproduction des Carnivores du Sud Ouest
contact@clinvetdugers.fr

1

Lola, American akita, 5 yo

- History
  → 2014 = Mating without pregnancy
  → 2015 = **Abortion** (45 – 55 days after mating)
  → No vulvar discharge
  → Repeated pseudopregnancy lactation

- New attempt
  → Ovulation = 02/08 (P4 = 12 ng/ml)
    ▸ AI = 03– 05/08 (39 ng/ml)
  → Pregancy confirmed = 25/08 – 8 embryos
    • No uterine abnormality

2

Progesterone follow-up

DATE	P4 (ng/ml)	
25/08 (23 days)	48	
01/09 (30 days)	42	(-12%)
08/09 (37 days)	36	(-14%)
15/09 (44 days)	27	(-25%)
17/09 (46 days)	3,5	(> 80%) → P4 supplementation

3

Pregnancy progesterone follow-up

- Physiological variation up to 20% in a-day
  → Morning > Afternoon

- Abnormal drop suspicion
  → 1st half og pregnancy
    ▶ P4 < 20-25 ng/ml (Minividas®)
    ▶ P4 dicrease > 20% in 2 to 4 days

4

Pregnancy progesterone follow-up

→ < 50 days of pregnancy
  ▶ < 10-15 ng/ml (Minividas®)
  ▶ Abortion without overt-signs: CEH, pyometra, etc..

5

Pregnancy progesterone follow-up

→ Parturition induction < 58 days of pregnancy
  ▶ P4 < 5-8 ng/ml (Minividas®)
  ▶ Nesting behavior
  ▶ Eadrly Milking secretion in primiparous bitch

6

How to treat

Progesterone insuffency

7

Natural and synthetic progesterone

- Natural micronized progesterone (100 or 200 mg®[H])
  - < 10-20 mg/kg, every 6 to 8 hours. Stop at least 48 hours before parturition day.
  - Pro: possible to monitor progesteronemia blood sample (6 hours' post-administration
  - Cons: frequency of drug administration
    - bitch: acromegaly and gestational diabetes, agalactia, uterine atony
    - Fetus: cryptorchidism in particular, masculinization of female fetus

Johnson CA. High-risk pregnancy and hypoluteoidism in the bitchTheriogenology 70 (2008) 1424–1430
Becher A and al. Luteal insufficicency in the bitch - symptoms, diagnosis, consequences and therapy. A review of the literature. Tierarztl Prax Ausg K Kleintiere Heimtiere. 2010;38(6):389-96.

8

Natural and synthetic progesterone

- Synthetic progestins
  - Megestrol acetate:2 mg/kg every 3 days IM. Stop at least 5 days before parturition
  - MPA 0,1 mg/kg/d *per os*
  - Altrenogest (Regumate®): 0.044 mg/kg every 12 to 24 hours. Stop at least 24 hours before parturition
  - Pro: easier to administer, suitable for small breeds, acute luteal insufficiency and bitches not balanced with natural progesterone
  - Cons: no progesteronemia follow-up can be done.
- Side effects of natural and synthetic:
  - bitch: acromegaly and gestational diabetes, agalactia, uterine atony
  - Fetus: cryptorchidism in particular, masculinization of female fetus

Johnson CA. High-risk pregnancy and hypoluteoidism in the bitchTheriogenology 70 (2008) 1424–1430
Becher A and al. Luteal insufficicency in the bitch - symptoms, diagnosis, consequences and therapy. A review of the literature. Tierarztl Prax Ausg K Kleintiere Heimtiere. 2010;38(6):389-96.

9

Uterolytic therapy
Contraction signs – Cervix opening and vulvar discharge

- Clenbutérol (Planipart®) 0,7 µg de clenbutérol/kg (0,26 ml/10 kg)
- Salbutamol inj., Ventoline® 20 microg/kg
- Terbutaline inj., Bricanyl® 0,03 mg.kg

- 3 times a day

10

Renji, Newfoundland, 4 yo

- 2016 : early resorption 2 embryos
- 2017: no pregnancy
  → Natural mating
  → Progesterone follow-up

- 2018 : new follow-up

11

Routine follow-up

- Progesterone Minividas®
  → 05/06: P4 = 3,4 ng/ml
  → 07/06: P4 = 12 ng/ml
  → 08/06: P4 = 21 ng/ml

- Vaginal swab
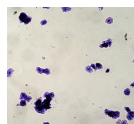
- US
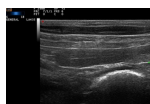
02/06   08/06
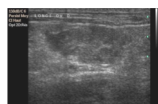
12

13

14

15

Freeman et al. 2013*

- 53 healthy » bitches
- 10 bitches with CEH
- Daily US after ovulation

- **Intra-luminal liquid = fertiliy reduction(p <0,05)**

* Freeman et al. Prevalence and effect of uterine luminal free fluid on pregnancy and litter size in bitches Therio 2013 (80): 73-76

16

Sub-clinical endometritis

Major cause of infertility in dogs (and cats)

17

Endometritis

Very known in some species

MUSCULARIS

MUCOSA

ENDOMETRIUM

Frequent cause of infertility

18

19

20

21

22

23
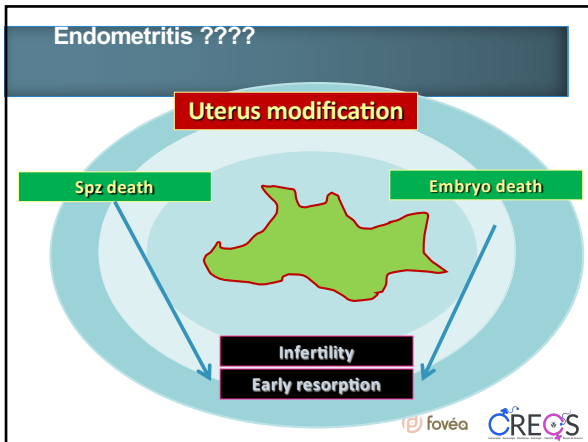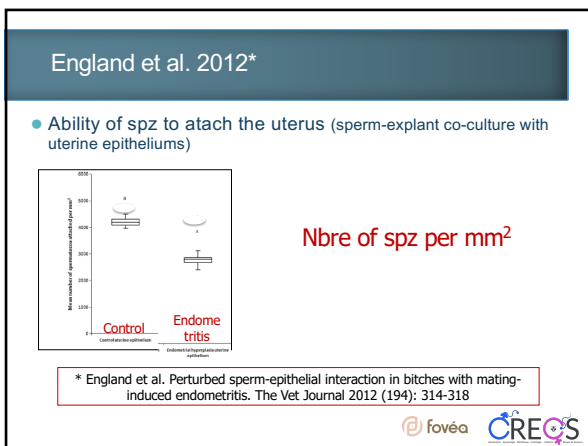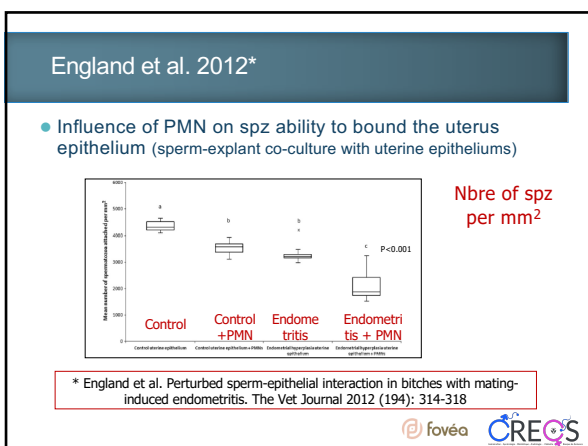
24
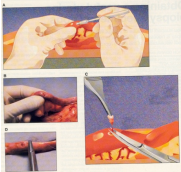
Biopsy?

Incisional, biopsy-punch, etc.

25
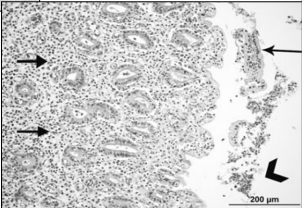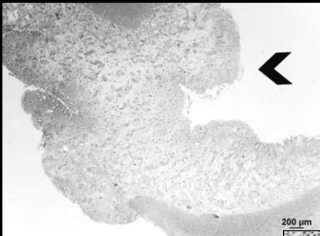
Biopsies

Findings in uterine biopsies obtained by laparotomy from bitches with unexplained infertility or pregnancy loss: An observational study

Fernando Mir [a,*], Emmanuel Fontaine [a,b], Olivier Albaric [c], Marty Greer [d], Florence Vannier [a], Donald H. Schlafer [e], Alain Fontbonne [a,b]

Theriogenology (79), 2013

26

27

Gifford et al. 2014*

- **399** incisional biopsies

  → Pregnant and non-pregnant bitches
    ‣ 68.7% for undetermined « infertility »
    ‣ 21.8% for abortion

  → In late diestrus

* Gifford et al. Histopathologic findings in uterine biopsy samples from subfertile bitches. JAVMA 2014 (244 (2)): 180-186

28

Gifford et al. 2014*

- Main lesions = **endometritis**
  → 170/399 (42.6%)
  → Lesion-association

- Among witch
  → 89 (52.4%) lymphatic and lymphoplasmocytary infiltration
  → 30 (17.6%) acute endometritis

* Gifford et al. Histopathologic findings in uterine biopsy samples from subfertile bitches. JAVMA 2014 (244 (2)): 180-186

29

DH Schlafer 2012

« The histological features of endometritis are in half of the endometrial biopsies taken from infertile bitches received in our laboratory. »

30

How to treat ?

Endometritis

31

NSAID's in farm animals and mare
Around ovulation and AI time

- Early endometrial inflammation is important for:
  - → uterine clearance of residual sperm,
  - → seminal fluid, and bacteria after sperm challenges during breeding

- Excessive inflammation reduces fertility and is directly related to tissue damage, which can lead to endometrial alterations such as fibrosis in response to repeated episodes of inflammation

No published data in carnivores

32

NSAID's in farm animals and mare
Around ovulation and AI time

- NSAID's reduce endometritis in mare and farm animals and enhance fertility
- Selective COX-2 NSAIDs do not affect:
  - → myometrial contraction, and therefore do not interfere with uterine clearance.
  - → Does not affect embryo displacement
  - → By contrast: meloxicam ne that inhibit COX-2 by 80% and COX-1 by 70% reduces embryonic mobility into the uterus

Friso AM et al. Periovulatory administration of firocoxib did not alter ovulation rates and mitigated post-breeding inflammatory response in mares. Theriogenology. 2019 Oct 15;138:24-30

Rojer H, Aurich C. Treatment of persistent mating-induced endometritis in mares with the non-steroid anti-inflammatory drug vedaprofen. Reprod Domest Anim 2010;45:e458e60.

Wilson JE, Chandrasekharan NV, Westover KD, Eager KB, Simmons DL. Determination of expression of cyclooxygenase-1 and -2 isozymes in canine tissues and their differential sensitivity to nonsteroidal anti-inflammatory drugs. Am J Vet Res 2004;65:810e8.

No published data in carnivores

33

AISDs in mare endometritis
Around ovulation and AI time

- Dexamethasone
  - → increased uterine PMNs influx
  - → decreased plasma concentration of the immunomodulatory steroidal hormones cortisol and estrogen
  - → finally reduced the generation of reactive oxygen species (ROS) by uterine PMN
    This latter mechanism would be particularly beneficial in protecting the endometrium from tissue damage by excessive extracellular ROS

Bucca S et al. The use of dexamethasone administered to mares at breeding time in the modulation of persistent mating induced endometritis. Theriogenology 70 (2008) 1093–1100

König T, et al. . Dexamethasone depresses the expression of L-selectin but not the in vivo migration of bovine neutrophils into the uterus. Theriogenology 2006;65:1227–41.

No published data in carnivores

34

AISDs in mare endometritis
Around ovulation and AI time

- When dexamethasone was administered at breeding time:
  - → a significant reduction of endometrial edema occurred
    - ▶ decrease in plasma concentration of the immunomodulatory steroidal hormones cortisol and estrogen
  - → A significant reduced post-breeding endometrial fluid accumulation.
    - ▶ may restore mucociliary flow, mucus composition and improve uterine clearance

Bucca S et al. The use of dexamethasone administered to mares at breeding time in the modulation of persistent mating induced endometritis. Theriogenology 70 (2008) 1093–1100

König T, et al. . Dexamethasone depresses the expression of L-selectin but not the in vivo migration of bovine neutrophils into the uterus. Theriogenology 2006;65:1227–41.

No published data in carnivores

35

New approach for infertility in carnivores
Endometritis to idiopatic

- Anti-Nuclear Antibodies could impair oocyte quality and embryo development,
  - → reduce pregnancy and implantation rates and women with recurrent pregnancy loss had a significantly higher incidence of ANA than controls
- Abnormal autoimmune conditions may impair all stages of fertility,
  - → implantation failure or pregnancy loss through different putative mechanisms

- Corticosteroid effect may be derived from
  - → an anti-inflammatory action or the regulation of immune cells as in the reduction of NK cells

Qing Zhu . A retrospective study on IVF/ICSI outcome in patients with anti-nuclear antibodies: the effects of prednisone plus low-dose aspirin adjuvant treatment. Reproductive Biology and Endocrinology 2013, 11:98

Yu Q et al. Efficacy of aspirin, prednisone, and multivitamin triple therapy in treating unexplained recurrent spontaneous abortion: a cohort study. Int J Gynaecol Obstet. 2019 Sep 15.

36

New approach for infertility in carnivores
Endometritis to idiopatic

- Anti-phospholipids antibodies and anti-beta (2) - glycoprotein I antibody
  - → thrombosis of placental blood vessels,
  - → dysfunctions of trophoblasts in the peri-implantation period
  - → imbalance of maternal hormones
- Low-dose aspirin for its anti-thrombotic effect
  - → may reduce uterine and intraovarian vascular resistance,
  - → improve blood perfusion
  - → increase oocyte maturation, the high-quality embryos rate, and the implantation rate

Qing Zhu . 2013, 11:98 , Yu Q et al2019 Sep 15.

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CRECS unpublished data
Treatments for bitch endometritis and infertility

- Prednisone (0.1-0.5 mg/kg/d) from heat to late pregnancy time
  - → Depending Creactive protein, ultrasonography and breeding history

+ DL-lysine acetylsalicylate (1-2 mg/kg/d)
  - ▶ before time of embryo implantation (<12 days post-ovulation) to late pregnancy (< 60 days post-ovulation).

+ ω 3 / ω 6 increase

  - → 1 capsule of 500mg/10-20 kg BW (salmon oil, sardines, herring ...), source of EPA and DHA to be swallowed or opened on a meal just before distributing it
    NB: no cod liver oil - no vial too oxidized, only capsules, preferably look for EPAX quality –
  - → Omega 3 lead to the release of anti-inflammatory substances after a cascade of reactions.

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38

Local treatments

Antiseptic and Anti-inflammatory

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39

Why a local treatment ?

- To remove mechanically inflammatory / infectious / macerated bloody discharge
- To destroy / prevent a biofilm leading to antibio-resistance

Muzny CA. Biofilms: An Underappreciated Mechanism of Treatment Failure and Recurre ce in Vaginal Infections. Clin Infect Dis. 2015 Aug 15;61(4):601-6

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40

Routine antiseptic molecules

- **Chlorhexidine and Polyvidone iodine**
  - → Good results in women vaginosis
  - *Verstraelen et al. Antiseptics and disinfectants for the treatment of bacterial vaginosis: A systematic review. BMC Infectious Diseases 2012, 12:148*
  - *Petersen EE. Arzneimittelforschung. Local treatment of vaginal infections of varying etiology with dequalinium chloride or povidone iodine…multicentric clinical study. 2002;52(9):706-15.*

- **Cytéal® at 1/10 dilution in rinsing, etc.**
  - → Hexamidine + Chlorocresol + Chlorhexidine unpublished data
- **< 7 to 14 days**
  - → drying out the vaginal mucosa leading to a secondary irritation
    - ▶ 5 to 20% among publications in women
    - ▶ No statistic in bitches but irritation also observed

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Essential oils: thymol and eugenol
Antiseptic and Anti-inflammatory

- Actions demonstrated *in vitro* and *in vivo* in women
  - → antibacterial
  - → antimycotic
  - → anti-inflammatory and antioxidant actions
- An antimicrobial synergistic effect has been found between thymol and eugenol
- These molecules can reduce the bacterial and mycotic adhesiveness to human vaginal cells that were incubated with *Escherichia coli, Staphylococcus aureus,* …
- once daily for 7 days

Need bitch investigations!

Braga PC.Inhibitory activity of thymol on native and mature Gardnerella vaginalis bio lms: in vitro study. Arzneimittelforschung. 2010;60:675–681. Sosto F, CANVA Study Group. Controlled study on thymol + eugenol vaginal douche versus econazole in vaginal candida- asis and metronidazole in bacterial vaginosis. Arzneimittelforschung. 2011;61:126–131. Dal Sasso M. Thymol: inhibitory activity on Escherichia coli and Staphylococcus aureus adhesion to human vaginal cells. J Essent Oil Res. 2006;18:455–61.

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Anti-inflammatory molecules = soothing products

- At time of diestrus and anoestrus
  - → Intra-vaginal – intra-uterine:
    - ♦ Opalgyne® (Benzidamine 0,1%) in rinse solution
      - • Nonsteroidal anti-inflammatory drug (NSAID) with local anaesthetic and analgesic properties *In vitro* antibacterial activity and also shows synergism in combination with other antibiotics against antibiotic-resistant strains of *Staphylococcus aureus* and *Pseudomonas aeruginosa.*

      Hay PE, Uthayakumar S, Peddie H, Lister P: A double-blind placebo- controlled trial of topical benzydamine douche twice a day in patients with bacterial vaginosis. Int J STD AIDS 1997, 8(Suppl 1):42.

43

Cystic endometrial hyperplasia

A frequent cause in cats (and dogs)

44

Definition

- Hyperplasia of the endometrium
- Abnormal dilatation and proliferation of the endometrial glands

45

Stages of the disease
Histological lesions (Dow 1957)

- Stage I: uncomplicated CEH:
  - →Increase in the number of endometrial glands
  - →Irregular aspect of the glands
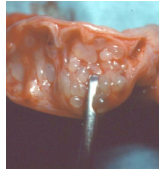
46

Stages of the disease
Histological lesions (Dow 1957)

- Stage 2 : CEH with plasma cells infiltate:
  - →No tissue destruction is visible histologically

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Stages of the disease
Histological lesions (Dow 1957)

- Stage 3 : CEH with acute endometritis (Mean age: 8 years)
  - →Areas of endometrial ulcerations and haemorrage
    - ❯ Intrauterine discharge /vulvar discharge
    - ❯ Endometrial congestion, edema, infiltration with neutrophils
  - →Myometrial inflammation in 40% of the cases

48

Stages of the disease
Histological lesions (Dow 1957)

- Stage 4 : CEH with chronic endometritis
  → Atrophy of the endometrium:
    ▸ Infiltration with plasma cells/lymphocytes
  → High modifications of the myometrium
    ▸ Hypertrophy/fibrosis if the cervix is opened
    ▸ Atrophy if the cervix is closed

49

- Histopathology

Histology: normal uterus
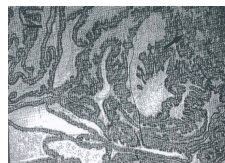
Histology: uterus with CEH:
« swiss-cheese » endometrium

50

CEH pathogenesis: roles of hormones

- Progesterone:
  → Endometrial proliferation
  → Uterine glandular secretions
  → Cervix closure
  → Decreased myometrial contractions
  → Decreased local immunity

- The effects of the hormones on the uterus are cumulative over several estrous cycles

- In cattery, spontaneous ovulation and repeated diestrus are frequent!

51

CEH therapy ?

- Mibolerone (Cheque drops®) – other testosterone
  - → 2,7 µg/kg once daily PO, not to exceed 180 µg/dog for 6 months, and bred at the next cycle.
  - → Side effect: clitoral hypertrophy (15-20%), creamy vaginal discharge, vaginitis, increased mounting and aggressive behaviors, anal gland inspissation, musky body odor, obesity, and epiphora.
  - → Seaman WJ. Canine ovarian fibroma associated with prolonged exposure to mibolerone. Toxicol Pathol. 1985;13(3):177-80.
- Digital crushing and/or hysteroscopy puncture
  - → No published data
  - → Not revelant in our practice (but very few cases performed)

- Uncommonly, bitches and queen are pregnant with CEH

52

"INES", Great dane, 4 yo

- Whelping in 2014

- 2015 – 2016
  - → 2 attempts: no pregnancy
    - ◗ Follow-up and matings
    - ◗ Progesterone follow-up

53

Follow-up

P_4 (ng/ml)

D 11 : 2 – 90% superficial cells

D 14 : 3,5

D 18 : 4

D 20 : 9

D 21 : 17 - AI

D 23 : 36 - AI
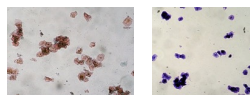
54

Estradiol 17 β ?

