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TREATMENT OF FELINE DIABETES MELLITUS, ANY NEWS?

Thursday 12 September | 08:30 - 10:30 | Amphitheater N. Skalkotas - Room A

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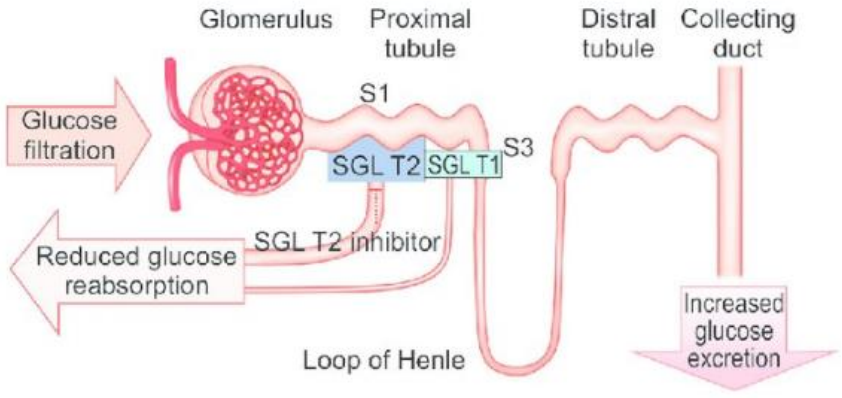
The main aims of treating cats with uncomplicated diabetes mellitus is achieving a good quality of life for both cat and owner. Good quality of life typically requires the elimination or serious reduction in the classic clinical signs of diabetes mellitus: polydipsia, polyuria, polyphagia, and weight loss; prevention of short-term complications (e.g. hypoglycemia, diabetic ketoacidosis [DKA]); and maintenance of stable bodyweight.
Traditionally feline diabetes mellitus has been treated with insulin. Insulin remains one of the important treatment options to treat feline diabetes but today is not the only effective option.
The management of feline diabetes mellitus has seen significant advancements recently, particularly with the introduction of sodium-glucose cotransporter 2 (SGLT2) inhibitors. This new class of drugs, which has been transformative in human medicine for type 2 diabetes, is now making strides in veterinary medicine. Here's a detailed look at the latest developments, alongside traditional insulin treatment and dietary management.

Introduction to SGLT2 Inhibitors

SGLT2 inhibitors function by inhibiting the reabsorption of glucose in the kidneys, leading to increased glucose excretion in the urine and consequently lowering blood glucose levels. This mechanism offers a novel approach to managing diabetes, reducing the reliance on insulin injections, which has been the cornerstone of feline diabetes treatment for years.
Mechanism of action of SGLT2:



Recent Approvals and Studies

Bexagliflozin (Bexacat):
Approval: In December 2022, the FDA approved bexagliflozin, marking it as the first oral medication for improving glycemic control in cats with diabetes not previously treated with insulin.
Efficacy: Studies have shown that bexagliflozin significantly reduces the need for insulin, lowers blood glucose, and decreases fructosamine levels, without causing hypoglycemia. A field study reported an 84% success rate in glycemic control and improvement in clinical signs such as

polyuria, polydipsia, polyphagia, and weight loss.

Velagliflozin (Senvelgo):

Approval: In August 2023, velagliflozin was approved as an oral solution for once-daily administration.

Efficacy: Similar to bexagliflozin, velagliflozin has demonstrated effectiveness in reducing blood glucose and improving clinical signs of diabetes in cats

Benefits and Challenges

Benefits:

Non-Invasive administration: One of the primary advantages of SGLT2 inhibitors is the elimination of the need for insulin injections, making diabetes management less stressful for both cats and their owners. Improved glycemic control: These medications help control hyperglycemia and reduce clinical signs associated with diabetes, potentially leading to a better quality of life for affected cats.