P4 (ng/ml)	E2 (pmol/l)
D 11 : 2	250
D 14 : 3,5	270
D 18 : 4	360
D 20 : 9	290
D 21 : 17	250
D 23 : 36	190
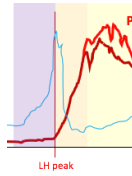
55

Physiological Estradiol profile in estrus

P4 (ng/ml)	E2 (pmol/l)
D 7 : 1,1	210
D 10 : 3	160
D 12 : 9	< 20
D 13 : 12	< 20
D 16 : 36	< 20
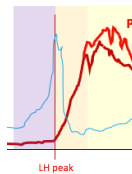
Proestrus : 30 - 100pg/ml = 100 - 367 pmol/l
Estrus : 15 - 21pg/ml = 50 - 75pmol/l

56

Diagnostic hypothesis

Ovulation ? Cyst ? Tumor ?
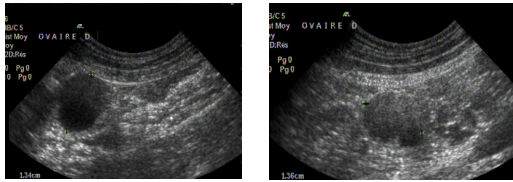
57

Ovarian ultrasound

- Mixed cyst : follicular with luteinisation

D18 = 4 ng/ml   D21 = 17 ng/ml

58
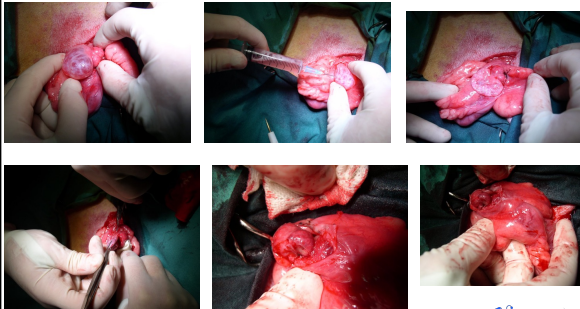
Treatments

US irrigation - Surgery

59

Laparotomy resection

60
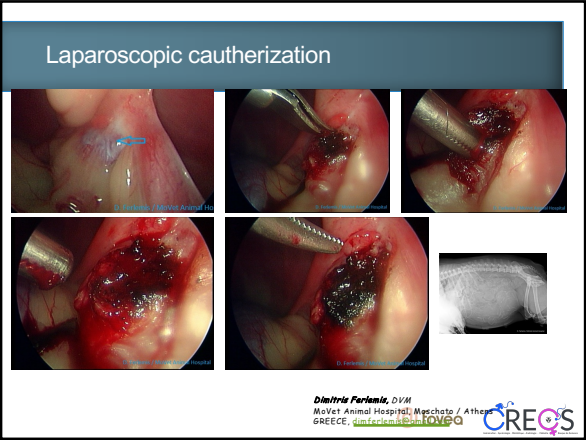
61
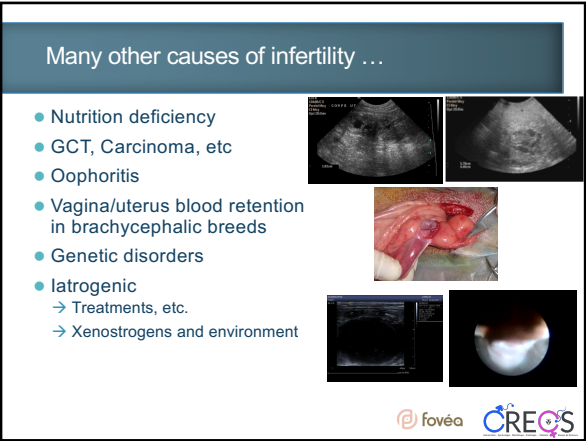
62
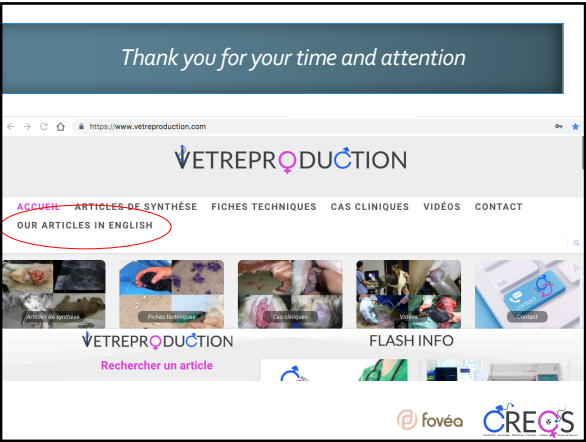
63

Post-partum diseases: metritis, mastitis, SIPS, placental retention, metrorragy and milk insufficiency

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1

Post-partum acute metritis

- A bacterial condition that occurs immediately after parturition or following an abortion.
- It usually occurs within a week of giving birth
- Acute inflammation of the endometrium and myometrium
  - → unlike pyometra, where only the endometrium and uterine mucosa are affected
- Etiology
  - → Abortion
  - → infection or fetal death
  - → Dystocia: obstetric manoeuvres or prolonged parturition
  - → Placental retention or fetal retention
  - → Poor hygienic conditions: pyodermatitis, environement, etc.

2

Main clinical signs

- Mucopurulent, malodorous, reddish-brown vulvar discharge
- Hyperthermia > 40° C
- Apathetic and litter disinterest
- Anorexia
- Agalactia and sometimes associated mastitis
- Vomiting and/or Diarrhea

3

Complications can quickly occur

- Peritonitis
  - → very intense abdominal pain
- Uterine gangrene and sudden death of the bitch
- Puerperal sepsis
  - → T > 41°C
- Puerperal pyohemia
  - → Germs may embolize in different organs
    - Mammary gland and gangrenous mastitis
    - Heart (valvular endocarditis, myocarditis)
    - Lung, spleen, liver, etc.

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4

Biological consequences

- Dehydration and sepsis may lead to
  - → polycythemia and hyperproteinemia, with pre-renal azotemia
  - → Urine density is isosthenuric (1.008 and 1.015) or hyposthenuric (density < 1.008) rather than hypersthenuric
    - Bitch is in a state of endotoxemia,
      - can interfere with the action of the antidiuretic hormone in the renal tubules
- Mild to severe leukocytosis (neutrophilia)
  - → Deviation to the left of the Arneth curve
  - → In case of endotoxemia and septic shock: leukopenia will occur
- ALKP and ALAT, GGT may be increased
  - → due to low liver perfusion and damage to liver cells
- If the animal remains lying down, CPKs and possibly ASTs will be slightly increased.
- Protein electrophoresis
  - → Drop in albumin from 5 to 15%
  - → net peak increase in alpha 2 globulin
    - related only to an acute inflammatory process
  - → discrete increase in beta or gamma globulins.
- Hypoglycemia is present in septic shock often associated with uterine rupture

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5

Vaginal cytology

- Acute inflammatory reaction
  - → large number of neutrophils and probably bacteria on a mucoid background.
    - Neutrophils appear degenerated with early or advanced karyolysis.
    - A number of bacteria can be found either in the free state or more frequently in phagocytes.
    - This should be observed in post-partum cytology
  - → Endometrial cells are sometimes visible.
  - → Muscle fibres from decomposing fetuses can also be observed during fetal retention
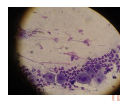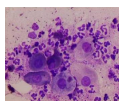
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6

Imaging soundness

- Xray: fetus and gaz uterine dilation

- US
  → Placental and fetal retention
  → Gaz into the uterine lumen
  → Peritonitis

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7

Treatments

**It is obvious that if no future reproduction is desired
Or
if metritis persists despite initial drug management
an ovariohysterectomy should be performed
without delay**

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Antibiotherapy

- IV if signs of septic shock, otherwise *per os*
- Broad-spectrum aerobic-anaerobic antibiotic
- a culture and antibiotic susceptibility test are recommended in case of recurrence in the kennel or female
  → β-lactamines : clavulanic acid + Amoxycilin in particular
  → Sulfamids-thrimetoprim
  → Fluoroquinolones is a critical antibiotic
- Usual posology
- Duration:
  → 10 days are normally sufficient, except in special cases (incomplete healing, etc.).

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9

Other treatments

- Rehydration plan and balance of potential electrolyte disturbances
- **Beware** of the risk of hypoglycemia and eclampsia, especially in miniature breeds
- Hyperthermia treatments
  → Estocelan®, 1 ml/10 kg SC, IM, slow IV
    ▸ very good antipyretic and safe in case of dehydration and pre-renal IR
    ▸ 1 single injection should be sufficient (and reduces contraction of smooth muscle fibres)
  → Acetylsalicylic acid: 10 - 20 mg/kg 1 to 2 times
  → Avoid other antypyretic NSAIDs in a dehydration context and kidney infection

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Other treatments

- Uterine drainage = Tocolytic
  → During postpartum metritis, avoid using prostaglandins as a first-line treatment:
    ▸ risk of uterine rupture (low unless post-caesarian, very prolific range and extremely distended uterus at the end of gestation)
    ▸ risk of retrograde pus ascent into the oviduct and abdomen
  → marked adverse reactions: vomiting, diarrhea, etc. Increases the risk of septic mastitis
  → Others: see dystocia lecture
- Uterine catheter drainage
  → It is possible to perform uterine rinsing of the uterus if it does not empty in 24 hours and a reproductive potential wishes to be preserved.
  → See infectious genital diseases previously

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Post-partum haemorrhage - Metrorragia

- Etiology
  → Poor involution of placental insertion areas
    ▸ particularly in caseof abrupt fetal extraction during cesarean section
    ▸ Placentitis (Al Bassam et al 1981) ?
  → Result of an inherited coagulopathy such as von Willebrand disease
  → Rodenticide intoxication in late diestrus
- Symptoms of the disease
  → Vulvar discharge appears excessively bloody
  → Rarely, the female will show signs characteristic of major blood loss
    ▸ lethargy, pallor of the mucous membranes and a small and rapid pulse.
    ▸ Attention : hematocrit of the dam after parturition is already lower (around 30%)

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Flow cytology

- Syncial cells with the appearance of trophoblasts ("Trophoblast like cells")
  - → very rarely identified in practice.
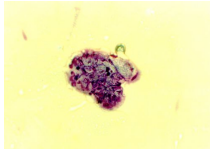
13

Medical treatments

- In case of limited bleeding, without clinical or hematological repercussions,
  - Treatment is not always necessary

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Medical treatments

- Etamsylate (Dycinone®): 12 - 25 mg/kg PO twice daily
  - → increasing resistance in the endothelium of capillaries and promoting platelet adhesion
  - → Inhibits biosynthesis and action of those prostaglandins which cause platelet disaggregation, vasodilation and increased capillary permeability
- Tranexamic acid (Exacyl®): 12 - 25 mg/kg PO twice daily
  - → Antifibrinolytic by reversibly binding four to five lysine receptor sites on plasminogen.
- Methylergometrine (Méthergin®) : 0.2 to 0.5 mg/15 kg SC
  Always useful to have in your fridge at the clinic
  - → Methylergometrine is a smooth muscle constrictor that mostly acts on the uterus

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Surgical treatments

- Ovario-hysterectomy

- Partial amputation of the hemorrhagic part of the horn
  - → very good healing
  - → without complication
  - → without further reduction in fertility

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CKC, 2 yo
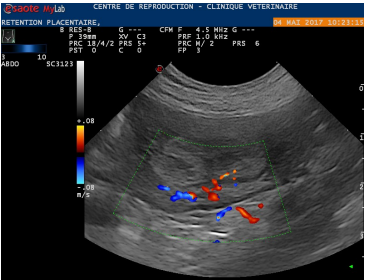
- Haemorrhagic vulvar loss remains 20 weeks after parturition
- Vaginal cytology
  - → Anestrus and Blood cells +++

17

Genital ultrasonography

18

Treatment

- Not always necessary to remove
  - → If bleeding stop
  - → If no inflammation/infection complications

- Only surgical treatment is efficient > 5 days post-partum

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Uterine prolapse

- Very rare in dogs or cats

- Unknown etiopathogeny
  - → Reduction in myometrial tone that allows the uterus to descend
  - → Prolonged and forced dystocia by disproportionate cause
  - → Incomplete placental separation
  - → Pain after parting
  - → Often idiopathic

20

Clinical signs ☺

- Uterine horns protruding from the vulvar lips
- Frequent rapid complications
  - → Rapid mutilation and contamination by self-mutilation (licking)
  - → Congestion and oedema (lack of venous return)
  - → Hemorrhagic shock
    - ▸ Rupture of ovarian or uterine pedicles (by traction on the meso)
  - → bladder globe/urethral stenosis
  - → Uterine rupture

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Mastitis

Congestive - Septic

25

Etiology

- Ascending nipple infection
  - → often associated with poor hygiene (skin, dental, etc.) of the bitch and/or the environment

- Hematogenous
  - → subclinical metritis is often associated

- Mammary congestion related to
  - → Lactation and non suckle nipple
  - → Trauma due to sucking and scratching puppies are contributing factors

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Germ and mastitis

- Most common bacteria
  - → *Staphylococcus sp.* (> 80% in bitches)
  - → *E.coli*
  - → Streptocoques
  - → !!! *Staphylococcus pseudintermedius* methicillin-resistant (MRSP)

- But what pathophysiology?
  - → Few studies...
    - Kuhn et al (1991): 68% of "healthy" bitches have bacterio+ (30/44) in low quantity
    - Schäfer-Somi et al. (2003):
      - *Escherichia coli, Klebsiella pneumoniae* and/or ss-haemolytic (haem.) *Streptococcus sp* isolated in the bitch nd the pup
      - *Staph. Intermedius* often isolated in the milk but not the litter

Milk bacteria are not, in most cases, the main cause of sepsis in neontates

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Clinical signs

- Dysorexia, apathy, and refusal to be sucked (grumbling, etc.)
- Severe hyperthermia (> 39.5° C)
- Mammary gland hot, painful, and often indignant in the mastitis region
- Purulent liquid, tinted with blood, comes out of the nipple under pressure
- Fluctuating and voluminous abscesses then appear in the mammary tissue
- Gangrenous evolution is frequent and very rapid (<48H)
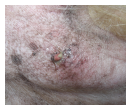
28

Ultrasound

- In our experience, mammary ultrasound is
  - → an early, sensitive and very useful examination.
  - → It shows the affected glands and abscesses in formation that are not yet palpable

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Milk and mammal gland cytology

- Few publications have been published on the usefulness of the cytological study (including cell count) of the bitch's milk.
- It is difficult to diagnose "beginner" mastitis but obvious in congestive septic mastitis.
- The smear is slightly different from a blood smear
  - → instead of attempting to obtain a smear with a rounded distal end, cells may be concentrated at the end of the smear by slow movement of the traction slide and removal of the slide, before the entire specimen is spread on the smear slide.

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Milk and mammal gland cytology

- "Normal" milky stasis (udder not recently sucked) is different from septic mastitis:
  - → In milky stasis
    - ‣ macrophages vary from 15 to 80% and neutrophils from 10 to 80%.
    - ‣ The cells have a normal morphology
  - → In septic mastitis
    - ‣ the cytological concentration of milk increases very significantly (up to 363.0 X 109/l; 363000/µl).
    - ‣ Most cells are neutrophils (80% of nucleated cells).
    - ‣ Erythrocytes in greater or lesser quantities are present.
    - ‣ The morphological study of the cells shows a marked process of caryolysis within the cells and significant cell degeneration.
    - ‣ Bacteria are often detected either in suspension in milk or (most importantly) phagocytized by macrophages and/or neutrophils.
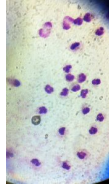
31

Bacteria culture and antibiogram

- For recurrent mastitis on a female or in a kennel/cattery
- Gangreneous mastitis refractory to first-line treatment.

- *Escherichia coli, staphyloccus spp. and streptococci β-hemolytica* are the most frequently isolated germs from septic mastitis milk culture.

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Mastitis – Local treatments

- Gongestion reduction
  - → Alcohol swabs
  - → Decongestant ointment (Vetebiol®) to be applied at least 4 times a day
  - → Gradually drain the congested mammals.
    - ‣ Be careful to disinfect the nipples properly.
    - ‣ To be done at least 4 times a day.
- Underlying abscesses, drain it:
  - → Warm compresses before the abscess ruptures
  - → Per-cutaneous drainage with a fine needle from the abscess or incision with a white blade
  - → Regular cleaning of the abscess once it has been broken: Bétadine solution® diluted 1/10, etc.
  - → If necessary: perform surgical removal of the necrotic tissue and close it on a large windowed drain.

- Gradually drain the remaining mammals that have not been sucked
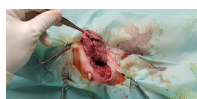
33

Mastitis – General treatments

- Control hyperthermia, dehydration and electrolyte disorders
  - → See metritis
- Antibiotic therapy
  - → Integrity of the blood-milk barrier:
    - ▸ Acute mastitis, barrier is broken allowing most antibiotics to reach the infected tissue.
    - ▸ Chronic mastitis, blood-milk barrier is restored and antibiotics diffuse according to the affinities of pH
      - • clindamycin or erythromycin are concentrated in acid milk.
    - ▸ Safety of the antibiotic for neonates
      - • Ampicillin and Marcolides often associated with pathogenic bacterial proliferation in the neonates.
      - • Tetracyclines can cause enamel defects and bone deformities
      - • Fluoroquinolones of joint and cartilage malformations (especially if prolonged)
      - • Aminosides have ototoxicity and nephrotoxicity.
  - → First intention:
    - ▸ Cephalexin (5-15 mg/kg per os 3 times daily)
    - ▸ amoxicillin/clavulanic acid (15 mg/kg per os 3 times daily)
    - ▸ 10 days is often enough

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Can neonates suchle the dam ?

- Mammary disorders are a major cause of neonatal sepsis in their sub-clinical forms (toxic milk syndrome).
- The choice to let the puppies suckle will depend on several parameters:
  - → affecting the general condition of the mother and/or puppies,
  - → safety of the antibiotic used
  - → ability of the breeder/owner to feed the puppies/kittens correctly in an artificial way.
- Puppies should be systematically removed in case of
  - → Abscess and open drainage
  - → or if at least two non-connected mammals are affected

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Milk insufficiency

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Etiology

- Unfavourable environment
  → Stress
  → Hot and Dry (< 50% humidity)
  → Insufficient food: quality and/or quantity

- Pain or systemic disease
  → Mastitis
  → Metritis
  → Etc.

- Premature parturition or Csection

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Allopatic treatments

- Dopaminergic ?
  → Metoclopramids: 0,5-1 mg/kg 4 times a day
    Domperidone : 1 mg/kg
    ‣ Psychic deleterious effect in children
    ‣ Efficacy not demonstrated
    ‣ Keller SR. Effect of metoclopramide treatment of bitches during the rst week of lactation on
      serum prolactin concentration, milk composition, and milk yield
      and on weight gain of their puppies AJVR 2018

- Stress and pain management
  → DAP®
  → Anxitane®
  → Etc.

NB: In case of complete agalactia, treatments are often disappointing.

Lévy X et al. Traitement des affections fonctionnelles de la mamelles chez le chien et le chat. Nouveau
praticien 2009

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Milk insufficiency: other treatments

- Homeopathic
  → Ricinus communis **5** CH + Alfalfa 6 DH
    ‣ 5 granules every 2 to 4 hours
- Essential oils
  → essential oil of fennel (3.5 ml) + star anise (1.5 ml)
    ‣ 3 drops, twice a day
- Phythothérapie
  → Galactogil® = Fennel + Aniseed

+ Fatigue Reduction
  → Silicea 9 CH : 1 dose a day
  → China Rubra 9 CH : 5 granules, 2 times a day

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Slide 1

Mammary gland disorders. Managing mammary tumors

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CREOS fovéa

1

Slide 2

Mammary neoplasia

IN BITCHES

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2

Slide 3

Epidemiological informations

- 1st malignant neoplasia in bitches
  → daily practice
  → statistical data show
- Prevalence 25 to 50% among studies
  → 50% bitches
    ▸ 3 times higher than in women
- 1% in males
- 6 to 10 yo
  → 16% around 10 yo
  → 45% 9 to 12 yo
- Entire = x 4 spayed bitches
- Inherited risk?
  → Poodles, Dachshunds, Cocker spaniels, and German shepherd

Age of spaying	Reduction of risk
< 1st estrus	99,50%
< 2nd estrus	92%
< 3rd estrus	74%
< 2,5 yo	0

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3

Epidemiological informations

- Around 50% are malignant
- Epithelial cells tumours > mixed tumours
  - Tubular adenoma, papillary adenoma, tubular carcinoma, papillary carcinoma, solid carcinoma, complex carcinoma and carcinosarcoma
- Localization
  - Inguinal mammals:1/3
  - Abdominal:1/4
  - Left side 60% ?

4

Etio-pathogenesis

- Many unknowns remain to this day
- Estrogens, progesterone, prolactin, pituitary hormones
- Carcinogenic molecules ?
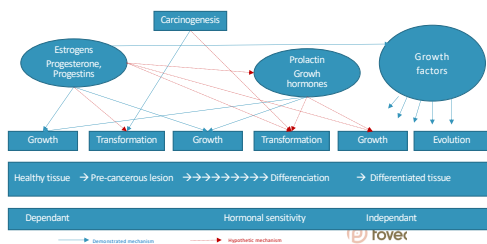
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Etio-pathogenesis

- Repeated and prolonged exposure to the various sex hormones (natural or synthetic) are factors that favour tumour differentiation.
  - Promoters but do not participate in tumor growth
    - as evidenced by the "progressive disappearance" of estrogen, progesterone and prolactin receptors as mammary tissue change
- Pseudo-lactation is believed to be responsible for
  - Accumulation of carcinogenic free-radicals
    - By hypoxia following acini distension
  - Repeated contact of these toxic products with the mammary epithelium could induce the formation of pre-neoplastic lesions or potentiate existing lesions.

6

Etio-pathogenesis

- Number of litters and the size of the litters do not seem to have any positive effect.
  - But this remains to be confirmed.
- Other factors have been proposed but not scientifically demonstrated!
  - Skinny bitches at puberty are less likely to develop mammary neoplasia than overweight bitches.
  - Home-diet food, especially if rich in beef or pork, would be more susceptible to mammary tumours.
  - Soya or cruciferous plants due to their phytoestrogen content

7

Clinical signs

- Most often
  - tumor detection takes place during a routine examination such as vaccination by simple palpation
  - Consultation for mammary mass most often correspond to masses already of a significant size or even extreme

8

Clinical signs

- Indirect in regards of metastasis localization :
  - lameness
    - bone metastases
    - Cadiot Ball syndrome
  - Polyuria-polydypsia
    - malignant hypercalcemia
  - Breathing difficulties
  - Skin carcinosis
  - Brain, eyes, nose, heart, Kidney, adrenal glands, spleen, liver, uterus

9

How to proceed?
Anamnesis

- Date of onset of tumor
- Rapid evolution
- History of the reproductive system (sterilization, contraception, pseudo-pregnancy, history of mammary tumor,...
- Appearance of other symptoms (cough, locomotor difficulties,...)

10

How to proceed?
Assessment of the tumor

- Look for all nodules
- Forms of the mass
- Adhesion with surrounding tissue

11

How to proceed?
Metastasis soundness

- Lymph nodes.
  - → Size is not proportional to malignancy
  - → Iliac/lumboaortic and sternal lymph nodes in regards of mass localizations
  - → Cutaneous metastases (cutaneous carcinosis)

12

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14

15

Clinical prognosis

Before any surgery

16

TNM clinical classification and prognosis

- Provides information on the progression of the disease
  - → but does not take into account the histological nature of the tumour

- T + N + M =
  - → Size of the tumor
    - ▪ Adhesion to the muscle and the skin

  - → Lymph node invasion

  - → Metastasis

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TNM staging : SIZE OF THE TUMOR
Multiple tumours are classified individually, nodule by nodule

- T0: no tumor
- T1: **tumor < 3cm** in maximum diameter
  - → T1a: non-attached
  - → T1b: adherent to the skin
  - → T1c: adherent to the muscle
- T2: tumour 3 to 5cm in diameter maximum
  - → T2a: non-attached
  - → T2b: adheres to the skin
  - → T2c: adherent to the muscle
- T3: **tumor > 5cm** in its maximum diameter
  - → T3a: non-attached
  - → T3b: adherent to the skin
  - → T3c: adherent to the muscle
- T4: cutaneous carcinosis

Stade I	T1 a,b ou c	N0(-) ou N1a(-) ou N2a(-)	M0
Stade II	T0	N1(+)	M0
	T1 a,b ou c	N1(+)	M0
	T2 a,b ou c	N0(+) ou N1a(+)	M0
Stade III	T3 a,b ou c	Tous les N	M0
	Tous les T	Tous les Nb	M0
Stade IV	Tous les T	Tous les N	M1

Clinical stage. Owen, OMS 1980 and WithrowSJ, Mac even EG, Clinical Veterinary oncology 1st ed. 1989

Stade I	T1	N0	M0
Stade II	T2	N0	M0
Stade III	T3	N0	M0
Stade IV	Tous les T	N1	M0
Stade V	Tous les T	Tous les N	M1

Simplified classification for vet. Rutteman. Dans Withrow SJ, Mac Ewen EG. Small Animal Clinical Oncology 3rd ed. 2001

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Slide 19

TNM staging = LYMPH NODES AND METASTASIS
Multiple tumours are classified individually, nodule by nodule

- N = Lymph node
  - → N0: No lymph node iinvasion
  - → N1: **Node Invasion**
- M = Metastases
  - → M0: no distant metastasis
  - → M1: **presence of distant metastasis**

- **Pay full attention to the classification used**
  - → .

Stade I	T1 a,b ou c	N0(-) ou N1a(-) ou N2a(-)	M0
Stade II	T0	N1(+)	M0
	T1 a,b ou c	N1(+)	M0
	T2 a,b ou c	N0(+) ou N1a(+)	M0
Stade III	T3 a,b ou c	Tous les N	M0
	Tous les T	Tous les Nb	M0
Stade IV	Tous les T	Tous les N	M1

Clinical stage. Owen, OMS 1980 and WithrowSJ, Mac even EG, Clinical Veterinary oncology 1st ed. 1989

Stade I	T1	N0	M0
Stade II	T2	N0	M0
Stade III	T3	N0	M0
Stade IV	Tous les T	N1	M0
Stade V	Tous les T	Tous les N	M1

Simplified classification for vet. Rutteman. Dans Withrow SJ, Mac Ewen EG. Small Animal Clinical Oncology 3rd ed. 2001

Slide 20

Stage prognosis
Clinical and extension assessment

- T threshold
  - → < 3 cm (stage 1)
    - 30% local recurrence into 2 years
  - → > 3 cm (stage 2 and 3)
    - 80% local recurrence into 2 years
  - → > 5 cm
    - 80% are malignant

- The diamer of the tumor is a powerful predictor of
  - → local recurrence
  - → distant metastasis,
  - → an independent prognostic factor (other factors) of survival rates.
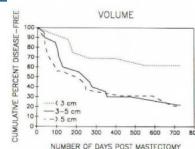
Slide 21

Stage prognosis
Clinical and extension assessment

- T threshold
  - → < 3 cm (stage 1)
    - 30% local recurrence into 2 years
  - → > 5 cm
    - 80% are malignant
- N invasion (stage 4)
  - → 21% survival at 1 year
  - → 0% survival at 2 years.
- Metastasis (stage 5)
  - → 0% survival at 1 year

Fine needle aspiration

Cannot be a reliable diagnostic method

representativeness of the sample
coexistence of several histological types in the same tumour
risk of vascular or lymphatic dissemination

The same applies to lymphatic nodes.

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Classification - Grading - Scoring

Anatomo-pahological analysis !

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Anatomo-pathology prognosis

- Reference diagnostic method for canine mammary tumors
- Different histological criteria
  - → mitotic index, dedifferentiation, cytonuclear pleomorphism, embolization image,...
  - → immunohistochemical
- Different grades and scores to propose a
  - → Mean survival rate (MSR),
  - → Risk of local recurrence and distant metastasis

- 2 classification systems
  - → World Health Organization[WHO] classification of 1999 and 2011
- 2 classification methods
  - → based on the human Nottingham grade
- Two studies published in 2017 and 2018 confirmed the quality of the 2011 classification, as well as the proposed scoring

Rasotto R. Prognostic Significance of Canine Mammary Tumor Histologic Subtypes: An ObservationalCohort Study of 229 Cases. Vet Pathol. 2017 Jul;54(4):571-578.
CanadasA. Canine Mammary Tumors; Comparison of Classification and Grading Methods in a SurvivalStudy.Vet Pathol. 2018 Oct 31:3009 [Epub ahead of print].

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Slide 25

Classification of bitch mammary tumor

Proposed Histologic Classification: 2010

1: Malignant Epithelial Neoplasms

Carcinoma–in situ
Carcinoma–simple
  a. Tubular
  b. Tubulopapillary
  c. Cystic-papillary
  d. Cribriform
Carcinoma–micropapillary invasive
Carcinoma–solid
Comedocarcinoma
Carcinoma–anaplastic
Carcinoma arising in a complex adenoma/mixed tumor
  —The benign counterpart is still detectable in the section.
Carcinoma–complex type
  —The epithelial component is malignant, and the myoepithelium is benign.
Carcinoma and malignant myoepithelioma
  —The epithelial and myoepithelial components are malignant.
Carcinoma–mixed type
  —The epithelial component is malignant; the myoepithelial mesenchymal component is benign; and the mesenchymal component is cartilage or bone.
Ductal carcinoma–malignant counterpart of ductal adenoma
Intraductal papillary carcinoma–malignant counterpart of intraductal papillary adenoma

2: Malignant Epithelial Neoplasms—Special Types

Squamous cell carcinoma
Adenosquamous carcinoma
Mucinous carcinoma
Lipid-rich (secretory) carcinoma
Spindle cell carcinoma
  Malignant myoepithelioma
  Squamous cell carcinoma–spindle cell variant
  Carcinoma–spindle cell variant
Inflammatory carcinoma (see Inflammatory Carcinoma section)

3: Malignant Mesenchymal Neoplasms—Sarcomas

Osteosarcoma
Chondrosarcoma
Fibrosarcoma
Hemangiosarcoma
Other sarcomas

4: Carcinosarcoma—Malignant Mixed Mammary Tumor

5: Benign Neoplasms

Adenoma–simple
Intraductal papillary adenoma (duct papilloma)
Ductal adenoma (basaloid adenoma)

With squamous differentiation (keratohyaline granules)
Fibroadenoma
Myoepithelioma
Complex adenoma (adenomyoepithelioma)
Benign mixed tumor

6: Hyperplasia/Dysplasia

Duct ectasia
Lobular hyperplasia (adenosis)
  Regular
  With secretory activity (lactational)
  With fibrosis–interlobular fibrous connective tissue
  With atypia
Epithelioisis
Papillomatosis
Fibroadenomatous change
Gynecomastia

7: Neoplasms of the Nipple

Adenoma
Carcinoma
Carcinoma with epidermal infiltration (Paget-like disease)

8: Hyperplasia/Dysplasia of the Nipple

Melanosis of the skin of the nipple

Goldschmidt et al. Classification and Grading of Canine Mammary Tumors - Vet Pathol 2011 48: 117

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Slide 26

Grading of malignant tumour

Table 2. Criteria for Histologic Malignant Grade

		Tubule Formation	Nuclear Pleomorphism	Mitoses per 10 HPF[a] / Hyperchromatism[b]
1 point	Peña[a]	Tubule formation > 75% of the specimen	Uniform or regular small nucleus and occasional nucleoli	0–9 mitoses/10 HPF
	Misdorp[b]	Well marked tubule formation	Mild nuclear pleomorphism and staining	Occasional hyperchromatic nuclei or mitotic figures per HPF
2 points	Peña	Moderate formation of tubular arrangements (10–75% of the specimen) admixed with areas of solid tumor growth	Moderate degree of variation in nuclear size and shape, hyperchromatic nucleus, and presence of nucleoli (some of which can be prominent)	10–19 mitoses/10 HPF
	Misdorp	Moderate tubule formation	Moderate nuclear pleomorphism and staining	2–3 hyperchromatic nuclei or mitotic figures per HPF
3 points	Peña	Minimal or no tubule formation (< 10%)	Marked variation in nuclear size and hyperchromatic nucleus, often with one or more prominent nucleoli	> 20 mitoses/10 HPF
	Misdorp	Few or no tubules	Marked nuclear pleomorphism and staining	2–3 hyperchromatic nuclei or mitotic figures per HPF

[a] Peña. HPF, high-power field.
[b] Misdorp.

Goldschmidt et al. Classification and Grading of Canine Mammary Tumors - Vet Pathol 2011 48: 117

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Slide 27

Classification and prognosis

- Excellent to good survival rate prognosis for:
  → Benign tumours
  → Carcinomas in mixed benign tumou
  → Complex carcinoma
  → Simple tubular carcinoma

1

Rasotto R. Prognostic Significance of Canine Mammary Tumor Histologic Subtypes:
An Observational Cohort Study of 229 Cases. Vet Pathol. 2017 Jul;54(4):571-578.
Canadas A. Canine Mammary Tumors: Comparison of Classification and Grading Methods in a Survival Study. Vet Pathol. 2018 Oct 31:3009 [Epub ahead of print]

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Slide 28: Classification and prognosis

Very low survival rate:
- Adenosquamous carcinomas
  - MST = mean survival rate = 18 months
  - Highest local recurrence rate = 50%
- Comedocarcinomas
  - MST = 14 months
- Solid carcinomas
  - MST = 8 months
- Carcinogenic sarcoma

Rasotto R. Prognostic Significance of Canine Mammary Tumor Histologic Subtypes: An ObservationalCohort Study of 229 Cases. Vet Pathol. 2017 Jul;54(4):571-578.
Canadas A. Canine Mammary Tumors: Comparison of Classification and Grading Methods in a SurvivalStudy. Vet Pathol. 2018 Oct 31:3009 [Epub ahead of print]

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Slide 29: Classification and prognosis

Most unfavorable survival rate
- Anaplastic carcinoma
  - TMS = 3 months, metastatic rate = 89%
- Carcinosarcoma
  - TMS = 3 months, metastatic rate = 100%
  - highest metastatic rates (89% and 100%, respectively).

Anaplastic mammary carcinoma. Cells are markedly pleomorphic and variably cohesive.

Rasotto R. Prognostic Significance of Canine Mammary Tumor Histologic Subtypes: An ObservationalCohort Study of 229 Cases. Vet Pathol. 2017 Jul;54(4):571-578.
Canadas A. Canine Mammary Tumors: Comparison of Classification and Grading Methods in a SurvivalStudy. Vet Pathol. 2018 Oct 31:3009 [Epub ahead of print]

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Slide 30: Grading and prognosis survival rate

Table 3. Histologic Malignancy Grade of Mammary Neoplasms

Total Score	Grade of Malignancy
3 to 5 Peña Misdorp	I (low) Well differentiated
6 to 7 Peña Misdorp	II (intermediate) Moderately differentiated
8 to 9 Peña Misdorp	III (high) Poorly differentiated

Goldschmidt et al.Classification and Grading of Canine Mammary Tumors - Vet Pathol 2011 48: 117
Rasotto R. Prognostic Significance of Canine Mammary Tumor Histologic Subtypes: An ObservationalCohort Study of 229 Cases. Vet Pathol. 2017 Jul;54(4):571-578.
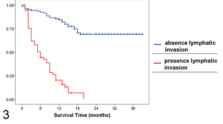
30

Lymph node invasion and MSR

- Excision margins are predictive
  - → only of local recurrence
- Lymphatic invasion and histological grade are predictive of
  - → local recurrence
  - → distance metastasis
  - → Survival rate
  - *but only in univariate analyses*

Rasotto R. Prognostic Significance of Canine Mammary Tumor Histologic Subtypes: An ObservationalCohort Study of 229 Cases. Vet Pathol. 2017 Jul;54(4):571-578.

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Treatments

SURGICAL

32

The extent of excision depends on many factors and there is no scientific consensus

33

Some anatomy reminds
Vascular and lymphatic distribution

34

Choice of surgery depends first on size and location

- < 0.5 cm : a nodulectomy can be considered

- < 1 cm: a local mastectomy

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Choice of surgery depends first on size and location

- > 1 cm:
  - local mastectomy : bitch ASA 2 or owner acceptance
  - Regional mastectomy
    - function of lymphatic drainage
    - Reduce the risk of lymphatic emboli
  - General mastectomy
    - Most often recommended
    - A bitch with a mammary tumor is 3 times more risky of developing another one
  - Bilateral mastectomy
    - in case of masses on both chains.
    - Two stage-operations 4 weeks apart: less debilitating, easier oncological resection, and less post-surgery complication
    - Select first the chain with the largest or most infiltrating masses

Mammals with a mass	Excision extension	Lymph node excision
M1	M1+M2+M3	Axilary LN
M2	M1+M2+M3	Axilary LN
M3	ENTIRE CHAIN	Axilary + Inguinal
M4	M4 + M5	Inguinal LN
M5	M4 + M5	Inguinal LN
Thoracic + Abdominal	ENTIRE CHAIN	Axilary + Inguinal

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Method of surgery

- Ligate blood and lymphatic vessels
  - → as early as possible
  - → as far away from the tumour
- Remove at least 1cm of "healthy" tissue around the tumour.
  - → optimum would be 3cm in all three dimensions around the mass.
- Rinse the wound before suturing the skin planes
- Limit post-operative complications
  - → limit the tension of the skin sutures,
  - → Limit the subcutaneous dead space.
  - → Compressive bandage
- Analgesia during and after surgery
  - → Morphine, methadone, fentanyl patch, etc.
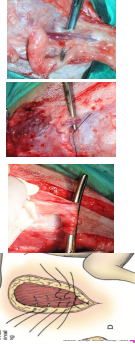
37

Ovariectomy at time of mastectomy ?

- Benefits of neutering at the time of diagnosis and treatment of a mammary tumour are still being debated
  - → Some studies have shown a better survival rate with concomitant sterilization
  - → but a meta-analysis rejects this statement

  Beauvais W, Cardwell JM, Brodbelt DC.The effect of neutering on the risk of mammary tumours in dogs--a systematic review. J Small Anim Pract. 2012 Jun;53(6):314-22

- In case of neutering
  - → start with spaying to limit the risk of tumor cells spreading into the abdomen

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Adjuvant therapies

Chemo- Radio and Immuno- therapies

39

Adjuvant chemotherapy

- Doxorubicin
  - 30 mg/m2 IV strict every three weeks, 6 sessions (maximum over a lifetime)
  - Side effects
    - cumulative cardiac toxicity
      - cardiac workup required before first and fourth.
    - Hair loss in woolly dogs (bichon, ...)
- Carboplatin (if doxorubicin impossible)
  - 300 mg/m2 IV strict associated with a short-time perfusion
  - Side effects:
    - myelosuppression.
    - Strict haematological follow-up
- GnrH (Suprelorin 4,7 then 9,4 ®, Virbac©, etc.)
  - a study showed a very high survival rate at two years (88%) for bitches with Grade II and III adenocarcinoma.
    Concannon P. Proceedings 3rd Int Symp non-sx contracept, 2006.
  - GnrH inhibits (over the long term) the secretion of LH, FSH, Estrogen and Testosterone.
  - GnRH also appears to antagonize the mitogenic effect of EGF
- Other historical protocols (not useful)
  - Vincristine+methotrexate+cyclophosophamide
  - 5-florouracil+cyclophosphamide given IV in the same day

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Other chemotherapy?

- Desmopressine (1-deamino-8-d-arginine vasopressin: DDAVP)
  - capable of inhibiting lymphatic and pulmonary metastasis in mice.
  - A study seems to show its interest in dogs
    - increased survival rate, and decrease in local recurrence rate as a function of time). Hermo GA, Torres P, et al. Vet J. 2008
- Aglepristone?
  - Anti-proliferative effect to be evaluated
- NSAIDS?
  - In women, reduction in mammary malignant tumor incidence with long-term use of aspirin
- Tamoxifen
  - Estrogen receptor blocker (0.5-1.0 mg/kg orally)
    Morris et al. 1993
- Testosterone ? Osipow et al. 1972
- Immunotherapy?
  - Mycobacterium bovis
  - Dimer of lysosyme at time and after surgery
  - Levamisol 5 mg/kg, 3x a week for 3 mo then weekly
  - Etc.

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Radiotherapy

- Radiotherapy is exceptionally recommended when
  - large lesions which cannot be completely removed
    - decrease the risk of local recurrence in post-op
  - In combination with chemotherapy tumours with a poor prognosis
    - Sarcoma
    - Carcinosarcoma
    - etc.
- Methods:
  - External radiotherapy
    - 12 sessions over one month, 3 times a week
    - Total dose 32 to 48 Gy
  - *In situ:*
    - Cobalt-ferrite-particles 100Å in magnetic *Sincai et al; 2001*

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MAMMARY TUMORS

PARTICULARITIES IN THE CAT

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Epidemiology

- 17% of all cat tumors
- 76% of all genital tumors in the female cat
- Mostly ageing cats: 10-12 yo
  → Siamese: + young
- > 80-90% carcinomas hormone-independent of simple type
  → involvement of a single neoplastic component: the epithelial lumen
- 85% are malignant
- 50 - 90% have already metastasized on the day of diagnosis
  → Most often regional lymph nodes (83%), lungs (83%), liver (25%) and pleura (22%)

Mass of limited size but Grade 3 mammary carcinoma with embolus

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Etio-pathogenies in female cats
Key role of sexual hormones

- 7 X less risk if the cat is sterilized before 6 months
  Dorn et al, 1968
- Induction of carcinomas by repeated, high-dose injections of progestin
  Hernandez FJ, Feline Pract, 1975 / Brodey RS, Adv Vet Sci Compp Med, 1970

- Viral catalyst (FelV, etc.) ?

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Tumours classification

- Adenocarcinoma: 75.8%
- Miscellaneous carcinoma: 9.7%
- Sarcoma : 0.8%
- Benign: 11,8%
  - → Adenoma, Fibroadenoma, Papilloma

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Prognosis, general informations

- Multiple mammary glands > 50% cases
- Often both chains at the time of diagnosis
- Malignant appearance:
  - → Muscle and skin adhesion
  - → Ulceration
  - → Heterogeneity
  - → Speed of growth

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Prognosis, TNM classification and MSR

- T = size of each mass
  - → T1 [stage I] < 2 cm < T2 [stage II] < 3 cm <T3 [stage III]
  - → Method of measuring the tumor size need standardization

Tumor size (in cm)	MSR (months)
< 2	12 to 54
2 < < 3	5,1 to 24
> 3	1,6 to 6

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Slide 49

Prognosis, TNM classification

- Lymph node
  - → stage III if present (NI)
- Metastases
  - → present in 50-90% of cases at diagnosis: stage IV
  - → In 120 cats autopsied: 80% lungs, 82% NL, 42% pleura, 23% liver
    Weijer NL, 1972
- NB: The presence of an enlarged LN
  - → does not necessarily mean tumour invasion.
  - → It may also be an inflammatory reaction (better prognosis).
  - → Standardization of a systematic evaluation
    - ▸ Cytology
    - ▸ Histology

Lymph node invasion	Negative	13 mo, median
	Positive	5 mo, median
Lymphovascular emboli / lymph mode invasion	Negative	21,83 mo, 33% death 1-y post surgery
	Positive	13,38 mo, 80% death 1 y post surgery

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Slide 50

TNM and Median Survival Rate

- This TNM classification makes it possible to create stages associated with survival rates
  - → TNM associated with survival rate need standardization among studies

TNM classification	Survival Rate
Stage 1	24 to 29 mo
Stage 2	13 mo
Stage 3	6 to 9 mo
Stage 4	1 mo

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Slide 51

Fine-needle aspiration and cytology

- Diagnostic in 66.7% of cases
- Exclude a mammary tumour in case of doubt
  - → *Vs* mastosis
    Casalli, Cytopath, 2007
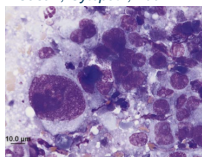
Epithelial cells from a feline mammary carcinoma have marked variation in cell and nuclear morphology.
One large nucleus contains an abnormally shaped macronucleolus (Wright stain, 1000×).
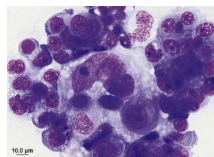
Pleural fluid from the same cat tightly cohesive clusters of epithelial cells with marked criteria of malignancy

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Method for a good FNA remind

- Small-gauge needles are used
  - → stain and briefly examine one slide to ensure that they are adequately cellular
    - ▸ reasons for poor cellularity are inadequate negative pressure (aspiration technique) and slow or shallow needle passages (nonaspiration technique).
      - • Aspiration tecchnique: Short-time and strong (but not excessive) negative pressure are applied by withdrawing the plunger to about three-fourths the volume of the syringe. Do not exist the mass under negative pressure.
      - • Non-aspiration technique: deedle passages should be quick and of sufficient length
- A minimum of four to five slides, representing collection attempts from several sites within the lesion
- If multiple masses are sampled, a new needle and syringe should be used with each mass.

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Method for a good FNA remind

- If blood vessels within the lesion have been ruptured, the tissue of least resistance will be peripheral blood.
  - → Too large a needle (<22-gauge), prolonged aspiration, or excessive force
  - → Once significant blood contamination has occurred, it is difficult to salvage the sample
- Squash preparation of the slides
  - → Care must be taken not to place excessive pressure on the slide, causing the cells to rupture.

A B C D

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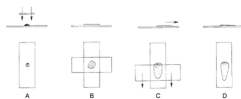
Anatomo-pathogology

- Poor prognosis correlated:
  - → Tumour classification: anaplastic >> adenocarcinoma

Tumor subtype	
Tubulopapillary	36 mo
Complex FMCs	27 mo, 32.6 mo
Noncomplex FMCs	15.5 mo
Non-MIMC	10 mo
Solid	8 mo
MIMC	4 mo, 7 mo

Prognostic factors for feline mammary tumours with respective categories and associated survival: statistically significant results, P < .01.

Pale pink areas represent necrosis randomly distributed between neoplastic epithelial cells
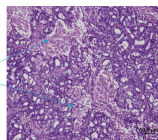
Zappulli V. et al. Prognostic Evaluation of Feline Mammary Carcinomas: A Review of the Literature. Vet Pathol. 2015 Jan;52(1):46-60

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Anatomo-pathogology

- Histological markers:
  - → Hormone receptors
    - ▸ In healthy mammary tissue: 100% progesterone and estrogen receptors
    - ▸ The less hormone receptors, the worst
      De las Mulas, Vet Path, 2004.
  - → COX 2
    - ▸ Absent in healthy tissue
    - ▸ Present in 96% of cats with a malignant mammary tumour.
  - → Ki 67 = proliferation marker
    - ▸ Highly correlated with survival rate. Castagnaro, Res Vet Sci, 1998

AgNORs, mean count per cell	
≤ 5.9	21% death 1-y postsurgery
> 5.9	79% death 1-y postsurgery
Mitotic index, %	
≤ 1.1	13 mo
> 1.1	7 mo
Ki67, mean positive cells, %	
≤ 25.2	12.5% death 1-y postsurgery
> 25.2	87.5% death 1-y postsurgery
≤ 36.1	14 mo
> 36.1	7 mo
ER, mean ± SD positive cells, %	
4.2 ± 11.8	Alive 2-y postsurgery
1.3 ± 5.3	Dead 2-y postsurgery

Zappulli V. et al. Prognostic Evaluation of Feline Mammary Carcinomas: A Review of the Literature. Vet Pathol. 2015 Jan;52(1):46-60

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Anatomo-pathogology

- → HER 2
  - ▸ Marker for genetic mutations that lead to aggressive tumours
  - ▸ Strongly correlated with COX-2 receptor expression
  - ▸ Expressed in 59.6% of mammary malignant tumour
  - ▸ HER 2 is a high prognostic factor in human medicine.
    DeMaria R, Cancer Res. 2005;Millanta, Vet Path, 2005;Dutra, Braz J Med Biol Res, 2004; De las Mulas, Breast Can Res Treat, 2003
- → VEGF expression
  Millanta, Breast Can Res, 2006 ;Heller, Vet Path, 2005

HER-2	
Negative, 0, 1+	18.7 mo
Positive, 2+, 3+	14.6 mo
VEGF, mean positive cells, %	
≤ 72	18.4 mo
> 72	14.2 mo

Zappulli V. et al. Prognostic Evaluation of Feline Mammary Carcinomas: A Review of the Literature. Vet Pathol. 2015 Jan;52(1):46-60

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Grading and Mean Survival Rate

	Death 1-y postsurgery	Death from surgery
Grade 1	0%	31 mo
Grade 2	42,40%	12 mo
Grade 3	100%	4 mo

Prognostic factors of feline mammary tumors with respective categories and associated survival: statistically significant results, P < .01.