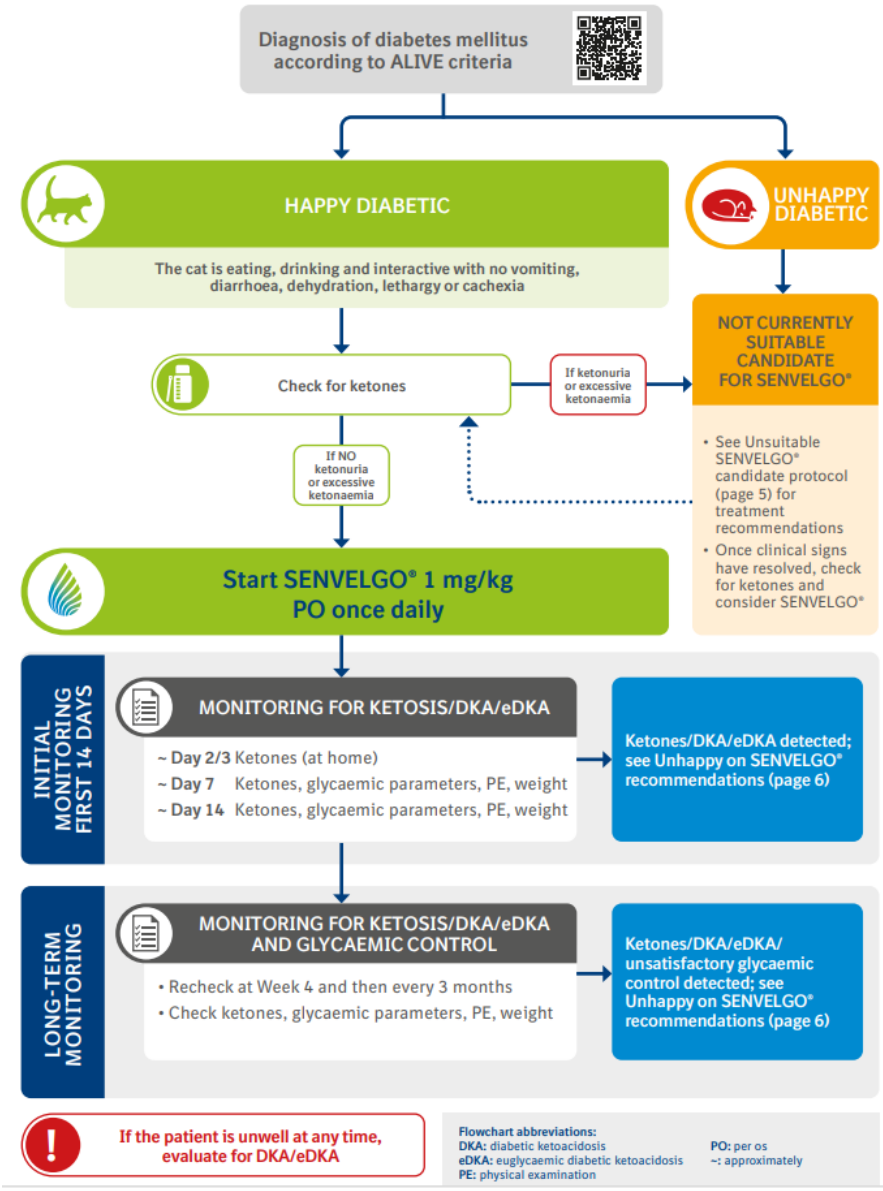
Challenges

Eligibility: Not all diabetic cats may be suitable for SGLT2 inhibitors. Cats need to have sufficient functional beta cells for these medications to be effective. Prior to initiating treatment, screening for ketosis should be performed. Clinical signs such as dehydration, lethargy, anorexia (inappetence), acute vomiting and cachexia alongside hyperglycemia and presence of blood or urine ketone bodies may indicate that the cat has diabetic ketoacidosis (DKA) or may be at higher risk of developing DKA.

Risk of Diabetic Ketoacidosis (DKA): Cats previously treated with insulin are at a higher risk of developing DKA when switched to SGLT2 inhibitors. Continuous monitoring and early detection of euglycemic ketoacidosis are critical.

In 2023 a group of feline diabetes experts from Europe and North America worked as Global Diabetes Advisory Board (GDAB). The GDAB worked on the treatment protocol end the monitoring for diabetic cats treated with velagliflozin (Senvelgo).

Below is the therapeutic and monitoring algorithm developed by the GDAB.