Zappulli V. et al. Prognostic Evaluation of Feline Mammary Carcinomas: A Review of the Literature. Vet Pathol. 2015 Jan;52(1):46-60

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Need to be improved …

"By standardizing future retrospective and prospective studies, preferably in collaboration with veterinary oncologists, we will be able to identify factors of prognostic importance and expand the molecular evaluation of TMFs. This would allow the use of specific targeted therapies and increase the value of TMFs as a model of breast cancer in women."

Zappulli V. et al. Prognostic Evaluation of Feline Mammary Carcinomas: A Review of the Literature. Vet Pathol. 2015 Jan;52(1):46-60

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Treatments

To be discussed with the owner

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Surgical treatment

- Removal of the mammary chain with local-regional NL
  - → Reduces the risk of local recurrence compared to partial removal
  - → but does not increase survival rate for cancerous tumors
    Weijer K, J Natl Cancer Inst, 1983

- Removal of both chains in one step
  - → seems very debilitated
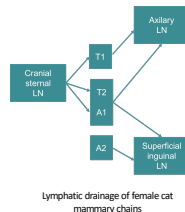
Lymphatic drainage of female cat mammary chains

60

61
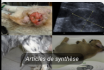
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Soft Tissue Surgery

Vicky Lipscomb (United Kingdon)
MA VetMB CertSAS DipECVS MRCVS
(Soft Tissue Surgery)

Vicky graduated from Cambridge University Veterinary School in 1996 and undertook a Small Animal Internship at the RVC. After a period working in small animal practice in Surrey she completed a Small Animal Surgery Clinical Training Scholarship at the RVC, achieving the European Diploma in Small Animal Surgery in 2002.
Following a period in private referral practice Vicky returned to the RVC in March 2003 where she is now Professor, Head of Small Animal Surgery and Clinical Director of the Queen Mother Hospital for Animals.

PRINCIPLES OF WOUND RECONSTRUCTION

Professor Vicky Lipscomb MA, VetMB, CertSAS, FHEA, Dipl.ECVS, MRCVS
Royal Veterinary College, University of London vlipscomb@rvc.ac.uk

Extensive traumatic wounds look impressive but the principles of managing all wounds are the same. Large wounds are rarely immediately life-threatening and it is important to triage and prioritise treatment of the most important clinical signs first. Understanding the stages of wound healing and performing initial wound management correctly is critical for producing a healthy granulating wound, which is the basis for performing reconstructive surgery. The initial goal of management of any open wound is the formation of a healthy bed of granulation tissue, from which decisions regarding further closure options and healing potential may be made.

Once the correct wound environment has been created, many defects will heal by contraction and epithelialization (second intention healing). However, second intention healing may be lengthy and costly or can result in complications, such as wound contracture (may be unsightly or interfere with limb function), large areas of fragile epithelium (may be hairless, unsightly and break open easily) or the wound may fail to heal completely. If these complications are present or anticipated, a carefully planned reconstructive procedure is required.

Reconstructive procedures do not need to be carried out on an emergency basis so there is always time to consider the options. It is extremely fortunate that dogs and cats have fur, loose skin, axillary and inguinal skin folds, a variety of direct cutaneous arteries from which to form axial pattern flaps, and a high success rate for full thickness free skin grafting. The donor defect flaps and grafts create in our patients can usually be closed primarily.

Remember:
- Many wounds will heal by second intention and you need to be able to recognise normal healing
- Intervening in a wound could cause more harm than good!
- We intervene in wounds that won't heal

Reconstructive surgery planning:
- The wound must be healthy!
- Consider tension and motion at the wound site when making the plan i.e. both before making an incision and before closing an incision. Close wounds parallel to skin tension lines if possible and assess tension by approximating the wound before closure by manually moving the skin or using sterile towel clamps to approximate closure.
- In addition to tension, wound closures in highly mobile areas (e.g. axilla, inguinal, tail base, foot pad and jaw regions) are subject to shear. Protect these areas during the extended healing period, e.g. bandaging and kennel rest, or even by placing negative-pressure wound therapy over the incision.
- If surgery is needed or preferred, it is it is usually best to choose the simplest technique first, in ascending order of options to consider:
  - Primary closure +/-undermining or other local tension relieving techniques
  - Local subdermal plexus flap: advancement, transposition, rotation, axillary or inguinal skin fold flaps
  - Axial pattern flap, full thickness free skin graft or distant subdermal plexus flap
  - Consider use of skin stretchers or expanders in combination with the above options.
  - Placing omentum from the abdomen into a wound fills the defect and promotes drainage, angiogenesis and the immune response to infection.
- The technique(s) employed for any specific wound will be determined by the overall condition of the animal, the nature of the wound and the wound environment, anatomical location of the wound and the experience of the surgeon.

- When considering all the options is a good idea, if possible, to have prepared "plan B" in case problems are encountered with "plan A".
- More than one reconstructive technique may be needed, or part of the wound may be left to finish healing by second intention.
- Depending on the case, it may be better not to tackle everything at once – consider the merits of performing one reconstructive procedure and evaluating the outcome before proceeding.
- Expect complications and be prepared to adapt to the outcome of each treatment.

General reconstructive surgery tips
- Follow Halstead's principles of surgery, including:
- Clip and drape widely to allow access to mobile skin and prevent tension on the skin to be manipulated.
- Assess for tension
- Plan the surgery carefully: revise anatomy and surgical techniques, discuss the case, measure twice, cut once, be meticulous in all aspects of perioperative care.
- Keep animals with drains hospitalised and barrier nurse the animal (gloves/apron) to minimise the risk of transferring a nosocomial infection to your patient from your practice. Cover Penrose drains with a dressing/bandage. Empty active drains using aseptic technique.

Skin stretching
Mechanical creep is when the skin's viscoelasticity allows it to elongate under constant **short-term loading**. Over time the skin will not only elongate (mechanical creep) but also lose its tendency to recoil when the load is removed: **stress relaxation**. We can take advantage of these properties to mobilize skin adjacent to a wound and relieve tension on the wound closure.

Pre-tensioning
This valuable technique takes advantage of mechanical creep and stress relaxation which can achieve up to 40% reduction in tension depending on the body location. It can be performed over the several days (48 to 72 hours) before definitive wound closure. It is essential that the peri-wound skin is healthy to achieve its full viscoelastic potential. Options for pre-tensioning:

1. Suture: simple continuous suture line through skin and superficial hypodermis of the wound edges with 2-0 or 0 nonabsorbable monofilament suture material. Similarly, even without a wound, "pre-suturing" can be performed around an area of planned excision whereby sutures are placed through the intact skin and the skin is plicated over the area of planned excision.
2. Externally applied skin stretching Velcro pads which are glued to the skin on each side of the wound with adjustable elasticized Velcro straps joining them across the wound.

Post-tensioning
If the surgeon becomes concerned about shear and tensile forces during surgical wound closure there are also options for protecting the surgical wound from dehiscence:
1. Externally applied skin stretching Velcro pads can be used postoperatively similarly to preoperatively to relieve tension on an incision.
2. Negative pressure wound therapy can be applied across a surgical wound to reduce both tension and motion. Postoperative incision management with negative-pressure wound therapy has shown promise with respect to decreased rates of surgical site infection, dehiscence, seroma, and hematoma in high-risk human patients.

Negative pressure therapy (NPWT)
Negative pressure wound therapy (NPWT) is a special type of active closed suction drainage system that may also help the healing process and can be used to help to keep skin flaps/grafts in apposition with the wound bed and/or protect high risk/high tension surgically closed incisions.

Negative-pressure wound therapy is the local application of sub-atmospheric pressure across a wound. A coarse, open cell (400 to 600 µm pore) foam or gauze is placed in or on the wound defect, with the drainage tubing placed above the dressing. Antimicrobial-impregnated dressings (silver-impregnated foam, biguanide-impregnated gauze) can also be used. The dressing and tubing are

covered by an occlusive dressing that creates a complete seal over the wound surface. The tubing is connected to a portable mechanical unit that applies constant suction negative pressure. Negative-pressure wound therapy can be combined with instillation of topical solutions (antiseptic or antimicrobial solutions) that are intermittently infused into the wound bed through a separate catheter system. The application of negative pressure wound therapy to reduce motion and tension, enhance acute open wound healing and/or protect skin flaps/grafts/surgical incisions is becoming increasingly common in veterinary medicine.

Omentalisation

The greater omentum is a large, double leaf, serous membrane of blood vessels and fat. It is ventrally attached to greater curvature of the stomach, spleen and left lobe of the pancreas, extends causally and then folds back on itself to attach to dorsal part of the stomach. Its blood supply is via the left and right gastroepiploic vessels and the splenic artery/vein, which lead into interconnecting omental vessels. The omentum contains numerous lymphoid clusters ("milky spots") whose satellite lymph ducts drain into the thoracic duct. In effect, the omentum is composed almost entirely of blood and lymph vessels. The omentum has multiple functions:

- Storage of fat
- Angiogenesis: rapid early onset of angiogenesis has been shown experimentally in tissues to which the omentum is applied (omental adipocytes produce an angiogenic factor, VEGF)
- Drainage properties via omental lymphatics.
- Immune defence: site of granulocyte production and macrophage differentiation which then phagocytose bacteria.
- Fibrinogenesis: produces fibrin which gives the omentum adhesion and filling properties in the face of tissue loss.
- Haemostasis: omentum possesses factors that accelerate prothrombin activation and transformation of fibrinogen to fibrin, accelerating intrinsic and common pathways of coagulation cascade.

FLAPS & GRAFTS FOR WOUND RECONSTRUCTION

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Subdermal Plexus Flaps

Subdermal plexus flaps (SPF) are 'local' flaps of skin which may be advanced, rotated or transposed into an adjacent wound to allow closure with minimal tension where excessive tension or distortion of local anatomy would be encountered attempting simple appositional primary closure of the wound. SPF are simple to perform, easily adaptable to a wound in any location and are particularly useful over the trunk of dogs and cats because the skin is usually loose and pliable in this region. They are also useful at sites where skin can only be recruited from one side of a defect. The secondary defects SPF create can usually be closed primarily or left to heal by contraction and epithelialization. Special types of SPF include axillary and inguinal fold flaps. Distant SPF differ in that the recruited skin is not adjacent but distant to the defect which means these procedures are not often performed as they involve multiple surgical procedures over several weeks.

Tips for performing local flaps:
- SPF rely on a good collateral blood supply via the subdermal plexus, therefore the width of the flap should not exceed its base and flaps are mobilized by blunt dissection deep to the subdermal plexus. Do not to damage the vascular plexus in the hypodermis and preserve any direct cutaneous arteries that are identified during undermining.
- The flap must be large enough to be closed over the wound without tension. If the flap is too small, the skin will be stretched into position rather than advanced/rotated/transposed, creating tension. Tension on the flap causes ischaemic necrosis due to poor vascular perfusion of the skin.
- With all flaps, move the skin around manually before you begin to assess the degree and direction of skin tension in the region.
- Suture flaps in place using intradermal sutures and then skin sutures/staples. Any "dog-ears" will flatten in time and don't usually require removal. If necessary, additional subdermal/subcutaneous vertical interrupted sutures prior to the continuous horizontal intradermal suture will provide added security and closure of dead space.
- Keep flaps moist during surgery.
- Place a drain if there is dead space for fluid accumulation under the flap.

Outcome of subdermal plexus skin flaps

Jones and Lipscomb 2019:
- 53 dogs and 23 cats received 92 subdermal plexus flaps
- advancement 34%, axillary fold, 22%, inguinal fold 22%, rotation17%, transposition 3%, distant direct 2%
- Post-op complications 51% at a mean of 6.9 days after surgery
- Outcome excellent 48%, good 36%, fair 14%, poor 2%.

With appropriate management of complications, a good to excellent outcome is often possible. Owners should be counseled about the likely need for additional visits and costs associated with treatment of postoperative complications.

Axial pattern flaps

Axial pattern flaps are specifically created to incorporate the associated direct cutaneous artery and vein at their base compared to SPF whereas the subdermal plexus blood supply is 'random'. Axial pattern flaps, therefore, have a more robust and predictable blood supply than subdermal plexus flaps which means they can support the subdermal plexus over a longer length of flap and have a surviving area approximately 50% greater than the equivalent sized random-pattern subdermal plexus flaps. The most commonly used axial pattern flaps are thoracodorsal and caudal superficial epigastric.

Indications for axial pattern flaps
- Large wounds of the flank and proximal limbs
- Wounds with a relatively poor blood supply, e.g. chronic non-healing wounds
- Wounds requiring greater tissue coverage, e.g. supply of muscle bulk in composite flaps

Tips for performing axial pattern flaps
- Clip a wide area for mobilisation of the flap and assessment of skin tension intra-operatively.
- Careful positioning of the patient is required before outlining the flap. The limb should be in a relaxed position, perpendicular to the trunk. The regional skin should be lifted up and then left to recoil.
- The regional landmarks and the proposed outline of the flap can be marked on the skin with a sterile pen and a ruler used to measure the length the flap can be transposed to, allowing for the loss of length from rotating the flap and from the inherent elastic recoil of the skin after incision, which makes defects look larger and flaps smaller! Large flaps require careful planning!
- Meticulous surgical technique is essential to prevent damage to the subdermal plexus and to the single DCA and vein supplying the flap. The flap survives by virtue of this one source of blood supply so it must be preserved! The distal end of the flap is very vulnerable, and clumsy manipulation or prolonged surgical times will result in distal avascular necrosis of the flap.
- The flap is undermined below the panniculus muscle or in the deep dermis, depending on the anatomic location, to avoid trauma to the blood vessels and the subdermal plexus.
- Dissection should begin at the tip of the flap and the blood vessels should be identified early in the dissection. Once the tip of the flap is elevated, stay sutures are placed to minimise trauma on handling of the flap. Once the flap is elevated, it should be protected in a saline-soaked swab until it is transposed into the recipient wound.
- Tension at the base of the flap is avoided and, if necessary, back-cut incisions may be made into the base or an island flap may be created. Transposition beyond 180°, twisting or kinking of the flap must be avoided to prevent tension that might compress the DCA and vein.
- Use an active suction drain if there is dead space. The tube should exit percutaneously through the adjacent skin rather than the flap, to avoid trauma to the blood vessels.
- Bandaging is effective at controlling the dead space and limiting motion of the limb but use only with caution as a bandage which is placed tightly may compromise circulation in the direct cutaneous vessels.
- The general guidelines below allow routine closure of the donor site. In animals with abundant loose skin at the donor site, wider flaps may be possible.
- If available a second surgeon can close the donor site while the first surgeon transposes the flap to save time (quicker surgery time helps viability). Skin staples also make flap closure quicker than skin sutures.
- The flap is sutured to the recipient bed in a 2-layer closure: subdermal strength holding layer that accommodates any tension and skin appositional layer +/- deeper vertical interrupted sutures in subcutaneous/subdermal tissues if necessary.

Outcome of axial pattern flaps
Field et al 2015:
- 49 dogs and 24 cats
- thoracodorsal, caudal superficial epigastric, reverse saphenous conduit, superficial brachial, deep circumflex iliac, superficial cervical, caudal auricular, lateral thoracic, cranial superficial epigastric, genicular, superficial temporal.
- Post-op complications 89%
- Complications: dehiscence, flap swelling, necrosis, infection, discharge, seroma
- Flap outcome: excellent 23%, good 41%, fair 30%, poor, 7%

Free Skin Grafts

Skin defects on the distal extremities present a unique reconstructive problem. If left to heal by second intention contraction is minimal so the dermis is repaired by migrating epithelium. This repair may result in a thin and vulnerable layer of hairless epithelium. Sufficient local skin for rotational or transposition skin flaps is rarely available. Relaxing incisions and "Z" plasties will only produce acceptable results if the defect is less than or equal to one-third the circumference of the affected limb. Axial pattern flaps do not reliably survive at lengths required to cover distal pelvic or thoracic limb defects. Full thickness free skin grafting is an excellent option to create a durable, cosmetic coverage of distal extremity defects in cats and dogs.

Classification of free skin grafts

A free skin graft is a piece of dermis that has been completely removed from its native blood supply and used to close another skin defect elsewhere. The graft is totally dependent upon the recipient bed for its nutrition and blood supply. Full thickness skin grafts are most commonly harvested in cats and dogs and include all of the epidermis and variable amounts of the dermis: all of the dermis is included for "thick" grafts and slightly less of the dermis for "thin" full thickness grafts. Grafts that have been harvested with much smaller amounts of dermis (often using a dermatome) may be referred to as "thin" or intermediate" full thickness grafts or split thickness grafts. Grafts can be prepared as single sheets, single "meshed" sheets, as strips, punch, or as pinch or seed grafts. Strips and punches as placed in pockets of granulation tissue and have increased "take" due to high SA:V ratio. In general, since the graft is dependent on the recipient bed for nutrients and blood supply, for thicker grafts, less graft "take" is possible but more hair growth is expected from the graft that does take. In veterinary practice, full-thickness skin grafts are preferable because they incorporate the hair follicles and therefore achieve a more cosmetically acceptable and durable result. The graft is taken from an area where there is sufficient loose skin available for primary closure of the donor site. The most convenient donor site is often the lateral thorax or flank.

Conditions suitable for free skin grafting:
- Region of the body that can be completely immobilised (i.e. distal extremity)
- A fresh, well vascularized soft tissue wound (with or without omentum) or a healthy bed of granulation tissue

Conditions that contra-indicate free skin grafting:
- Any region that cannot be completely immobilized with a bandage
- Contaminated/infected wounds
- [Over exposed bone or tendons – depends on how large an area this represents in relation to the wound]
- [Actively bleeding wound – can resolve bleeding first]
- Fat, chronic ulcers, chronic granulation tissue (these are all avascular)

Thin full thickness meshed sheet grafts

All fat and subcutaneous tissue is removed from a full thickness sheet of skin. To increase the size of the graft, enhance conformation of the graft to a wound, allow good drainage and improve graft "take", the graft is meshed by making staggered stab incisions in rows into the graft with a scalpel blade. Can't put too many holes in, they contract quickly, improving graft adherence and resulting in an excellent cosmetic result with full hair growth in most cases. The prepared graft is stretched over the wound (to improve adherence to wound bed), trimmed to size and sutured into the recipient bed using fine monofilament 1.5 metric sutures at the edges. Sutures can also be placed through mesh holes in the centre of the graft.

Punch and strip grafts

Small punches of dermis (taken with an 8 or 10mm skin biopsy punch) or 3-5mm strips of graft, with the subcutaneous fat removed, are placed into pockets within the granulation tissue of a wound, with a single suture to hold them in place (suture at both ends of a strip). These grafts have a large surface area to volume ratio and survive well. The graft provides extra foci of active epithelial cells that will complete neo-epithelialization.

Protection of the graft

After the graft has been carefully placed in the wound, it is just as crucial that the mechanical environment around the surgery site is controlled so that even a small amount of movement cannot interfere with adhesion and neo-vascularization of the graft. The forces attaching the graft to the wound are very tenuous for the first 72 hrs and are not full strength for 8 – 10 days. This is best accomplished using a modified Robert Jones type bandage (in some cases incorporating a splint into the bandage as well), or an external fixator (for patients with concurrent orthopaedic trauma).

Full thickness free skin graft outcome

Riggs et al 2015:
- 20 cats and 32 dogs
- Full thickness free skin grafts on distal extremity
- Success = full thickness graft viability >75% of original area > 1 week postop
- Success higher in cats (77%) than dogs (38%)
- Post-op complications 50% (graft failure, donor dehiscence, bandage sores)

References

1. Field EJ, Kelly G, Pleuvry D, et al. 2015. Indications, outcome and complications with axial pattern skin flaps in dogs and cats: 73 cases. J Small Anim Pract 56:698–706
2. Jones C, Lipscomb V, 2019: Indications, complications, and outcomes associated with subdermal plexus skin flap procedures in dogs and cats: 92 cases (2000–2017), J Am Vet Med Assoc 255:933–938
3. Riggs J, Frazer Jennings JL, Friend EJ, et al 2015. Outcome of full-thickness skin grafts used to close skin defects involving the distal aspects of the limbs in cats and dogs: 52 cases (2005–2012). J Am Vet Med Assoc 274:1042–1047

EXPLORATORY LAPAROTOMY: VISUAL TOUR, TIPS AND TRICKS

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I didn't have a diagnosis and I still don't!

There is no indication or justification for performing an exploratory laparotomy without some knowledge of what disease process may be occurring or without an intention to perform biopsies for the purpose of achieving a diagnosis. The decision to operate is based on, as a *minimum*: history, physical examination, radiographic or ultrasound findings, laboratory tests on any abdominal fluid retrieved, and a consideration as to whether you are likely be able to deal with the expected findings at surgery.

How should I drape the abdomen?

Drapes reduce contamination by creating a sterile field around the surgical site. To achieve this drapes have to be both adequate in size (i.e. large), and remain dry (i.e. non permeable). Conventional 4 way draping remains the mainstay of draping technique. A recent change in veterinary practice is the availability of economical disposable draping systems. Adhesive skin barriers have not been demonstrated to provide a preferential additional barrier to these. It is acceptable to cut one central hole in a large disposable drape to save on cost.

Do I need to use abdominal retractors? What else will help me see what I am doing?

Yes. The most versatile abdominal retractors are Balfour retractors. The blade attachment helps to stabilize the retractor and prevent it rotating. An alternative is Gosset or Posse retractors. You may be able to use Weitlanders or similar retractors in cats and very small dogs. Abdominal retractors are essential to achieve thorough abdominal exploration – these are not optional! If you do not have good overhead surgical lighting then buy a headtorch. Dedicated surgical headtorches are obviously much more expensive than camping headtorches but both can significantly improve surgical visualisation.

What is the value of suction?

Suction allows the abdomen to be effectively lavaged to reduce the contamination burden and is an essential requirement for many abdominal surgeries, certainly those with effusion (haemoabdomen, peritonitis). It is really important to remove all the fluid after you have finished lavage because failure to do this leads to dissemination of the contamination and dilution of the host inflammatory response. Suction also improves visualization so improves efficiency and safety of surgery.

Do I need diathermy?

No. You can perform abdominal surgery using fine haemostatic forceps to crush small vessels and ligatures for larger vessels. Diathermy is likely to improve the efficiency and speed of many surgeries but only becomes a requirement for complex/lengthy surgical procedures where placement of multiple ligatures is not possible or practical e.g. adrenalectomy.

What about using stapling equipment in the abdomen?

Surgical staplers (such as the various types of linear and linear cutter staplers) may be used in a wide variety of abdominal surgeries. They are employed with the aim of reducing surgical time, reducing tissue trauma/manipulation, minimising surgical contamination by intestinal contents and/or to provide easy and secure closure of gastrointestinal, liver or splenic tissue. This type of equipment is a luxury not a necessity and the proposed advantages are most beneficial for critically ill animals.