Insulin Treatment

In recent years pharmaceutical

companies have gradually removed from the market the animal-derive insulin (mainly pork or beef insulins) and replacing them with human recombinant insulin or insulin analogues. Since 2000, the human insulin is available only at a concentration of 100 U/ml. Only Caninsulin® and ProZInc® are still formulated at the concentration of 40 U/ml. Therefore is essential use the proper syringe for the insulin type. The insulins can be short acting, intermediate acting or slow acting. The rapid-acting insulin (eg. Humulin R®) is in solution and can be administered subcutaneously, intramuscularly or intravenously. This is reccommended exclusively for the treatment of diabetic ketoacidosis through intravenous infusion or intramuscular. Generally, in uncomplicated diabetes therapy, long-acting insulins (insulin glargine, detemir, PZI) or mixed (Caninsulin®) insulin are used. Caninsulin® and ProZinc® are the only insulin products registered for veterinary use. Caninsulin is a mixed porcine insulin. 30% is fast-acting and 70% ultralente-acting. Protamine Zinc Insulin (PZI), as its name implies, is insulin combined with zinc (metal ion) and protamine (a strongly basic protein extracted from salmon testes). This combination prolongs insulin's duration of action. Both in dogs and cats this insulin should be administered every 12 hours. It is recommended to start with a dosage of 1 U / cat BID for cats <4 Kg weight and 1,5-2U / cat BID for those > 4 kg. Insulin glargine (Lantus ®) is a synthetic insulin. Glargine has a pH of about 4 and then is poorly soluble at physiological pH. This allows the formation of subcutaneous microprecipitates. This allows a late, long and relatively constant insulin absorption from the injection site. The formation of microprecipitates is highly dependent on pH and glargine should therefore not be diluted. From studies in healthy and diabetic cats it seems that the administration every 12 hours to obtain an optimal glycemic control. The recommended dose is the same as the Caninsulin ® and ProZinc®. In a study conducted in Australia, the use of glargine insulin in combination with a diet low in carbohydrates and high in protein (Purina DM®) resulted in remission of diabetes in all 8 cats in which it was used. Subsequent studies have not demonstrated the same percentages, but it seems to be that insulin works best in the cat and most likely result in a remission of the disease. From studies in healthy cats and diabetics seems to be administered every 12 hours to obtain an optimal glycemic control.

In BOX 1 is indicated the protocol for the management of the diabetic cat with insulin

Box 1. Protocol for the management of diabetic cats with insulin

Diagnosis and initial evaluations

- Diagnosis of diabetes mellitus (history, physical examination, hyperglycaemia, glycosuria, increased fructosamine).
- Routine laboratory evaluation (complete blood count, serum biochemistry, urine analysis, urine culture).
- Serum TT4, DDGR lipase, or SpecfPLI measurement, if indicated.
- Abdominal ultrasonography.
- Cease diabetogenic drugs.
- Administer long-acting insulin (e.g., glargine, detemir, or PZI): 1–1.5 U/cat b.i.d.
- Institute treatment for concurrent problems (e.g., stomatitis, urinary tract infection).
- Prescribe a commercial high-protein (>40% protein metabolizable energy), low-carbohydrate diet.
- Feed 45–60 kcal/kg/day.
- If overweight, dose to reduce 0.5%–2% weight loss per week.
- Dietary recommendations for concurrent disorders (e.g., chronic kidney disease, food allergy) have priority over a specific diabetic diet.

- Give owner instructions (requires at least one hour).
  - Provide written instructions.

Reevaluation 1 week after diagnosis

- . History, physical examination, body weight

- If the cat is a good eater, administer food and insulin at the clinic. For cats that are unwilling to eat at the clinic, food and insulin to be given at home and the blood glucose curve (BGC) started upon arrival at the clinic (as soon as possible).

• Measure glucose every two hours for the remainder of the day (ideally for 12 hours, or even longer if the nadir is not reached).
• Measure fructosamine.
• Adjust insulin dosage, if required, by 0.5 U/injection. In case of symptomatic hypoglycaemia, reduce 25%–50% of the dose.

Re-evaluation 2–3 weeks after diagnosis

• Repeat all procedures performed at the first re-evaluation (history, physical examination, body weight, BGC, fructosamine).
• Introduction to home monitoring (HM) and instruction on all relevant technical aspects (requires at least 0.5 hours).
• Owner should generate a BGC once per week in the initial stabilization period.
• After the stabilization period (e.g., adequate glycaemic control obtained), owner should perform a BGC every 3–4 weeks.
• All the BGCs should be sent to the clinic and the decision about insulin adjustments should be always be made by the clinician.
• Adjust insulin dosage if required, by 0.5 U/injection; n case of symptomatic hypoglycaemia, reduce 25%–50% of the dose.

Re-evaluation 6–8 weeks after diagnosis

• Repeat all procedures performed in first re-evaluation (history, physical examination, body weight, BGC, fructosamine, dose adjustment). BGC may not be required if the cat appears clinically well, if blood glucose measured close to the time of insulin administration is 180 to 250 mg/dL, and fructosamine is 350 to 450 µmol/L.
• Evaluate owner administration technique for those doing home monitoring
• Assess home monitoring results.

Re-evaluation 10–12 weeks after diagnosis and then every four months

•Repeat all procedures done six to eight weeks after diagnosis.