Entering the abdominal cavity

The incision should extend from the xiphoid to the pubis for an exploratory laparotomy. Once the skin is incised continue with a scalpel through the subcutaneous fat and fascia to the abdominal wall. Undermining of the skin to improve exposure of the abdominal wall is **not** necessary and should be avoided because it could predispose the patient to seroma formation and the fascia of the linea alba

receives some of its blood supply from this tissue. The linea alba is easy to identify in the cranial and mid abdomen as a white fibrous zone between the paired rectus abdominis muscles (wider in cats than dogs). It is quite narrow and becomes more difficult to identify in the caudal abdomen of both dogs and cats. Inadvertently straying off the midline (most commonly the result of poor patient positioning) may result in bleeding if the rectus abdominis muscle is incised. Enter the abdominal cavity by incising over the umbilical scar along the linea alba with a scalpel blade. This is a protected site as falciform fat always lies directly below the umbilicus so inadvertent laceration of abdominal organs is unlikely. Once a small hole is made through the linea alba extend the incision cranially with scissors. Once again, the cranial abdominal contents are protected from inadvertent laceration by falciform fat. Now that the incision is large enough, place your fingers into the abdominal cavity, elevate the abdominal wall and extend the incision caudally with scissors. Removing the falciform fat greatly improves visualization of the cranial abdomen. In deep chested dogs or when performing cranial abdominal surgical procedures, extending the incision alonside the xiphisternum will further increase exposure. In male dogs, the skin incision is extended lateral to the prepuce, the preputial branch of the caudal superficial epigastric artery is ligated and the preputial muscle fibres are incised (remember to re-align and suture the preputial muscle during closure). The prepuce is reflected laterally and the dissection continued to the midline linea alba.

Examination of the abdominal organs
Revising and knowing the abdominal anatomy in detail costs nothing. Explore the entire abdomen in a systematic manner (develop a routine), even if an obvious lesion is discovered.

Assessment and biopsy of abodminal organs ⌊SEP⌋
Biopsies should be performed on the organs that could be associated with the presenting clinical signs of the patient. For many patients, biopsies of the liver, stomach, duodenum, jejunum, ileum, mesenteric lymph node and pancreas are routinely performed, especially those with chronic vomiting and diarrhoea. Rarely biopsies of the spleen or kidneys are required. Avoid biopsies of the colon (rarely indicated and safer to get samples from colonoscopy). Pancreatitis secondary to performing a biopsy is very rare and should not prevent surgeons performing a biopsy when required.

Help – I don't know how to deal with what I have found inside the abdomen!
Improve the exposure by enlarging the incision, using retractors, excising the falciform fat and utilising suction. Performing the duodenal and colonic manoeuvres, packing uninvolved organs out of the way with large abdominal swabs and retracting the stomach with stay sutures is often useful. Perform a systematic examination of the entire abdomen. Carefully dissecting away any omental adhesions often makes the situation lot clearer. Consider asking a colleague for advice and/or an assistant to scrub in. Listen to your doubts – do not cut something if you are not certain what it is. Note the time and make sure you do not spend excessive time pushing tissue around without making progress. If you recognise that you do not have the ability, equipment or the postoperative care facilities to manage the case then take appropriate biopsies and close the abdomen. By performing a biopsy you make the procedure useful if the owner elects to pursue the case further.

Before closure of the abdomen
Perform a swab count and repeat after body cavity closure. Collect all used swabs in one dish, write down the count, note any dropped swabs, do not pass swabs off with biopsy material, unfold swabs to count them. Change contaminated gloves and instruments. Lavage the abdominal cavity to reduce contamination and the warm patient. Place an abdominal drain if indicated.

Abdominal wall closure
Abdominal wall closure can be performed using a simple continuous pattern is much quicker, and just as safe as interrupted sutures, provided:
- A 0.5cm-1cm bite of the correct fascial tissue is included in every pass of the needle on both sides of the incision. Distance between suture bites should also be 0.5 to 1 cm.
- Placement of sutures is in the transition between the linea alba and the rectus abdominus fascial sheath. You do not need to include the rectus abdominis muscle itself and closure of the peritoneal lining is not recommended, neither contribute to wound strength.
- Appropriate suture material such as longlasting monofilament absorbable suture (e.g. PDS,

Biosyn or Maxon) or, if cost is an issue, monofilament nylon, is used. Shorter lasting absorbable sutures (e.g. Caprosyn, Monocryl) or chromic catgut are not defensible choices.

- An adequate number of throws must be used on each knot for the suture material used.
- Sutures should accurately appose the tissue but excessively tight sutures diminish longterm wound strength (Stone et al 1986).

external sheath

rectus abdominis
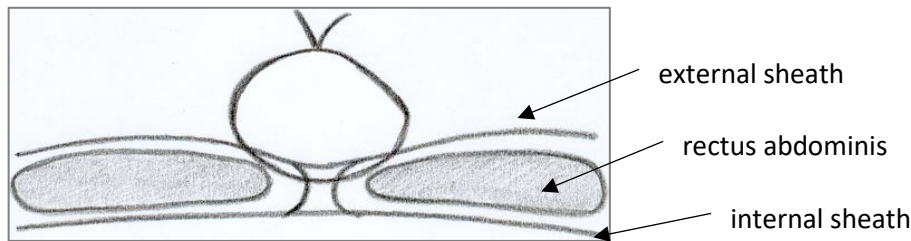
internal sheath

> Sutures should pass through the external sheath of the RA as well as the linea alba.

Coeliotomy complications

Haematomas and seromas can be avoided by good surgical technique and avoidance of undermining on each side of the incision. Wound infections can be minimised by correct aseptic and surgical technique, good postoperative care and correct antibiotic usage. Abdominal wound dehiscence is rare and usually the result of poor surgical technique, e.g. sutures too far apart (gap) or too close together (tissue necrosis), trapping fat between the incision edges, taking too small a bite of tissue, not placing the suture through the correct fascial tissue or selecting inappropriate suture material. A retrospective study of 200 dogs and cats that underwent exploratory coeliotomy (Boothe et al 1992) revealed a wound incision complication rate of 4%, with a trend for operations that lasted > 3 hours. Larger animals did not demonstrate a higher rate of coeliotomy complications.

References and further reading

1. Boothe HW, Slater MR, Hobson HP et al 1992: Exploratory coeliotomy in 200 nontraumatized dogs and cats. Vet Surg 21(6), 452-457
2. Keats MM, Weeren R, Greenlee P et al 2004: Investigation of the Keyes skin biopsy instrument for intestinal biopsy versus a standard biopsy technique. J Am Anim Hosp Assoc 40(5):405-10
3. Shales CJ, Warren J, Anderson DM et al 2005: Complications following full-thickness small intestinal biopsy in 66 dogs: a retrospective study. J Small Anim Pract 46(7):317-21
4. Swinbourne F, Jeffery N, Tivers MS, Artingstall R, Bird F, Charlesworth T, Doran I, Freeman A, Hall J, Hattersley R, Henken J, Hughes J, de la Puerta B, Rutherford L, Ryan T, Williams H, Woods S, Nicholson I (2017) The incidence of surgical site dehiscence following full thickness gastrointestinal biopsies in dogs and cats and associated risk factors. JSAP 58(9): 495-503

LEAKING ENTERECTOMY: PREVENTION IS BETTER THAN CURE!

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All gastrointestinal tract surgery carries a risk of incisional breakdown leading to lifethreatening peritonitis which has a mortality rate of 50-80%. Risk factors for peritonitis are difficult to identify but may include hypoalbuminaemia, presence of pre-operative peritonitis, intestinal trauma or foreign bodies (Allen et al 1992, Ralphs et al 2003). In a study of 208 dogs and cats with intestinal foreign bodies, longer duration of clinical signs, linear foreign body and multiple intestinal procedures were associated with increased mortality (Hayes 2009). The mortality rate following re-laparotomy in a series of dogs that had recurrent peritonitis due to intestinal wound breakdown was 56% (Barfield et al 2016) and it is imperative that everything possible is done at the first surgery to maximize the potential for healing of the gastrointestinal surgery.

What do I need to know about intestinal tract healing?
The intestinal wall is composed of four layers: serosa, muscularis, submucosa and mucosa. The submucosa contains a large proportion of connective tissue (mainly collagen) and is the strength holding layer for all intestinal surgery. The mucosa provides a barrier to the movement of intraluminal bacteria or endotoxins into the portal vasculature. This barrier becomes progressively compromised when bowel is obstructed. The intestine heals rapidly, regaining 80% of its original tensile strength by 14 days. Colonic healing is slightly delayed compared to the rest of the GI tract, regaining @ 50% strength regained by 14 days. The end of the inflammatory/lag phase of intestinal healing (days 1-4) before the proliferative/repair phase (days 3-14) gets properly underway and lays down collagen is typically when dehiscence will occur.

Atraumatic surgery and accurate apposition of the tissue layers optimises intestinal healing. Inversion or eversion of all layers, eversion of the mucosa or tissue overlap will retard intestinal healing. Appositional sutures also cause less intestinal lumen narrowing than an inverting pattern and less adhesions than an everting pattern. Other factors that may retard healing include nutritional compromise or hypoproteinaemia (albumin <20g/l), chemotherapy, leucopaenia, corticosteroids and radiotherapy. It is generally recommended that any chemotherapy is delayed until 2 weeks post-operatively.

Does it make a big difference how I handle the bowel at surgery?
Exposure and handling of bowel will result in desiccation and abrasion. Poor tissue handling causes increased inflammation and a greater risk of adhesion formation, motility disorders and peritoneal fluid production. Even with careful attention to surgical technique, myoelectrical activity of the gastrointestinal tract is decreased for 24 hours post-operatively.

It is important to try to avoid spilling intestinal contents (especially colonic contents/faeces) as doing so will increase the risk of post-operative infection. Where possible, the part of the intestinal tract involved is exteriorized and isolated from the rest of the abdomen using moistened, large laparotomy swabs. Layering 3-4 swabs allows removal of any swabs that become contaminated during the procedure and decreases the risk of contamination. Stay sutures can be placed to manipulate the intestine, and these can be lifted to avoid spillage when the lumen is entered. Before making an incision, the intestinal contents are milked away from the incision site. Inevitably, spillage of intestinal contents will occur and this is not a disaster so long as the abdomen is thoroughly lavaged with several litres of sterile saline to dilute the contamination. Local irrigation of the surgical site is performed first, followed by general abdominal lavage prior to closure. The lavage solution must be completely removed using suction. Replace contaminated instruments and gloves before closing the abdomen. If there is pre-existing peritonitis place an abdominal drain before closure (Adams et al 2009).

Sutures and needles for intestinal surgery

Use a swaged-on round-bodied needle and an absorbable, monofilament suture that maintains sufficient strength past the 14-21 days required for the intestines to regain normal wound strength e.g. PDS, Biosyn or Maxon. These suture materials are strong and long lasting therefore can be used at a relatively fine gauge (1.5 metric for small and large intestine) resulting in less tissue trauma and with good knot security. Shorter lasting monofilament absorbable sutures are also used successfully for GI surgery but Monocryl losses 90% of it's tensile strength by 14 days so be cautious if any factors that might delay healing are present.

How can I assess intestinal viability?

Serosal colour is very important – variations on purple, grey, black, green all indicate unviable tissue. Obvious necrosis will appear as a thin black-purple wall and a clear line of demarcation between viable and non-viable tissue. Another method of assessment is to make small stab incisions in the serosa and look for bleeding. In the small intestine viability is best assessed by evaluating a combination of serosal colour, wall texture, peristalsis and pulsing of the jejunal arteries. Objective measures of tissue necrosis, e.g. fluorescein and pulse oximetry, may not be more accurate than subjective assessments, and are rarely available. It is worth re-assessing the tissue 10-15 minutes after correction of the obstruction because the appearance of the tissue often improves. Unless the location is particularly tricky due to adjacent important structures, the safest plan is to generously apply the principle of "if in doubt cut it out".

What and how much bowel can I resect?

Fortunately, large regions of the small bowel can be resected. Short bowel syndrome (resection of so much bowel that the body cannot compensate, at least initially) is rarely reported in small animals, and is only likely to be seen in animals that have had more than 70-80% of the small intestine resected. Whether an animal will develop clinical signs depends on many factors, including the location and amount resected, whether the ileocaecocolic valve is resected, and the health and adaptation of the remaining intestine. Think carefully before considering surgery that involves the common bile duct, pancreatic ducts and proximal duodenum (shares an intimate blood supply with the right limb of the pancreas) because resection involving these structures is technically challenging and introduces additional complications.

How can I re-enforce my enterectomy?

Omentalisation

Wrapping omentum around the wound provides gastrointestinal surgery sites with additional blood supply, as well as promoting lymphatic draining and helping infection control. Omentum adheres to surgical sites and areas of inflammation. Experimental studies have shown that omentum can revascularise areas of intestinal ischaemia and prevent perforation.

Serosal Patch

Serosal patching provides support that is more mechanically robust than omentum but is not needed as often. It has been shown experimentally that it can seal off small perforations in dogs with GI wounds. The anti-mesenteric border of healthy jejunum is sutured either side of the suture line in question. The sutures penetrate the submucosa of both portions of intestine. Two intestinal loops can be sutured together first to create a larger patch. When patching around an enterectomy site make sure that the loop is gentle so as not to cause obstruction and that the sutures do not compromise the vasculature at the mesenteric border.

When should I feed my patient after intestinal surgery?

Adequate nutrition is critical to wound healing and patient survival. Feeding should begin as soon as the patient is able to/wants to eat and is awake enough, usually @ 12-24hrs after surgery (Ralphs et al 2003). It is contra-indicated to feed a patient that is still sedated as this predisposes to regurgitation and aspiration pneumonia. Feeding stimulates motility and blood flow in the intestinal tract reducing the likelihood of ileus and adhesions. Feeding also provides the patient with valuable fluid and electrolytes. There are no grounds for delaying feeding in an attempt to reduce tension or minimize leakage at an enterotomy or enterectomy site. Peristaltic contractions are *greater* in

strength in fasted (compared to fed) patients. Give water first, followed by a small amount of food later if there is no vomiting. The diet should be tailored to the patient but feeding multiple small meals of a highly digestible diet (e.g. low fat, low fibre) is recommended for the first few days. If the animal will not eat, consider enteral tube feeding sooner rather than later. In debilitated patients, place a gastrostomy or oesophagostomy tube at the time of surgery in the anticipation that enteral nutrition will be required, if the tube is not needed then it does not matter.

How can I tell if dehiscence is occurring?
Dehiscence occurs 2-5 days post-operatively and the animal will show some or all of: vomiting and anorexia, clinical signs of progressive septic shock (tachycardia, weak pulses, pale mm, prolonged CRT, pyrexia), abdominal pain and distension. Definitive diagnosis is made on the basis of cytology of retrieved abdominal fluid: neutrophils are degenerate and contain intracellular bacteria. The differences between peritoneal and serum glucose and lactate concentrations are also reliable indicators of septic peritonitis. In peritonitis peritoneal glucose is low and lactate is high. Occasionally it may not be possible to confirm peritonitis, but repeat surgery (following patient stabilisation) is warranted in clinically deteriorating patients.

References and further reading
1. Adams R, Doyle R, Bray J, Burton C (2012) Closed suction drainage for treatment of septic peritonitis of confirmed gastrointestinal origin in 20 dogs. Vet Surg 43(2): 843-851
2. Allen, DA, Smeak DD, Schertel ER (1992) Prevalence of small intestinal dehiscence and associated clinical factors: a retrospective study of 121 dogs. J Am Animal Hosp Assoc 28, 70-76
3. Barfield DM, Tivers MS, Holahan M, Welch K, House A, Adamantos S (2016) Retrospective evaluation of recurrent secondary septic peritonitis in dogs (2000-2011): 41 cases. J Vet Emerg Critical Care 26(2): 281-287
4. Hayes, G (2009) Gastrointestinal foreign bodies in dogs and cats: a retrospective study of 208 cases. J Small Animal Practice 50: 576-583
5. Ralphs SC, Jessen CR, Lipowitz AJ 2003: Risk factors for leakage following intestinal anastomosis in dogs and cats: 115 cases (1991-2000). J Am Vet Med Assoc 223(1):73-7
6. Shales CJ, Warren J, Anderson DM, et al. Complications following full-thickness small intestinal biopsy in 66 dogs: a retrospective study. J Small Anim Pract 2005; 46(7):317–321
7. Swinbourne F, Jeffery N, Tivers MS, Artingstall R, Bird F, Charlesworth T, Doran I, Freeman A, Hall J, Hattersley R, Henken J, Hughes J, de la Puerta B, Rutherford L, Ryan T, Williams H, Woods S, Nicholson I (2017) The incidence of surgical site dehiscence following full thickness gastrointestinal biopsies in dogs and cats and associated risk factors. JSAP 58(9): 495-503
8. Weisman DL, Smeak DD, Birchard SJ, Zweigart SL 1999: Comparison of a continuous suture pattern with a simple interrupted pattern for enteric closure in dogs and cats: 83 cases (1991-1997). J Am Vet Med Assoc 214(10):1507-10
9. Ullman SL, Pavletic MM, Clark GN (1991) Open intestinal anastomosis with surgical stapling equipment in 24 dogs and cats. Vet Surgery 20, 385-391

SURGICAL ASPECTS OF LOWER URINARY TRACT TRAUMA

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Contrast radiography is critical for identifying the site of urinary tract rupture before surgery therefore allowing selection of the correct surgical approach. The *extent* of damage to the kidney, ureter, bladder or urethra may only become fully apparent at surgery.

Bladder
The bladder is the most common (@70%) site of urinary tract rupture following trauma. Exploratory laparotomy is performed to identify and repair the defect. All unviable bladder tissue must be resected. A single layer, full thickness, simple continuous appositional closure is quick, provides accurate apposition of the strength-holding submucosal layer, and is suitable for most repairs. If the defect is small or irregular in shape then interrupted sutures may be easier. Many absorbable, monofilament synthetic suture materials are suitable choices for bladder closure, 1.5 or 2 metric depending on the thickness of the bladder wall. Polydioxane suture has been shown to be superior to other sutures in the presence of most types urinary tract infections (no absorbable sutures last well in the presence of Proteus infection). The abdomen is thoroughly lavaged before closure and the bladder incision is omentalised, or if there is concern about the bursting strength of the repair a serosal patch may be used.

If a large amount of bladder is resected the bladder may be reconstructed over a cystostomy tube, which will also maintain decompression in the immediate post-operative period. In people, excision of over 75% of the bladder (excluding the trigone) with closure over a 5ml Foley catheter results in development of a 300ml bladder capacity within 3 months. Catheterise the urethra and ureters and avoid them. One or both ureters can be re-implanted in the bladder at another location if necessary.

The neurovascular supply to the bladder enters dorsally in the trigone region; cystectomy of this area is complicated and carries greater risk of urinary incontinence. Successful management of >90% bladder necrosis was reported in one dog with a seromuscular colonic augmentation procedure (Pozzi et al 2006), in which the external wall of the colon became the cranial wall of bladder, and an ileocystoplasty procedure in another dog (Schwarz et al 1982) – both these bladder injuries occurred as a complication of ovariohysterectomy. A dog with an extensive proximal urethral and trigone defect secondary to massive pressure necrosis and abscess formation from a large proximal urethral calculus was managed successfully using a rectus abdominis muscle flap (Savicky and Jackson 2009).

Urethra
The urethra may rupture during blunt abdominal trauma and also as a consequence of laceration from pelvic fracture fragments (common in male dogs and cats). Other important causes of urethral rupture include iatrogenic perforation during catheterisation (particularly in cats) and obstruction due to urolithiasis.

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                    ┌─────────────────────┐
                    │   Urethral trauma   │
                    └─────────────────────┘
                               │
                               ▼
                ┌────────────────────────────┐
                │ Correct fluid, electrolyte  │
                │  and acid-base imbalances   │
                └────────────────────────────┘
                               │
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            ┌──────────────────────┐        ┌──────────────────────────────┐
            │  Attempt urethral    │──no───▶│ • Antegrade catherisation    │
            │  catheterisation     │        │ • Cystostomy tube            │
            └──────────────────────┘        │ • Cystocentesis              │
                        │                    │ • Abdominal drain            │
                       yes                   └──────────────────────────────┘
                        ▼
            ┌──────────────────────────────┐
            │ Retrograde urethrocystogram   │
            │ to determine site of rupture  │
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| Healing over indwelling catheter | Primary urethral repair by resection and anastomosis | Urethrostomy proximal to lesion: perineal (cat) or prepubic | (Permanent cystostomy tube) |

If the urethra can be catheterised because there is a reasonable degree of longitudinal integrity then healing over an indwelling urethral catheter is simple to manage and can produce satisfactory results (2/10 cats developed a stricture on longterm follow-up, Meige et a 2008). The catheter must be soft and flexible e.g. silicone Foley catheter. Anterograde guidewire assisted urethral catheterisation via the bladder (using fluoroscopy) may be useful when retrograde catheterisation attempts have failed.

If the urethra cannot be catheterised then debridement and suture repair by resection and anastomosis is indicated. Surgical magnification is helpful, particularly in cats. Injuries of the intrapelvic portion of the urethra will require a ventral pubic osteotomy for access. Debridement must be thorough because suturing unhealthy urethral tissue risks dehiscence or second intention healing resulting in stricture. Adequate dissection is needed to prevent tension on the urethral repair, which also promotes stricture formation. Place full thickness, interrupted sutures using fine, absorbable monofilament suture e.g. 1 or 1.5 metric PDS II over a urethral catheter. Use stay sutures to manipulate the ends of urethra and correctly orientate the two urethral ends relative to each other, taking care to avoid rotation. For some cases of complete urethral transection a second catheter may need to passed in an antegrade manner via a cystotomy incision to identify the end of the proximal urethra. Leakage of urine into the intrapelvic or subcutaneous tissues results in extensive cellulitis and tissue necrosis so lavage and placement of a drain is indicated.

Diversion of urine postoperatively for 5-7 days aids healing. Use of indwelling urethral catheter following primary repair is controversial because it has the potential to damage urothelium, interfere with healing, promote stricture formation and result in ascending infection. Indwelling urethral catheters should be soft, flexible and of a small diameter to minimise interference with the urethral repair. No differences in outcome were found between dogs that underwent primary urethral anastomosis with either a cystostomy tube, indwelling catheter or both for 7 days postoperatively (Cooley et al 1999).

If primary repair is not possible, or fails, then a salvage surgery such as a perineal or prepubic urethrostomy may be performed depending on the location of the trauma. A perineal rather than a prepubic urethrostomy is performed whenever possible in cats as this procedure is associated with fewer complications. Transpelvic urethrostomy produces a more cranial stoma to a perineal urethrostomy by using bone rongeurs are used to remove a section of ventral ischium. Both perineal and prepubic urethrostomies in dogs have a high rate of complications. Complications of prepubic urethrostomy include urethral obstruction due to kinking of the urethra, subcutaneous leakage of urine in the postoperative period leading to tissue necrosis, stricture, dehiscence, urinary incontinence, peristomal skin irritation and urine scald. Subpubic urethrostomy is similar to prepubic urethrostomy except that the urethral stoma is positioned caudal to the brim of the pubis.

Prognosis

Complete recovery is expected after prompt repair of a traumatic bladder tear. A series of 20 dogs and 29 cats with urethral rupture revealed that type of surgical correction, time to surgery and type/duration of urinary diversion were not significantly associated with outcome, which was instead governed by the extent of other injuries (Anderson et al 2006). In a study of 26 cats with uroperitoneum (mostly bladder and urethral injuries), 16 were discharged from the hospital and the prognosis again depended largely on the extent and severity of other injuries (Aumann et al 1998). In a series of 10 animals with ureteral rupture due to blunt trauma ureteronephrectomy was performed in 6 animals, all of which were discharged from the hospital. Ureteroneocystostomy was performed in two animals, both of which died of acute renal failure postoperatively (Weisse et al 2002).

References

1. Anderson RB, Aronson LR, Drobatz KJ et al 2006: Prognostic factors for successful outcome following urethral rupture in dogs and cats. J Am Anim Hosp Assoc 42(2), 136-46
2. Aumann A, Worth LT, Drobatz KJ 1998: Uroperitoneum in cats: 26 cases (1986-1995). J Am Anim Hosp Assoc 34, 315
3. Baines S, Rennie S, White R 2001. Prepubic urethrostomy: A long-term study in 16 cats. Vet. Surg 30, 107–113
4. Bernarde A, Viguier E 2004: Transpelvic urethrostomy in 11 cats using an ischial ostectomy. Vet Surg 33:246
5. Bilbrey S, Birchard S, Smeak S 1991: Scrotal urethrostomy: a retrospective review of 38 dogs (1973-1988). J Am Anim Hosp Assoc 27:560
6. Cooley AJ, Waldron DR, Sith MM et al 1999: The effects of indwelling transurethral catheterisation and tube cystostomy on urethral anastomoses in dogs. J Am Anim Hosp Assoc 35, 3421-347
7. Hosgood G, Salisbury SK 1988: Generalized peritonitis in dogs: 50 cases (1975-1986). J Am Vet Med Assoc 193, 1448
8. Mehl ML, Kyles A, Pollard R et al 2005: Comparison of 3 techniques for ureteroneocytostomy in cats. Vet Surg 34(2), 114-119
9. Meige F, Sarrau S, Autefage A 2008: Management of traumatic urethral rupture in 11 cats using primary alignment with a urethral catheter. Vet Comp Orthop Traumatol 21, 76-84
10. Ruda L, Heiene R 2012: Short and longterm outcome after perineal urethrostomy in 86 cats with feline lower urinary tract disease. J Small Anim Pract 53, 693-698

HAEMOABDOMEN: HOW AND WHEN TO OPERATE

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Confirming a haemoabdomen is present
A peritoneal tap using a needle and syringe or over-the-needle catheter will retrieve fluid that looks like blood grossly and on cytology and has a PCV/TP similar to the dog's peripheral blood. The PCV of fluid that looks haemorrhagic grossly should always be measured: fluids with a PCV of 5-10% may appear very bloody but do not represent true haemoabdomen and an alternative cause for their effusion should be sought. The blood should not clot; if it does it is possible the spleen may have inadvertently been penetrated.

Differential diagnosis of haemoabdomen
1. Ruptured splenic mass: In one study 70% of dogs presenting with acute non-traumatic haemoabdomen had splenic haemangiosarcoma (Pintar et al 2003). In another study more than 95% of dogs with splenic rupture were diagnosed with splenic neoplasia (Johnson et al 1989). Haematoma, haemangioma or other splenic tumours are also possible.
2. Ruptured liver mass: A primary or secondary neoplastic liver mass may rupture and cause haemoabdomen. A ruptured mass is most likely to be haemangiosarcoma or hepatocellular carcinoma but benign lesions are also possible.
3. Trauma to an abdominal organ (e.g. liver, spleen, kidney) or large vessel
4. Bleeding and/or perforated gastrointestinal mass (more likely to cause melaena) or adrenal mass
5. Coagulopathy caused by angiostrongylosis (Willesen et al 2008, Humm & Boag 2008) is not fully understood but seems to be able to manifest in different ways including haemoabdomen. It is important not to get caught out by this as surgery is contraindicated so examine a faecal smear for angiostrongylosis larvae if you have any suspicions.

Stabilisation and pre-op care
Hypoperfused patients are treated to effect with crystalloid +/- colloid fluids. An initial bolus rate, which is a proportion of the traditional "shock" fluid rate of 60-90 ml/kg, is given based on the severity of the presenting cardiovascular parameters e.g. 20-40ml/kg over 20 minutes. Subsequent fluid boluses and rates are tailored to the response of cardiovascular parameters (heart rate and rhythm, pulse profile, blood pressure, capillary refill time) to the fluid therapy. The aim is to replace intravascular deficits prior to surgery and therefore improve cardiovascular parameters e.g. mean arterial blood pressure @ 70mmHg, until surgical haemostasis can be achieved. A blood transfusion is required if fluid therapy is not sufficient for stabilisation and/or if the PCV drops very low (e.g. <20%) due to ongoing haemorrhage and fluid therapy.

Use ECG and blood pressure monitoring before, during and after surgery because animals with poor perfusion may develop cardiac arrythmias and animals with splenic masses are particularly prone to this, particularly those with anaemia and haemoabdomen (Marino et al 1994). Treatment of the hypoperfusion with fluid therapy is the main therapy for any cardiac arrhythmias. Anti-dysrhythmic medication is considered if cardiac arrhythmias associated with hypotension persist.

APTT and PT clotting tests are useful prior to surgery to identify potential for ongoing bleeding due to disseminated intravascular coagulation (DIC), which is common in animals with a splenic mass or splenic torsion.

Imaging
Abdominal radiographs may identify a splenic or liver primary mass but are often not able to distinguish between these two locations with certainty and usually can't identify abdominal metastases. Thoracic radiographs are essential to check for pulmonary metastases.

Abdominal ultrasound is extremely useful for accurately locating the primary mass, in particular whether it is in the spleen or liver (or adrenal, gastrointestinal tract). It may identify if the primary

mass the looks disrupted/ruptured (i.e. consistent with being the cause of haemoabdomen), identifies any other masses in the liver, spleen, enlargement of sublumbar lymph nodes. Identification of hepatic masses, however large, should not be a basis for recommending euthanasia because large regenerative hepatic nodules are common in older dogs; biopsy should be obtained at surgery. Pre-operative abdominal ultrasound is reassuring for the inexperienced surgeon who may be happy to perform a splenectomy but would struggle to address a bleeding hepatic mass or adrenal neoplasm.

Ultrasound guides any possible fine needle aspirate attempts but aspiration of a splenic mass is often unhelpful/contraindicated in cases of haematoma/haemangioma/sarcoma as usually just see blood. May be more useful for other liver/splenic masses (including metastatic disease) but false negatives are still common.

Echocardiography is useful to look for primary or secondary haemangiosarcoma because one of the predilection sites for this tumour is the right atrium. As many as 25% of dogs with splenic haemangiosarcoma have concurrent right atrial haemangiosarcoma.

You can justify the extra cost of performing a thoracoabdominal CT if available on the basis that it is more sensitive than radiographs for detecting pulmonary metastases and replaces the information obtained on abdominal ultrasound.

Surgical tips for splenectomy
Perform a total splenectomy, it is easier than a partial splenectomy and indicated if neoplasia is known or suspected.

Make a large ventral midline abdominal incision from xyphoid to pubis and use abdominal retractors. Large swabs are useful for packing other abdominal organs out of the way.

Use suction to remove intra-abdominal haemorrhage for good exposure and visibility.

A heavy spleen can compress CVC, reducing venous return and affecting CO so consider your positioning of the spleen during removal and use an assistant if available.

The main splenic pedicle can be clamped on entry to the abdomen prior to splenectomy to stop ongoing haemorrhage and improve visualisation. A congested, torsed spleen must be handled carefully because it is at risk of rupturing and the pedicle should not be untwisted prior to splenectomy. The twisted pedicle may be clamped and/or mass ligated to allow removal of the spleen followed by further division and ligation of the pedicle.

Remember to examine the entire abdomen in animals suspected of having neoplasia. Only 50% of dogs with splenic HSA and grossly abnormal livers at exlap had metastatic HSA on liver biopsy histopathology (Clendaniel et al 2014).

You will need lots of haemostatic forceps and swabs. Remember to count all swabs at the beginning of surgery and before closing the abdomen.

Measure blood in the suction bottle and weigh swabs (1ml of blood =1.3gs) to estimate amount of blood loss intra-operatively.

Begin removal of the spleen at the tail end and choose one of the techniques below:

i) Double ligate and divide all the hilar vessels. Double ligation with a transfixing ligature is recommended for the splenic artery and vein. When the head of the spleen is reached you can try and preserve the short gastric vessels and transect the gastrosplenic ligament. This method is time consuming and unnecessary.

ii) The "fast" technique described by Hosgood 1989 is to ligate the short gastrics, left gastroepiploic and the splenic a + v distal to the branch supplying the pancreas. This may be difficult to do if there are lots of adhesions to a ruptured splenic mass or if the anatomy is distorted because of a splenic torsion or GDV.

iii) An efficient compromise that works well for most cases is to ligate bunches that include the main 7-8 vessels just away from the hilus. Care still needs to be taken to preserve the splenic branches to the left limb of the pancreas to avoid ischaemic necrosis of the pancreas. Don't need to preserve short gastrics.
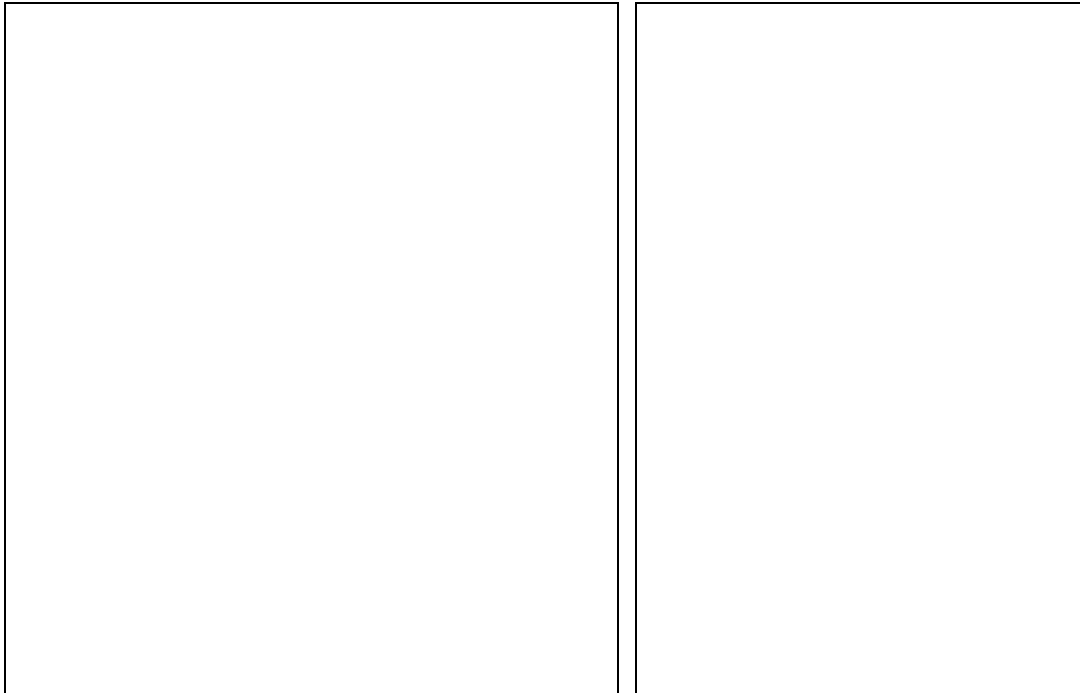
ii) Hosgood et al 1989: ligation of short gastrics, left gastropeiploic & splenic vessels

iii) blue circles are ligation sites for a quicker splenectomy than ligation of all the hilar vessels

If available both an ultrasonically activated scalpel (Royals et al 2005) and a vessel sealant device (Rivier and Monnet 2011) have been used safely for splenectomy in dogs.

Following splenectomy (particularly for splenic torsion) consider performing a gastropexy in breeds of dog known to be at increased risk for GDV but there is no evidence to support this concept currently (Goldhammer et al 2010).

Submit the entire spleen, or as much of the splenic mass as possible for pathology because multiple sections may be required to diagnose haemangiosarcoma.

Monitor mucous membranes, heart rate, pulse quality, blood pressure and PVC/TP regularly postoperatively as haemorrhage is the main complication following splenectomy.

The need for prophylactic antibiotics is mostly dictated by the underlying disease and can be justified in animals who are immunosuppressed, critically ill, in shock and/or likely to undergo a relatively long surgery. Patients with a haemoabdomen do not usually have an infection so postoperative antibiotics are rarely indicated.

References and further reading
1. Clendaniel DC, Sivacolundhu RK, Sorenmo KU, Donovan TA, Turner A, Arteaga T, Bergman PJ (2014) JAAHA 50(4), e6-10
2. Collard F, Nadeau ME, Carmel EN (2010) Laparoscopic splenectomy for treatment of haemangiosarcoma in a dog. Vet Surg 39(7), 870-2

3. Crawford AH, Tivers MT, Adamantos SE (2012) Owner assessment of dog's quality of life following treatment of neoplastic haemoperitoneum. Vet Rec 170, 566
4. Goldhammer MA, Haining H, Milne EM et al (2010) Assessment of the incidence of GDV following splenectomy in dogs. J Small Anim Pract 51(1), 23-8
5. Hosgood G, Bone DL, Vorhees WD et al (1989) Splenectomy in the dog by ligation of the splenic and short gastric arteries. Vet Surg 18(2), 110-3
6. Pintar J, Breitschwerdt EB, Hardie EM et al (2003): Acute nontraumatic haemoabdomen in the dog: a retrospective analysis of 39 cases (1987-2001), J Am Anim Hosp Assoc 39, 518
7. Rivier P and Monnet E (2011) Use of a vessel sealant device for splenectomy in dogs. Vet Surg 40, 102-5
8. Royals SR, Ellison GW, Adin CA (2005) Use of an ultrasonically activated scalpel for splenectomy in 10 dogs with naturally occurring splenic disease. Vet Surg 34, 174-8

SURGICAL DISEASES AND TECHNIQUES OF THE BILIARY TRACT

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Cholecystotomy or choledochotomy

An aspirate of bile can be taken from the gallbladder using a 25g needle so long as the biliary tract is not obstructed. It is rarely indicated to incise into the gallbladder (cholecystotomy) as alternatives are recommended instead e.g. cholecystectomy for a diseased gallbladder and retrograde catheterization of the common bile via the duodenum is much easier than antegrade catheterisation via the gallbladder. A choledochotomy (incision into the common bile duct) may occasionally be indicated for a dilated bile duct with an obstructing cholelith that cannot be flushed back into the gallbladder. The common bile duct incision is repaired over a stent using fine suture (1 or 1.5 metric) and surgical magnification is extremely helpful. Occasionally a cholelith obstructing at the major duodenal papilla can be removed by incising over the intramural bile duct (sphincterotomy) via a duodenal incision.

Cholecystectomy

Removal of the gallbladder may be performed for severe cholecystitis (with or without cholelithiasis), mucocoele, neoplasia or trauma to the gallbladder/cystic duct. Patency of the common bile duct must be established before cholecystectomy. Gently mobilise the gallbladder away from the liver by blunt dissection (fingers, Q-tips or moist swabs work well). This is easier to do when the gallbladder is moderately full. The cystic duct and artery is dissected clear of all surrounding tissue and ligated before excision (be careful to avoid traumatizing a hepatic duct when doing this). Carefully inspect the stump for bile leakage, a hepatic duct can be ligated or cauterized if necessary. Pack the empty gallbladder fossa with cold saline soaked swabs if necessary to stop any liver haemorrhage after dissection. Laparoscopic cholecystectomy has also been successfully reported in dogs with uncomplicated or incidental gallbladder mucocoeles.

Cholecystoduodenostomy

Obstruction of the common bile duct that cannot be relieved by catheterisation and flushing is treated by diverting the bile flow via anastomosis of the gallbladder directly to the duodenum (or jejunum if there is too much tension). This is not a benign procedure as it is less physiological for bile to enter directly into the duodenum from the gallbladder and the gallbladder itself must be healthy. The gallbladder is dissected out and mobilised as for a cholecystectomy. It is important that the gallbladder is mobilised sufficiently to ensure there is no tension on the suture lines and that the cystic artery is not damaged or twisted. The gallbladder is sutured to the seromuscular layer of an easily reached region of proximal duodenum (antimesenteric surface). The area is carefully packed off with swabs and parallel incisions are made in the gall bladder and duodenum (if an incision has been made in the proximal duodenum for attempted common bile duct catheterization the same incision can be used for the anastomosis). The incisions should be as long as possible (dictated by the size of the gallbladder) as it is essential that the anastomotic opening is large enough to prevent the inevitable backflow of intestinal contents from being trapped inside the gallbladder. If the new stoma is large enough then clinical disease associated with reflux into the gallbladder is usually not recognised. A stoma <2.5cm is suggested to predispose to stricture and ascending cholangiohepatitis. Both sides of the gallbladder and duodenal incisions are sutured to each other using a full thickness simple continuous suture pattern. The remaining free side of the gallbladder is folded over the stoma suture lines and a final suture line is placed from the gallbladder to the seromuscular layer of the duodenum to seal off the new anastomosis. Cholecystoenterostomy can also be performed using endoGIA stapling equipment at open surgery. The prognosis following biliary diversion is overall worse than for cholecystectomy and is especially guarded in cats.

Catherisation of the common bile duct

The patency of the common bile duct can be determined by catheterization of the major duodenal papilla via a duodenotomy incision on the antimesenteric surface @5cm distal to the pylorus. Look

for where the common bile duct enters the duodenum externally and then identify the raised mucosal papilla on the mucosal surface of the duodenum 1-2cm aboral to this (allows for the distal intramural portion of the common bile duct). Catheterise the common bile duct in a retrograde manner using a soft, fine catheter (3.5-5F cats/small dogs, 8-12F larger dogs). If leaving a catheter in place to ensure continued patency of the common bile duct attach to the duodenal mucosa with an absorbable suture. If permanent palliation is the goal a non-absorbable suture can be used. Leave the end of the catheter in the duodenal lumen and it will pass when the suture weakens (or you can also remove the catheter using an endoscope). Choledochal stenting is a relatively quick technique that is particularly useful for animals with reversible disease (e.g. pancreatitis) and nice to try in any patient before proceeding with a salvage cholecystoenterostomy surgery, especially in severely compromised animals for which a long anaesthetic is not desirable. In animals with neoplasia the stenting procedure is usually palliative until the results of biopsy are known as definitive surgery is often not recommended due to the guarded prognosis.

Extrahepatic biliary tract obstruction (EHBO)
EHBO may be intraluminal or extraluminal. The most common cause of biliary obstruction in both dogs and cats is inflammatory disease (pancreatitis, hepatitis, cholecytitis or a combination of these) resulting in compression or inflammation of the common bile duct. In mildly clinically affected animals where there is doubt regarding current biliary tract obstruction it may be prudent to monitor clinical progression, hyperbilirubinaemia and progressive biliary tract distension over several days but any animal with severe or rapidly progressive haemodynamic compromise should be operated on without delay. Animals (especially dogs) with pancreatitis causing EHBO rarely need surgery as this should improve or resolve with appropriate medical therapy over 7-10 days but in very severely affected animals or those not improving on medical management a common bile duct stent can be placed to temporarily relieve obstruction, confirm the diagnosis by biopsy and facilitate further medical management. Choleliths are often an incidental finding and in absence of other biliary tract signs or obstruction are themselves not an indication for surgery. At exploratory laparotomy be sure to identify the gallbladder, cystic duct and common bile duct and gently palpate them. Gallbladder patency may be observed by gently squeezing it then waiting a minute for relaxation of the sphincter and flow of bile. The goal of surgery is to thoroughly explore the abdomen, achieve a diagnosis through biopsy of abnormal organs and either remove a disease gallbladder or provide biliary decompression or diversion. Animals with inflammatory disease have a high mortality (up to 50%) and morbidity rate following surgery. Animals with underlying neoplasia have an extremely guarded prognosis and biliary diversion surgery is not likely to extend survival, although can have good prognosis following partial or complete resection of benign biliary cystadenomas in cats.

Gallbladder mucocoele
This condition is characterised by hyperplasia of the mucus-secreting glands within the gallbladder mucosa and accumulation of thick gelatinous mucus within the gallbladder lumen. Shetland Sheepdogs, Cocker Spaniels, Miniature Schnauzers and dogs with endocrinopathies may be predisposed. Results of retrospective studies suggest that perioperative mortality rates are high (22-32%) but if the animal survives to discharge the longterm prognosis following cholecystectomy is good. Generally early or prompt surgical intervention is indicated due to the high morbidity and mortality associated with biliary tract obstruction or bile peritonitis. When removing a gallbladder mucocoele check the patency (retrograde flush if necessary via duodenum) of the common bile duct first. Concurrent obstruction of the hepatic ducts and common bile duct is reported in up to 30% of cases. Submit the gallbladder for histopathology and culture.

Bile peritonitis
Any portion of the biliary tree can be ruptured by blunt or penetrating abdominal trauma, as a complication of biliary tract surgery or as a sequel to prolonged EHBO and the presence of bile leakage into the abdomen is an indication for exploratory laparotomy. Bile salts cause inflammation, haemolysis and tissue necrosis in the abdomen but sterile bile peritonitis may cause only ascites and icterus for weeks resulting a delayed presentation. The bile salts hyperosmolality result in fluid shifting from the circulation into the peritoneal cavity eventually causing dehydration and progressive hypovolaemic shock. Bacterial infection profoundly worsens the pathology and prognosis. Perforation of the gallbladder or a tear in the cystic duct warrants a cholecystectomy. Localisation of

a laceration in the extrahepatic biliary system can be quite tricky. The most common site of traumatic common bile duct rupture is just distal to the entrance of the last hepatic duct. If a hepatic duct is avulsed then it may be ligated. Lacerations of the common bile duct may be repaired over a stent using surgical magnification and very fine suture if the bile duct is large enough and if the animal presents before significant adhesions develop. Survival following appropriate treatment of bile peritonitis of any cause is likely to be poor if the biliary effusion is septic (27-45%) but may be excellent (87-100%) if the effusion is non-septic.