Goals of therapy

• Clinical signs: resolution of polyuria/polydipsia and polyphagia, and normal body weight
• Blood glucose concentration: ideally between 250 mg/dL (before insulin administration) and 80 mg/dL (nadir)
• Fructosamine concentration: ideally 350–450 µmol/L (please note: fructosamine concentration is the least important variable for evaluation of metabolic control)
• Diabetic remission is obtained in 25%–50% of newly diagnosed diabetic cats

New prospectives: incretins

The incretin-based therapy is revolutionizing the management of the human diabetic patient. Such products are able to replace insulin, they are safe and are also available as long-acting drugs. These hormones (Glucagon-like peptide-1 [GLP-1] and glucose- dependent insulinotropic peptide [GIP]) that are secreted from the intestine after ingestion of food. The GLP-1 slows gastric emptying and increases the state of satiety while in the pancreas increases insulin secretion and suppresses the secretion of glucoagone during hyperglycemia with a glucose-dependent mode of action. There is also a protective effect for beta cells by limiting oxidative damage and promoting the expansion of the beta cell mass. In humans with type 2 diabetes GPL-1 showed an efficacy equal to insulin to maintain glycemic control. The risks of hypoglycemia are low. Another big advantage is represented by the duration of action: while insulin must be administered daily, long-acting GPL-1 provides one administration weekly. In cats GPL-1 was well tolerated in healthy cats. In diabetic cats, a recent study showed that can be useful in combination with insulin. However further studies are needed in order to recommend this type of therapy routinely.

Dietary Management

Dietetic Requirements:

High-Protein, Low-Carbohydrate diet: cats are obligate carnivores, and their diet plays a crucial role in managing diabetes. A diet high in protein and low in carbohydrates is recommended to help stabilize blood glucose levels. Commercially available prescription diets for diabetic cats often follow this nutritional profile.

Consistency in feeding: Maintaining a consistent feeding schedule helps in managing blood glucose levels.

Weight management: obesity can exacerbate diabetes. Weight loss in overweight cats should be gradual and supervised by a veterinarian to avoid complications.

Benefits of Dietary Management:

Improved glycemic control: proper diet can help in stabilizing blood glucose levels and reducing the need for high doses of insulin.

Potential for remission: In some cases, especially in newly diagnosed diabetic cats, a strict diet can lead to remission, reducing or even eliminating the need for insulin therapy.

Conclusion

The advent of SGLT2 inhibitors represents a significant breakthrough in the treatment of feline diabetes mellitus, offering new hope for better management and improved outcomes. Traditional insulin therapy and dietary management remain critical components of treatment, ensuring comprehensive care for diabetic cats.

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FELINE DIABETES MELLITUS: HOW THE TECHNOLOGY CAN HELP IN MONITORING

Thursday 12 September | 08:30 - 10:30 | Amphitheater N. Skalkotas - Room A

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Monitoring options for feline diabetes mellitus include clinical signs, continuous glucose monitoring systems (CGMSs) or blood glucose curves (BGCs), urinary glucose and glycated proteins (fructosamine and glycated hemoglobin). None of the monitoring options are perfect, and results from the different options may conflict. Decisions about monitoring options should consider the kind of treatment (eg., insulin vs SGLT2i) owner's financial situation, level of motivation, and overall expectations regarding their pet. Some owners are willing and able to monitor their cat regularly and are highly compliant with clinical recommendations. Others may approach their responsibilities as pet owners with a different philosophy and may be reluctant to follow suggested protocols if substantial cost or time is required. In these circumstances, the veterinarian must carefully advocate for the patient's needs while acknowledging the owner's position.

History and Physical Examination

The most relevant parameters for assessment of glycemic control are owner opinions regarding their pet, specifically, status of PU/PD/PP, body weight, and general health. Bodyweight is emphasized since insulin-underdosed diabetics tend to lose weight and insulin-overdosed diabetics tend to gain weight. Well-controlled diabetics have stable, near ideal, body weight. Objective findings on PE are used in concert with owner thoughts. If the owner is satisfied, body weight stable, and PE consistent with good glycemic control, further testing is only directed at avoiding overdose. Owners should specifically report any possible hypoglycemic episodes (e.g., weakness, ataxia, "acting intoxicated"). Persistence or recurrence of clinical signs or unwanted change in weight are suggestive of poor glycemic control or presence of a concurrent disease. Serum fructosamine concentration and evaluation of the results of a continuous glucose monitoring system (e.g. FGMS) or blood glucose curves (BGCs) may help characterize the issue, guide changes in treatment, and may indicate the need for additional testing.