References and further reading

1. Amsellem PM, Seim HB, MacPhail CM, et al: Long-term survival and risk factors associated with biliary surgery in dogs: 34 cases (1994–2004). J Am Vet Med Assoc 229:1451–1457, 2006
2. Buote NJ, Mitchell SL, Penninck D, et al: Cholecystoenterostomy for treatment of extrahepatic biliary tract obstruction in cats: 22 cases (1994–2003). J Am Vet Med Assoc 228:1376–1382, 2006
3. Fahie MA, Martin RA: Extrahepatic biliary tract obstruction: a retrospective study of 45 cases (1983–1993). JAHHA 31:478–482, 1995
4. Kirpensteijn J, Fingland RB, Ulrich T, et al: Cholelithiasis in dogs: 29 cases (1980–1990). J Am Vet Med Assoc 202:1137–1142, 1993
5. Ludwig LL, McLoughlin MA, Graves TK, et al: Surgical treatment of bile peritonitis in 24 dogs and 2 cats: a retrospective study (1987–1994). Vet Surg 25:90–98, 1997
6. Mayhew PD, Weisse C: Treatment of pancreatitis-associated extrahepatic biliary tract obstruction by choledochal stenting in seven cats. J Sm Anim Pract 49:133–138, 2008
7. Mayhew PD, Richardson RW, Mehler SJ, et al: Choledochal tube stenting for decompression of the extrahepatic portion of the biliary tract in dogs: 13 cases (2002–2005). J Am Vet Med Assoc 228:1209–1214, 2006
8. Mehler SJ, Mayhew PD, Drobatz KJ, et al: Variables associated with outcome in dogs undergoing extrahepatic biliary surgery: 60 cases (1988–2002). Vet Surg 33:644–649, 2004
9. Papazoglou LG, Mann FA, Wagner–Mann C, et al: Long-term survival of dogs after cholecystoenterostomy: a retrospective study of 15 cases (1981–2005). J Am Anim Hosp Assoc 44:67–74, 2008
10. Pike FS, Berg J, King NW, et al: Gall bladder mucocele in dogs: 30 cases (2000–2002). J Am Vet Med Assoc 224:1615–1622, 2004
11. Worley DR, Hottinger HA, Lawrence HJ: Surgical management of gallbladder mucoceles in dogs: 22 cases (1999–2003). J Am Vet Med Assoc 225:1418–1422, 2004

WE SHOULD GIVE LESS ANTIBIOTICS, BUT WHERE IS THIS SAFE IN SOFT TISSUE SURGERY?

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Are you sometimes guilty of giving peri-operative antibiotics "just in case" without being entirely sure of your rationale? Have you ever wondered what to do with a "nightmare" post-op infection? …. then this lecture is for you!

Why is it important to reduce or avoid antibiotic use in our patients?
1. Risk to the patient - drug side effects, increased cost, increased risk of infection/MDR infection/nosocomial infection
2. Risk to your practice - increased MDR population contributing to nosocomial infection
3. Risk to human medicine – an estimated 4 million human deaths were linked to antimicrobial resistance in 2019, including 1.3 human deaths directly caused by resistant bacteria (Murray et al, The Lancet 2022)

Contamination versus infection: Every surgical wound is contaminated but only a proportion become infected. Bacteria contaminating a wound at surgery can progress to cause infection when they start multiplying, disrupting healing and damaging tissues.

Nosocomial infection: Infections that develop in patients due to being colonised with bacteria from your practice, often with multidrug resistant profiles. Strict asepsis and atraumatic/optimal surgical technique, barrier nursing and isolation facilities and rational decision making for antibiotic use are far more important than the antibiotics given in preventing surgical site infection (SSI), especially nosocomial SSI.

Antibiotics cannot compensate for poor aseptic technique. If the infection rate in your practice for clean surgeries e.g. routine neutering is >5% then you need to re-evaluate aseptic protocols in your practice rather than antibiotic protocols. Atraumatic surgical technique also makes a difference to development of SSI. Inexperienced surgeons suffer higher infection rates.

Surgery time affects SSI:
- SSI rate: 1.5% > 90mins versus 8% < 90mins
- SSI rate doubles every 30 mins after 60 mins of surgical time

Anaesthesia time (independently form surgery time) affects SSI:
- SSI rate increases by 0.5% every minute > 60 mins anaesthesia

Aim of **prophylactic = *preventative*** antibiotics is to prevent bacterial contamination at time of surgery developing into infection (SSI). To achieve this **prophylactic** antibiotics need to be present at the surgical site at the time of the 1st incision, at an effective concentration & effective against the likely bacteria and stop at the end of surgery (absolute max 12-24 hours post-op). Ensure you carefully assess patient to determine correct use of antibiotics including class & duration of surgery, as well as other patient factors.

Class of surgery	Antibiotics?	Post-op SSI rate
Clean	x	2-4.9%
Clean-contaminated	√/x	3.5-4.5%
Contaminated	√	4.6-9.1%
Dirty	√	6.7-17.8%

SSI rates are lowest for clean and clean-contaminated surgeries (< 5%) and these rates are **not** reduced by prophylactic antibiotics. **Stop antibiotics after clean or contaminated surgeries**: In human medicine the same infection rate was seen if antibiotics were used < 24 hrs or for 5 days after clean, clean-contaminated and contaminated surgeries.

The only class of surgery that requires **post-op (= therapeutic**) antibiotics is dirty surgeries where an infection is already present. If infection is suspected but not proven therapeutic may be given but if possible avoid temptation to continue antibiotics into the post-op period. Better if unsure to monitor the patient closely for signs of infection and treat based on C&S results. If you remove the source of infection at surgery you can also consider not giving post-op antibiotics in selected dirty surgeries.

The basic principle for surgical patients with tubes, drains or catheters is that antibiotic use is not dictated by presence of tube, drain or catheter, only by the underlying patient condition. It is better to start antibiotics AFTER tube, drain or catheter removal if needed, based on C&S than to select for a resistant bacteria by administering antibiotics whilst a tube, drain or catheter is still in place. For example, we would expect a nosocomial urinary tract infection following several days of a cystostomy tube or indwelling urethral catheter so to culture at tube/catheter removal and then prescribe short course of antibiotics. Patients with longterm cystostomy tubes will have a urinary tract infection and only receive antibiotics if they show clinical signs attributable to their urinary infection.

Healthy granulation tissue is the goal of appropriate wound management. Once you achieve healthy granulation tissue throughout a wound you can **stop antibiotics** as the wound has moved into the repair phase, the patient is systemically well and the granulation tissue is a barrier to infection. Note that appropriate wound management can succeed in spite of not being able to select an appropriate antibiotic due to an MDR infection – the body has an extraordinary capacity to heal itself and fight infection given the correct wound environment.

Summary and key points:
- It is critical to use less antibiotics where possible, it also benefits the patient!
- Nosocomial infection is your biggest enemy
- Antibiotics are not a substitute for proper asepsis and atraumatic surgical technique
- Only DIRTY surgeries need post-op therapeutic antibiotics

Further Reading
1. Abelson et al: Positive impact of an emergency department protocol on time to antimicrobial administration in dogs with septic peritonitis. JVECC 2013, 23: 551-556
2. Black et al: Antimicrobial therapy and aerobic bacteriologic culture patterns in canine intensive care unit patients: 74 dogs (Jan-June 2006). JVECC 2009: 489-495
3. Dickinson et al: Impact of appropriate empirical antimicrobial therapy on outcome of dogs with septic peritonitis. JVECC 2015, 25: 152-159
4. Kalafut et al: Comparison of initial and postlavage bacterial culture results of septic peritonitis in dogs and cats. JAHHA 2018, 54: 257-266
5. Weese et al: ACVIM Consensus Statement on Therapeutic Antimicrobial Use in Animals and Antimicrobial Resistance. JVIM 2015, 29: 487-498

Vector-Borne
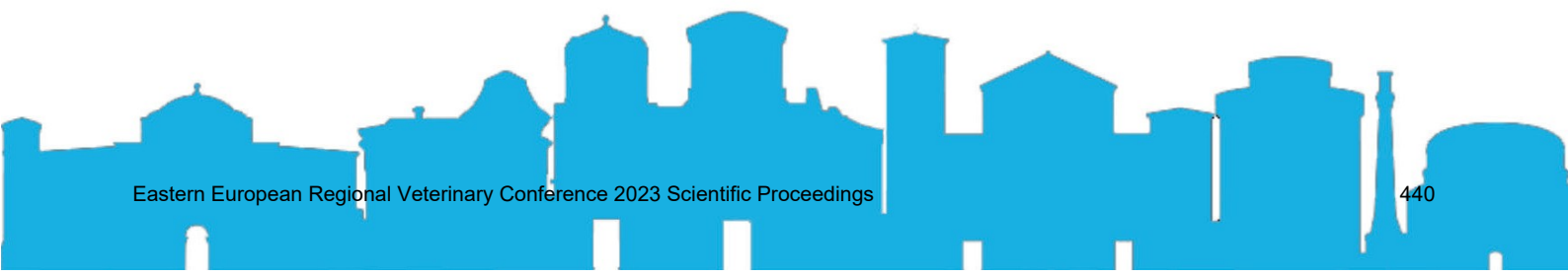
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ANGIOSTRONGYLUS VASORUM: KEEPING AN EYE ON THIS EXPANDING PARASITE

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Introduction

Angiostrongylus vasorum is a nematode parasite, causing Canine Angiostrongylosis (CanA), an important and potentially fatal parasitic disease of dogs. Until around 20-30 years ago, the presence of this parasite in Europe was "patchy", showing up in specific pockets within certain countries like France, the UK, Denmark, Italy, and Spain. Nowadays, the distribution of the parasite is progressively spreading throughout Europe, extending into previously established areas of existence and even encroaching upon new regions once believed to be free from infection[1]. The countries where the parasite is reported to expand in the last decades are Portugal, Finland, Sweden, Switzerland, Austria, the Netherlands, Germany, Belgium, Poland, Greece, Slovakia, Serbia, and Hungary, with a prevalence in dogs ranging from 0.5% to 3%[1,2].

Although CanA poses a serious and potentially lethal threat to dogs, it can be effectively treated. Thus, it is critical that veterinarians keep a vigilant eye and consider CanA in the differential diagnosis in all cases where even a single compatible sign is documented in a clinical case. One of the core aims of the European Society for Dirofilariosis and Angiostrongylosis (ESDA, https://www.esda.vet/) is to establish standardized procedures for diagnosing, preventing, and treating *A. vasorum* infections and to serve as a European hub for disseminating new advancements to veterinarians across Europe, through the creation of official Guidelines. In this article, some basic information about CanA, including common clinical presentations, diagnosis, treatment, and prevention, are presented under the auspice of ESDA.

Biology and Epizootiology

Adult *A. vasorum* (males measure from 1.4 to 1.8 cm and females from 1.8 to 2.5 cm in length), live in the pulmonary arteries and right chambers of the heart of canids and other carnivores. *Angiostrongylus vasorum* has an indirect life cycle with terrestrial gastropods (slugs and snails) serving as intermediate hosts. The female parasites lay eggs and the first-stage larvae (L1) develop and hatch in the lung capillaries. Then L1 pass into the respiratory tract, ascend to reach the pharynx, are swallowed, pass through the digestive tract, and eventually are excreted into the environment through the animal's faeces. In order for the life cycle to persist, L1 must either be ingested by slugs or snails or actively penetrate their bodies, where they undergo development and ultimately reach the third (infective) larval stage (L3). Various small vertebrates (frogs, reptiles, birds) serve as paratenic hosts of the parasite. When infected intermediate or paratenic hosts (or free L3 that exit gastropods in slime) are consumed by a final host, L3 transit from the intestine to the mesenteric lymph nodes, where they undergo two moults before migrating through the portal veins to the pulmonary arteries. There, they reach maturity and commence reproduction (prepatent period: usually 7-8 weeks)[3].

Younger dogs are more prevalently infected, probably due to age-related behaviour (scavenging, playing and consuming gastropods or paratenic hosts) and immature immune system[4,5]. Dogs that live in sympatry with foxes are in higher risk of infection as foxes are considered the reservoir of the parasite. However, other wild carnivores like wolves, jackals, coyotes, polecats, Eurasian badgers and red pandas have been found to serve as definitive hosts as well[6,7]. The expansion of the parasite's distribution in the last decades is attributed to various factors such as the climate change that influences gastropods ecology, the environmental changes that drive wildlife closer to humanised environments and vice versa, and the intensified movements of dogs (travels with owners, trade, adoptions)[1,7]. It is expected that gradually more areas, currently considered free of infection, will become enzootic in the future.

Clinical Canine Angiostrongylosis

The clinical picture of canine angiostrongylosis (CanA) may be vastly polymorphic and may present as acute or hyperacute, although subclinical infections are also recorded. There may be mild signs for an undetermined period of time, followed by sudden aggravation of the disease with a fast and deadly outcome, if left untreated. The cardiopulmonary system is usually the most affected as adult parasites, eggs lay in the pulmonary arteries, and larvae make their way from the vascular to the respiratory system. Clinical signs include abnormal lung sounds, cough, tachypnoea, and dyspnoea (ranging from mild to life-threatening), chronic fatigue, exercise intolerance, pale mucous membranes, tachycardia and syncope. Haemoptysis may also occur in rare cases. Severe pulmonary lesions may lead to pulmonary hypertension[8,9].

Bleeding diathesis, attributed to mechanisms of hyperfibrinolysis that haven't been fully deciphered yet, is a common finding in CanA, present in about 60% of clinical cases[10]. As a result, spontaneous epistaxis, petechiae, ecchymoses, bleeding of the oral mucosa, integument, or sclera, haemoptysis, post-surgical hematomas, haematochezia, and haematuria may occur. Intracranial and pulmonary haemorrhages stand out as particularly severe manifestations and in some cases, extensive bleeding in the central nervous system (CNS) or body cavities can lead to a fatal outcome[10,11].

Bleeding and aberrant migration of larvae in the CNS is the cause of neurological signs in CanA. The associated clinical signs include reduced mental status, cranial nerve deficits, ataxia, seizures, intense lumbar pain and various degrees of paresis and paralysis. In a few cases the parasites (adults or larvae) cause ocular angiostrongylosis with various degrees of ocular discomfort and sometimes hyphaema. Occasionally, irreversible ocular lesions and loss of vision have been reported due to bilateral panuveitis, lens subluxation, secondary glaucoma, and retinal detachment[12]. Furthermore, non-specific clinical signs may be present in CanA, including gastrointestinal signs, i.e., vomiting, diarrhoea, anorexia, and weight loss[4].

Diagnosis

Diagnosis of angiostrongylosis is achieved by a) the detection of L1 in the faeces of the infected animal, and b) the detection of specific antigens by serological tests. Antibody detection by ELISA[13] can in some cases support diagnosis, but is not always helpful due to the persistence of antibodies produced in the past, especially in enzootic areas[6]. Paraclinical examinations e.g. Doppler echocardiography, lung sonography and biochemical/haematological examinations can support the suspicion of angiostrongylosis but do not allow an ultimate diagnosis.

The technique of choice for the detection of larvae in faeces is the Baermann method. $ZnSO_4$ flotation can also be used but is less sensitive, while a direct faecal smear is not recommended due to its low sensitivity; however, it can be used as an initial and rapid diagnostic approach[14,15]. Proper storage of the sample is critical for a reliable result, as the larvae must be alive and motile for the Baermann migration method to work. If immediate processing of a fresh sample is not possible, it should be stored at 4-7 ºC until examination, ideally within 24 hours. Repetition of the examination in up to three different samples may be necessary to detect L1, which may have an intermittent presence in the faeces.

Morphological identification of L1 in the faeces is necessary, as larvae of other nematode species may be found in dog faeces. These species are the lung nematodes *Crenosoma vulpis*, *Oslerus osleri* and *Filaroides* spp., or the larvae of the intestinal nematode *Strongyloides* spp.

Broncho-alveolar lavage, tracheal swabs, or fine-needle lung aspirates may also be used to detect L1 but these methods are invasive, laborious, require anaesthesia and have low sensitivity[6].

A commercially available, sensitive, specific, vet-friendly, in-clinic test can be used for the detection of *A. vasorum* circulating antigen in the blood of infected dogs[16]. Still, it is recommended that both the Baermann and the serological test are applied in case of CanA suspicion. A positive Baermann method is proof of infection while any result of the serological test is an indication that should be supported by additional examinations.

Various paraclinical and laboratory examinations can be performed to support CanA suspicion and evaluate the severity of the disease. Such examinations include radiography, lung sonography echocardiography M.R.I. of the CNS, ophthalmoscopy, blood cells count, PT, aPTT, D-dimers, FDP, fibrinogen and ATIII evaluation, and serum electrophoresis[17].

Treatment

There is effective treatment against CanA and the molecules currently used are fenbendazole, moxidectin and milbemycin oxime[6,18].

Administration of fenbendazole at the dose of 25-50 mg/kg for 5-21 consecutive days, twice a day, in finely ground tablets, given with a meal to promote absorption effectively treats CanA, even though in many countries this molecule is not licenced for *A. vasorum*.

Two veterinary products are licenced in Europe to date against CanA. The first one is a tablet containing milbemycin oxime and praziquantel, and the other one is a spot-on formulation containing moxidectin 2.5% and imidacloprid 10%.

Supportive treatment, e.g. oxygen supplementation, bronchodilators, and antibiotics (in case of secondary bacterial infections) may be necessary in some cases. Furthermore, corticosteroids at immunosuppressive doses may be used to reverse immune-mediated thrombocytopenia and to prevent any occurring anaphylactic reaction due to parasites' death. In dogs with haemorrhagic diathesis transfusion of whole blood, packed red blood cells or plasma, may be helpful to replace erythrocytes and/or coagulation factors. Phosphodiesterase type 5 inhibitors (sildenafil) may relieve pulmonary hypertension. If right heart congestive failure is observed, angiotensin-converting enzyme inhibitors and diuretics can be administered. Tranexamic acid (20 mg/Kg iv) seems to be the choice treatment in dogs with haemorrhages.

Prevention

Prevention of CanA should be applied in all areas where the infection is prevalent. The spot-on formulation containing moxidectin 2.5% in combination with imidacloprid 10% is licensed for this purpose, while two oral formulations are experimentally proven effective in preventing of CanA. The first of these products contains milbemycin oxime and spinosad, and the second contains milbemycin oxime with afoxolaner. These chewable tablets, given monthly, have the potential to prevent dogs from developing angiostrongylosis[19,20].

Conclusions

Regardless of the prevalence of the disease in a particular region, the possibility of CanA should be considered when a dog displays even a single sign that aligns with the disease. Furthermore, pet owners in enzootic areas should be educated about the risk of angiostrongylosis, and that the disposal of faeces of dogs is critical to minimize infection of intermediate hosts. Dog owners should remain attentive when animals play, roam and scavenge in areas where slugs and snails are present. Finally, routine screening of dogs through periodic parasitological examinations is crucial for early detection of the infection and timely antiparasitic treatment. This will prevent the development of clinical disease and will interrupt the biological cycle of the parasite. In this context, annual examination (faecal and serological) for *A. vasorum* in dogs living in enzootic areas is recommended.

References

1. Morgan ER, Modry D, Paredes-Esquivel C, Foronda P, Traversa D. Angiostrongylosis in animals and humans in Europe. *Pathogens*. 2021;10(10):1236. https://doi.org/10.3390/pathogens10101236
2. Fuehrer HP, Morelli S, Unterköfler MS, Bajer A, Bakran-Lebl K, Dwużnik-Szarek D, Farkas R, Grandi G, Heddergott M, Jokelainen P, Knific T, Leschnik M, Miterpáková M, Modrý D, Petersen HH, Skírnisson K, Vergles Rataj A, Schnyder M, Strube C. *Dirofilaria* spp. and *Angiostrongylus vasorum*: Current Risk of Spreading in Central and Northern Europe. *Pathogens*. 2021;10(10):1268. https://doi.org/10.3390/pathogens10101268
3. Morgan ER, Shaw SE, Brennan SF, De Waal TD, Jones BR, Mulcahy G. *Angiostrongylus vasorum*: a real heartbreaker. *Trends Parasitol.* 2005;21(2):49-51. doi: 10.1016/j.pt.2004.11.006. PMID: 15664523.
4. Morgan ER, Jefferies R, van Otterdijk L, McEniry RB, Allen F, Bakewell M, Shaw SE. *Angiostrongylus vasorum* infection in dogs: Presentation and risk factors. *Vet Parasitol*. 2010;173(3-4):255-61. doi: 10.1016/j.vetpar.2010.06.037.
5. Blehaut TR, Hardstaff JL, Chapman PS, Pfeiffer DU, Boag AK, Guitian FJ. Spatial, demographic and clinical patterns of *Angiostrongylus vasorum* infection in the dog population of Southern England. *Vet Rec*. 2014;175(6):148. doi: 10.1136/vr.102186.

6. Elsheikha HM, Holmes SA, Wright I, Morgan ER, Lacher DW. Recent advances in the epidemiology, clinical and diagnostic features, and control of canine cardio-pulmonary angiostrongylosis. *Vet Res.* 2014;45(1):92. doi: 10.1186/s13567-014-0092-9.

7. Veronesi F, Deak G, Diakou A. Wild mesocarnivores as reservoirs of endoparasites causing important zoonoses and emerging bridging infections across Europe. *Pathogens.* 2023;12(2):178. doi: 10.3390/pathogens12020178.

8. Glaus T, Schnyder M, Dennler M, Tschuor F, Wenger M, Sieber-Ruckstuhl N. Natural infection with *Angiostrongylus vasorum*: characterisation of 3 dogs with pulmonary hypertension. *Schweiz Arch Tierheilkd.* 2010;152(7):331-8. German. doi: 10.1024/0036-7281/a000076.

9. Kranjc A, Schnyder M, Dennler M, Fahrion A, Makara M, Ossent P, Morgan J, Deplazes P, Glaus TM. Pulmonary artery thrombosis in experimental *Angiostrongylus vasorum* infection does not result in pulmonary hypertension and echocardiographic right ventricular changes. *J Vet Intern Med.* 2010;24(4):855-62. doi: 10.1111/j.1939-1676.2010.0529.x.

10. Willesen JL, Langhorn R, Nielsen LN. Hemostatic Dysfunction in dogs naturally infected with *Angiostrongylus vasorum*-A narrative review. *Pathogens.* 2022;11(2):249. doi: 10.3390/pathogens11020249.

11. Glaus T, Sigrist N, Hofer-Inteeworn N, Kuemmerle-Fraune C, Mueller C, Geissweid K, Beckmann K, Wenger M, Novo Matos J. Unexplained bleeding as primary clinical complaint in dogs infected with *Angiostrongylus vasorum*. *Schweiz Arch Tierheilkd.* 2016;158(10):701-709. doi: 10.17236/sat00088.

12. Ciuca L, Meomartino L, Piantedosi D, Cortese L, Cringoli G, Rinaldi L, Lamagna B. Irreversible ocular Llesions in a dog with *Angiostrongylus vasorum* Infection. *Top Companion Anim Med.* 2019;36:4-8. doi: 10.1053/j.tcam.2019.05.001.

13. Schucan A, Schnyder M, Tanner I, Barutzki D, Traversa D, Deplazes P. Detection of specific antibodies in dogs infected with *Angiostrongylus vasorum*. *Vet Parasitol.* 2012;185(2-4):216-24. doi: 10.1016/j.vetpar.2011.09.040.

14. Morelli S, Diakou A, Colombo M, Di Cesare A, Barlaam A, Dimzas D, Traversa D. Cat respiratory nematodes: current knowledge, novel data and warranted studies on clinical features, treatment and control. *Pathogens.* 2021;10(4):454. doi: 10.3390/pathogens10040454.

15. Morelli S, Traversa D, Diakou A, Colombo M, Russi I, Mestek A, Chandrashekar R, Beall M, Paoletti B, Iorio R, Tsokana A, De Cristofaro D, Barlaam A, Simonato G, Di Cesare A. A Comparison of copromicroscopic and molecular methods for the diagnosis of cat aelurostrongylosis. *Animals (Basel).* 2022;12(8):1024. doi: 10.3390/ani12081024.

16. Schnyder M, Stebler K, Naucke TJ, Lorentz S, Deplazes P. Evaluation of a rapid device for serological in-clinic diagnosis of canine angiostrongylosis. *Parasit Vectors.* 2014;7:72. doi: 10.1186/1756-3305-7-72.

17. Venco L, Colaneri G, Formaggini L, De Franco M, Rishniw M. Utility of thoracic ultrasonography in a rapid diagnosis of angiostrongylosis in young dogs presenting with respiratory distress. *Vet J.* 2021;271:105649. doi: 10.1016/j.tvjl.2021.105649.

18. Di Cesare A, Traversa D. Canine angiostrongylosis: recent advances in diagnosis, prevention, and treatment. *Vet Med (Auckl).* 2014;5:181-192. doi: 10.2147/VMRR.S53641.

19. Böhm C, Schnyder M, Thamsborg SM, Thompson CM, Trout C, Wolken S, Schnitzler B. Assessment of the combination of spinosad and milbemycin oxime in preventing the development of canine *Angiostrongylus vasorum* infections. *Vet Parasitol.* 2014;199(3-4):272-7. doi: 10.1016/j.vetpar.2013.10.024.

20. Lebon W, Tielemans E, Rehbein S, Dumont P, Yoon S, Beugnet F, Jeannin P, Larsen D, Halos L. Monthly administrations of milbemycin oxime plus afoxolaner chewable tablets to prevent *Angiostrongylus vasorum* infection in dogs. *Parasit Vectors.* 2016;9(1):485. doi: 10.1186/s13071-016-1773-1.

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DIROFILARIA, WHERE WE'VE BEEN AND WHERE WE'RE GOING?

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The diagnosis of the first cases of Dirofilaria immitis and repens was sporadic. Over time, rapid and accurate diagnostics as well as adequate therapy and prevention have developed. Regardless of the efforts of science to stop the spread of diseased individuals, the number of animals susceptible to Dirofilaria grows every day. The reasons are multifactorial, a significant increase in several dogs and cats as pets, traveling to endemic areas of unprotected pets, traveling from endemic areas of infected pets (Simon at all, 2012), an increase in the number of vectors (Fuehrer 2022), the spread of certain types of mosquitoes to a new area, changes in climate conditions, wild animals...

On the other hand, the advancement of diagnostics, therapy, and prevention reduces the number of sick individuals every day. A big role in prevention is played by the education of public opinion as well as the education of professionals. (Morchón et al., 2022).

Joint efforts on continuous prevention, improved medications, reducing the number of vectors, and disrupting the development cycle of parasites are the directions for future actions.

References:

1. European Society of Dirofilariosis and Angiostrongylosis. ESDA. Available online: http://www.esda.vet/index.php
2. Fuehrer HP, Morelli S, Unterköfler MS, Bajer A, Bakran-Lebl K, et al. *Dirofilaria* spp. and *Angiostrongylus vasorum*:Current Risk of Spreading in Central and Northern Europe. Pathogens, 2021; 10: 1268.
3. Morchón R, Carretón E, González-Miguel J, Mellado-Hernández. I. Heartworm disease (*Dirofilaria immitis*) and their vectors in Europe – new distribution trends. Front Physiol. 2012; 3:196.
4. Morchón R, Montoya-Alonso JA, Rodríguez-Escolar I, Carretón E. What Has Happened to Heartworm Disease in Europe in the Last 10 Years? Pathogens. 2022 11:1042.
5. Fuehrer HP, Auer H, Leschnik M, Silbermayr K, Duscher G, Joachim A. *Dirofilaria* in Humans, Dogs, and Vectors in Austria (1978-2014)-From Imported Pathogens to the Endemicity of *Dirofilaria repens*. PLoS Negl Trop Dis. 2016, 10 (5): e0004547.

Veterinary Forensics

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She graduated from the Faculty of Law of Democritus University of Thrace in 2015, where she continued her studies in the Department of International Studies obtaining two master's degrees, in "International and European Energy Law" (2018) and "International and European Studies" (2020), with specialty in human rights and humanitarian law.

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Companion animal abuse in Greece:
a) the applicable criminal legislation;
b) the role of police, prosecuting agencies and courts

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Animal abuse has been at the core of animal welfare and legal protection in Western countries for many decades, even centuries, depending on the morality and sensitivity of each individual society to animal use and animal care issues. In Greece, many special criminal laws governing animal maltreatment had been implemented and enforced in the past. Until 2020, all types of crime against animals (active cruelty including unlawful animal killing, neglect or passive violations of animal welfare, and/or animal abandonment) were treated as misdemeanors. Then, the National Parliament responded to the increasing interest of the Greek citizens by classifying the unlawful animal killing and the majority of the severe acts of animal cruelty as felonies, raising the penalties and assisting the investigation and the prosecution of these crimes. In this keynote lecture the applicable Hellenic legislation in the cases of suspected criminal offences against companion animals is presented thoroughly. Moreover, the role of police, prosecuting agencies and criminal courts is noted in order for the Greek veterinarians to be able to respond diligently and efficiently as forensic experts in companion animal practice.

Selected References:
- Thomas D. Improving the Law for Animals: a Campaigning Lawyer's Perspective. Liverpool Law Review; 2022; 43:107-121.
- Reyes CL, Brewster MP (Eds). Animal cruelty: a multidisciplinary approach to understanding, 3rd ed. Carolina Academic Press, Durham, North Carolina, USA 2023.
- Doukas D, Tontis D. Non-accidental injuries in dogs and cats: review of post-mortem forensic evaluations and the social significance of small animal practice. J Hellenic Vet Med Soc 2022; 73(1): 3543-3552.
- Hellenic criminal legislation on companion animal unlawful killing, cruelty, neglect and abandonment. ***Available on request at: arkalaitzi@uth.gr***

Companion animal euthanasia / death during veterinary care:
a) current Greek legislation;
b) criminal and civil Justice issues for veterinarians

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Euthanizing companion animals (very old, with incurable/painful diseases, severe injuries or behavioral problems) is a common feature of veterinary practice. Moreover, the unexpected death of a pet during veterinary care may become a central professional issue for veterinary medical establishments (hospitals, clinics). It is not uncommon, the veterinarian's recommendation for pet euthanasia, as well as the pet death during care, to be perceived by the animal owner as a feature of veterinarian's lack of knowledge, inexperience, negligence or incompetence. As companion animals are, according to the Greek law, an object of property, some civil liability and claiming compensation issues are raised. Finally, in extreme scenarios, an owner may accuse the veterinarian as a perpetrator of intentional companion animal abuse or killing. Animal cruelty and unlawful death are criminal offenses classified as felonies, resulting in the veterinarian's prosecution. In this keynote lecture, the applicable Hellenic legislation on companion animal practice, including euthanasia, is presented thoroughly. However, current legislation is not fully detailed with analytical provisions concerning errors and levels of medical responsibility by veterinarians: criminal and civil liability as well as administrative, disciplinary and medical liability. The need of a modern legislation on veterinary medical liability issues, along with a new Code of Veterinary Ethics in Greece, is also noted.

Selected references:
- Mc Eachern Nunalee MM, Weedon RG. Modern trends in veterinary malpractice: how our evolving attitudes toward non-human animals will change veterinary medicine. Animal Law 2004; 10: 125-161.
- Passantino A, Fenga C, Morciano C, Morelli C, Russo M, Di Pietro C, Passantino M. Euthanasia of companion animals: a legal and ethical analysis. Euthanasia of companion animals: a legal and ethical analysis. Ann Ist Super Sanita 2006; 42: 491-5.
*- Hellenic criminal and civil legislation on veterinary practice, animal euthanasia and companion animal abuse. **Available on request at:** arkalaitzi@uth.gr*

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Veterinary Forensic Sciences: basic principles, procedures and applications in companion animal practice

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Veterinary Forensic Sciences (or Veterinary Forensics) has nowadays been emerged as a distinct branch of Veterinary Sciences. Veterinary Forensics can be applied to the investigation of a variety of criminal and/or civil medicolegal cases involving possible violations of animal law and/or veterinary legislation. The range of interests of veterinary forensics is very broad including:

- animal physical cruelty/abuse;
- animal sexual abuse;
- animal abuse in correlation to interpersonal violence;
- unlawful killing;
- animal poisoning;
- non-accidental injuries;
- sharp force trauma;
- blunt force trauma;
- strangulation, suffocation, and asphyxia;
- environmental and situational injuries/death (thermal, chemical, electrical, hyperthermia, hypothermia, and drowning);
- firearm animal injuries and ballistics;
- animal neglect;
- animal hoarding;
- legal investigations in shelter medicine;
- animal fighting and bitemark analysis;
- legal investigations in shelter medicine;
- animal sudden death;
- anesthesia-related deaths;
- veterinary malpractice and veterinary civil liability; and,
- pet insurance issues and sale agreements.
  Veterinary Forensics may use a wide range of scientific practices such as:
- animal crime scene investigation (CSI);
- estimation of time since death according post-mortem changes;
- veterinary forensic necropsy, gross pathology and histopathology;
- veterinary forensic radiology and imaging; veterinary forensic toxicology;
- veterinary forensic entomology;
- animal genetic evidence and DNA analysis;
- veterinary forensic clinical examination and clinical pathology;
- evidence documentation according chain of custody process; and,
- veterinary forensic report writing and its submission to specific authorities (e.g. Police, courts).

In conclusion, veterinarians as forensic experts have an undoubtedly crucial role in the investigation and prosecution of the various crimes against companion animals (according the definition of animal abuse, cruelty and neglect which varies among different jurisdiction). Moreover, veterinarians may provide their forensic expertise in companion animal cases related to Civil Justise, including veterinary malpractice and civil liability as well as pet insurance issues and companion animal sale agreements.

Selected references:

- Brooks JW. Veterinary Forensic Pathology, vol-1 & vol-2. Springer, Cham, Switzerland, 2018.
- Byrd JH, Norris P, Bradley N. Veterinary Forensic Medicine and Forensic Sciences. CRC Press, Boca Raton, Florida, USA, 2018.
- Maxwell VM and Smith-Blackmore M. Investigating Animal Abuse Crime Scenes: A Field Guide, CRC Press, Boca Raton, Florida, USA 2023.
- Merck MD. Veterinary Forensics: Animal Cruelty Investigations, 2nd ed. Wiley-Blackwell. Ames, Iowa, USA, 2013.
- Otteman K, Fielder L, Lewis E. Animal Cruelty investigations: A Collaborative Approach from Victim to Verdict. Wiley Blackwell, Hoboken, NJ, USA.
- Rogers ER, Stern AW. Veterinary Forensics. Investigation, Evidence Collection and Expert Testimony. Taylor & Francis, Boca Raton, Florida, USA, 2018.

Dead victims of companion animal cruelty and/or neglect: forensic investigation procedures and report writing instructions

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A veterinarian may be asked by the police to provide a forensic report to describing factual observations and him/her expert opinion in cases of dead companion animals with the suspicion that they are victims of (active) cruelty and or/ (passive) neglect, which are criminal offences. The specific scientific knowledge and the great awareness of the legal requirements related to forensic investigations will enable veterinarians to be better prepared to handle criminal evidence. Veterinary forensic services in a case of a dead companion animal (or massive deaths) should comprise a full post-mortem examination (forensic necropsy) and supporting laboratory tests. The objective of a forensic necropsy is not only to establish the cause, the manner and the time of death, but also to recognize, identify, collect, preserve, and examine physical evidence associated with the death. Moreover, the evidence related to animal abuse must follow a chain of custody: the animal cadaver itself, samples, photographs and any vital information from the environment (crime scene investigation by the veterinarian). The use of standard operation procedures (SOP) for veterinary forensic investigations is the key to provide reliability, efficiency, and consistently quality in case documentation by the veterinary forensic expert [e.g. the minimum standards for veterinarians who perform forensic postmortem examinations provided by the International Veterinary Forensic Sciences Association (IVFSA) since 2019]. These standards cover the preliminary procedures, evidence documentation, external and internal postmortem examination and documentation, lesion and injury descriptions, ancillary tests, and the instructions for writing the postmortem examination report. Finally, the official forensic opinions and interpretations by the veterinarian for a dead companion animal case (due to cruelty acts and/or neglect omissions) must be formulated after consideration of all available information.

Selected references:
-International Veterinary Forensic Sciences Association (IVFSA). Veterinary Forensic Postmortem Examination Standards, 2019. Accessed at: https://www.ivfsa.org/wp-content/uploads/2020/11/IVFSA-Veterinary-Forensic-Postmortem-Exam-Standards-Approved-2020.pdf
- Brooks JW. Veterinary Forensic Pathology, vol-1 & vol-2. Springer, Cham, Switzerland, 2018.
- Byrd JH, Norris P, Bradley N. Veterinary Forensic Medicine and Forensic Sciences. CRC Press, Boca Raton, Florida, USA, 2018.
- Maxwell VM and Smith-Blackmore M. Investigating Animal Abuse Crime Scenes: A Field Guide, CRC Press, Boca Raton, Florida, USA 2023.
- Merck MD. Veterinary Forensics: Animal Cruelty Investigations, 2nd ed. Wiley-Blackwell. Ames, Iowa, USA, 2013.
- Otteman K, Fielder L, Lewis E. Animal Cruelty investigations: A Collaborative Approach from Victim to Verdict. Wiley Blackwell, Hoboken, NJ, USA.
- Rogers ER, Stern AW. Veterinary Forensics. Investigation, Evidence Collection and Expert Testimony. Taylor & Francis, Boca Raton, Florida, USA, 2018.

Live victims of companion animal cruelty and/or neglect: forensic investigation procedures and report writing instructions

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A veterinarian may be asked by the Police to provide a forensic report to describing factual observations and him/her expert opinion in cases of live companion animals with the suspicion that they are survived victims of (active) cruelty and or/ (passive) neglect, which are criminal offences. The specific scientific knowledge and the great awareness of the legal requirements related to forensic investigations will enable veterinarians to be better prepared to handle criminal evidence. Veterinary forensic services in a case of a live companion animal should comprise a full clinical examination, paraclinical examinations (e.g. imaging) and supporting laboratory tests. The objective of the forensic clinical investigations is to recognize, identify, collect, preserve, and examine physical evidence associated with the non-accidental injuries or chronic lesions due to neglect. Moreover, the evidence related to animal abuse must follow a chain of custody: samples from the animal body, photographs and any vital information from the environment (crime scene investigation by the veterinarian). The use of standard operation procedures (SOP) for veterinary forensic clinical investigations is the key to provide reliability, efficiency, and consistently quality in case documentation by the veterinary forensic expert [e.g. the minimum standards for veterinarians who perform live animal examinations provided by the International Veterinary Forensic Sciences Association (IVFSA) since 2019]. These standards cover the preliminary procedures, evidence documentation, clinical and paraclinical examinations, lesion and injury descriptions, ancillary tests, and the instructions for writing the live animal clinical examination report. Finally, the official forensic opinions and interpretations by the veterinarian for a live companion animal case (survived of cruelty acts and/or neglect omissions) must be formulated after consideration of all available information.

Selected references:
- International Veterinary Forensic Sciences Association (IVFSA). Standards Document for the Forensic Live Animal Examination, 2019. Accessed at: https://www.ivfsa.org/wp-content/uploads/2020/11/IVFSA-Veterinary-Forensic-Live-Animal-Exam-Standards-Approved-2020.pdf
- Brooks JW. Veterinary Forensic Pathology, vol-1 & vol-2. Springer, Cham, Switzerland, 2018.
- Byrd JH, Norris P, Bradley N. Veterinary Forensic Medicine and Forensic Sciences. CRC Press, Boca Raton, Florida, USA, 2018.
- Maxwell VM and Smith-Blackmore M. Investigating Animal Abuse Crime Scenes: A Field Guide, CRC Press, Boca Raton, Florida, USA 2023.
- Merck MD. Veterinary Forensics: Animal Cruelty Investigations, 2nd ed. Wiley-Blackwell. Ames, Iowa, USA, 2013.
- Otteman K, Fielder L, Lewis E. Animal Cruelty investigations: A Collaborative Approach from Victim to Verdict. Wiley Blackwell, Hoboken, NJ, USA.
- Rogers ER, Stern AW. Veterinary Forensics. Investigation, Evidence Collection and Expert Testimony. Taylor & Francis, Boca Raton, Florida, USA, 2018.

Companion animal euthanasia / death during veterinary practice: forensic investigation procedures and final documentation

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Euthanasia of companion animals (very old, with incurable/painful diseases, severe injuries or behavioral problems) is a very common procedure in veterinary clinics and hospitals. Also, the unexpected death of companion animals during a veterinary practice (e.g. during anesthesia, or during a surgical procedure or post-operatively, or post administration of a specific medication) are not uncommon. In many of such cases, the veterinarian's recommendation for animal euthanasia, as well as the pet death during veterinary practice may be perceived by the animal owner as a feature of veterinarian's lack of knowledge, inexperience, negligence or incompetence raising civil liability and compensation issues. More rarely, an owner may accuse the veterinarian as a perpetrator of the crime of companion animal cruelty and unlawful killing. This keynote lecture is focused on the forensic procedures must be followed by the veterinary expert for the investigation and documentation of the above cases. The need of a critical, combined evaluation of: a) the animal's medical file (medical history, clinical symptoms, paraclinical laboratory findings, type of medication, type and quantity of anesthetics, etc.); b) the gross lesions during necropsy; and, c) the findings of the supporting laboratory tests after necropsy (e.g. the histopathological lesions, the toxicological detection and quantification of anesthetics or other drugs residues in animal tissues etc.) is emphasized thoroughly.

Selected references:
- Banco B, Grieco V, Servida F, Giudice C. Sudden death in a dog after doxorubicin chemotherapy. Vet Pathol 2011; 48(5): 1035-7. doi: 10.1177/0300985810377185.
- De Lay J. Anesthesia-related deaths. In: Brooks JW. Veterinary Forensic Pathology, vol-2. Springer, Cham, Switzerland, 2018, pp 89-96.
- Levy JK, Bard KM, Tucker SJ, Diskant PD, Dingman PA. Perioperative mortality in cats and dogs undergoing spay or castration at a high-volume clinic. Vet J 2017; 224:11-15. doi: 10.1016/j.tvjl.2017.05.013.
- Pang D, Rondenay Y, Helie P, Cuvelliez SG, Troncy E. Sudden cardiac death associated with occult hypertrophic cardiomyopathy in a dog under anesthesia. Can Vet J 2005; 46(12):1122-5.
- Remmers G, Hayden DW, Jaeger MA, Ervasti JM, Valberg SJ. Postanesthetic death in a cat with myopathy. Vet Pathol 2015; 52(1): 186-188. doi: 10.1177/0300985814524797.

Sudden and unexpected death in Dogs: causes and post-mortem diagnosis

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Dogs (owned and stray) are nowadays companion animals in very high populations in Western countries. Moreover, many dog individuals are used very commonly as valuable working animals (therapy dogs, military and police dogs, shepherd dogs etc.) Therefore, the sudden and unexpected death of a dog is a painful event for the owner as well as other persons knowing the animal. Very commonly the canine sudden and unexpected death is raising the suspicion of animal abuse, an event which constitutes an ex oficcio prosecuted criminal offence. According to the law, a veterinarian is responsible to investigate the manner of dog death. A full necropsy is the only scientific method to answer the basic question what caused the sudden and unexpected death of a dog. Causes of canine death can be categorized as: a) natural, e.g. infectious diseases; b) accidental e.g. high-rise syndrome; and, c) non-accidental canine abuse (accompanied by a complaint to Police); the necropsy is characterized as forensic or diagnostic respectively. Finding the cause of dog death in each case is the key: a) for the efficient prosecution of perpetrator in cases of death due to cruelty; b) for taking preventing actions for the protection and safety of the rest companion animals (e.g. in death due to an infectious disease, or death due to intrafamily animal abuse). The present keynote lecture focuses on the most common causes of dog sudden and unexpected death, presenting the gross lesions per cause during postmortem examination. Moreover, the diagnostic value of the supporting laboratory examinations (histopathological, microbiological, toxicological, etc.) is emphasized.

Selected references:
- Harms NJ, Guest BB, Allen AL. Investigating the sudden death of a dog. Can Vet J 2010; 51(2): 210-2.
- Olsen TF, Allen AL Causes of sudden and unexpected death in dogs: α 10-year retrospective study, Can Vet J 2000; 41(11): 873-5.
- Parry N. Sudden and unexpected death in small animal patients: Part 1.UK Vet 2008; 13 (8): 1-6.

- Parry N. Investigating cases of sudden and unexpected death in small animal patients. UK Vet 2008; 13 (9): 1-5.
- Piegari G, Cardillo L, Alfano F, Vangone L, Iovane V, Fusco G. Pathological, bacteriological and virological findings in sudden and unexpected deaths in young dogs. Animals (Basel) 2020; 10(7): 1134.

Sudden and unexpected death in Cats: causes and post-mortem diagnosis

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Cats (owned and stray) are nowadays companion animals in very high populations in Western countries. In general, the sudden and unexpected death of a cat is a painful event for the owner as well as other persons knowing the animal. Very commonly the feline sudden and unexpected death is raising the suspicion of animal abuse, an event which constitutes an ex oficcio prosecuted criminal offence. According to the law, a veterinarian is responsible to investigate the manner of cat death. A full necropsy is the only scientific method to answer the basic question what caused the sudden and unexpected death of a cat. Causes of feline death can be categorized as: a) natural, e.g. infectious diseases; b) accidental, e.g. high-rise syndrome; and, c) non-accidental feline abuse (accompanied by a complaint to Police); the necropsy is characterized as forensic or diagnostic respectively. Finding the cause of cat death in each case is the key: a) for the efficient prosecution of perpetrator in cases of death due to cruelty; b) for taking preventing actions for the protection and safety of the rest pets (e.g. in death due to an infectious disease, or death due to intrafamily animal abuse). The present keynote lecture focuses on the most common causes of cat sudden and unexpected death, presenting the gross lesions per cause during postmortem examination. Moreover, the diagnostic value of the supporting laboratory examinations (histopathological, microbiological, toxicological, etc.) is emphasized.

Selected references:
- Olsen TF, Allen AL. Causes of sudden and unexpected death in cats: a 10-year retrospective study. Can Vet J 2001; 42(1): 61-62.
- Parry N. Sudden and unexpected death in small animal patients: Part 1.UK Vet 2008; 13 (8): 1-6.
- Parry N. Investigating cases of sudden and unexpected death in small animal patients. UK Vet 2008; 13 (9): 1-5.
- Toma C, Popa R, Haralambie MC, Haralambie OR, Marica R. Hemorrhage and sudden death in a cat with pancreatic hemangiosarcoma. Vet Sci 2022; 10(1):8. doi:10.3390/vetsci10010008.
 - Wilkie LJ, Smith K, Luis Fuentes V. Cardiac pathology findings in 252 cats presented for necropsy; a comparison of cats with unexpected death versus other deaths. J Vet Cardiol 2015; 17 Suppl 1: S329-40. doi: 10.1016/j.jvc.2015.09.006.

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