Serum fructosamine and glycated hemoglobin (HbA1c)

Serum fructosamine and glycated hemoglobin (HbA1c) are two glycated proteins that result from the irreversible, non-enzymatic binding of glucose to serum proteins or hemoglobin in the RBC, respectively. In cats, serum fructosamine reflects the mean blood glucose concentration during the preceding 1 to 2 weeks, while HbA1c can be considered as an index of the average plasma glucose concentration over the preceding 2 to 3 months. Serum fructosamine and HbA1c are not affected by acute changes in blood glucose. Higher average glucose concentrations result in greater amounts of blood fructosamines and HbA1c. Lower fructosamine, independent of blood glucose, has been observed with hypoproteinemia, azotemia, hypoalbuminemia, hyperlipidemia, and hemolysis

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Urine Monitoring

Owner monitoring of urine for glucse and ketones can be useful. Most diabetics have varying amounts of glucose present in virtually every urine sample, with an occasional negative. Persistent absence of sugar may be indicative of insulin overdosage or excellent control. Ketonuria suggests inadequate control and decompensation. Upon seeing ketones in the urine of a pet who rarely has them, the owner should contact the veterinarian. Owners should not

adjust insulin dosage on the basis of morning urine glucose because this commonly leads to overdose and increases the likelihood of insulin-induced hypoglycemia. Monitoring ketonuria is particularly important in monitoring diabetic cats treated with SGLT2 inhibitors. Indeed, the appearance of ketonuria dictates that SGLT2 inhibitor therapy should be discontinued and insulin treatment started.

Single Blood Glucose

A single blood glucose measurement is rarely useful in monitoring DM in animas that are receiving insulin with the exception of finding a low result, always indicative of an overdose. Single glucose measurements may be sufficient when an owner believes the cat is virtually asymptomatic, the PE is unremarkable and serum fructosamine concentrations are indicative of good glycaemic control (e.g. less than 100 mcmol/L above the upper reference range of the laboratory). In such cases, glucose concentrations between 180 and 250 mg/dL around the time of the insulin injection are consistent with good glycemic control and additional blood glucose measurements are not usually necessary. With SGLT2 inhibitor treatment, blood glucose usually has minimal fluctuations throughout the day, and therefore, a single blood glucose can be useful in monitoring cats treated with SGLT2 inhibitors.

Portable Blood Glucose Meters

During the initial adjustment phase and in subsequent long-term management phases of therapy, if signs of DM persist, signs recur, or fructosamine concentrations are high, single glucose measurements should be avoided and a BGC obtained instead. Serial BGCs can provide guidelines for making rational adjustments in insulin therapy. Blood glucose concentrations are typically determined by a hand-held portable blood glucose meter (PBGM). To avoid multiple venipunctures, one may collect capillary blood from the. Several portable glucose meters are available. The accuracy of PBGM devices designed for people varies considerably when used in cats. Some PBGM devices designed for humans are sufficiently accurate and precise to monitor feline blood glucose concentrations. However, most give lower results than laboratory reference methods. This bias may result in an incorrect diagnosis of hypoglycemia or the misconception that the animal's glycemic control is better than it actually is. The AlphaTRAK blood glucose meter (Abbott Animal Health) is specifically designed for use in dogs and cats and is more accurate and precise than the PBGMs designed for humans. Additional advantages of the AlphaTRAK are the small volumes of blood needed (0.3 mcL) and the extended measurement range (20 to 750 mg/dL). Conversely, AlphaTRAK tends to overestimate blood glucose values, potentially missing hypoglycemia.

Blood Glucose Curves and Insulin Dose Adjustments

Up to a few years ago, the BGCs were the most objective monitoring tool for making rational adjustments in insulin therapy. They allow the identification of subclinical hypoglycemia; thus, the insulin dose can be decreased before clinical signs develop. Moreover, when the clinical signs suggest poor control of the disease, the BGCs may help to characterize the underlying problem (e.g., insulin doses are too low or insulin action is too short), thus allowing insulin changes. However, this monitoring method has several limitations, the most important of which is the inability to detect inter- and intra-day glycemic variability. For this reason, the author recommends using this monitoring method only in situations where the use of a CGMS is not possible.

There are several situations when a BGC could be performed: (1) at 5-7 days after the start of insulin therapy; (2) at 7-14 days after an insulin dose change; (3) at 5-7 days after the first dose of a new kind of insulin; (4) at least every 3 months even in well-controlled diabetics; (5) any time clinical signs recur in a controlled patient; and (6) when hypoglycemia is suspected.

When conducting a BGC, the cat should be seen early in the morning and blood glucoses sampled every 1 to 2 hours throughout the day. One should begin just prior to the first insulin dose and continue until the next dose is due. Most cats respond well to the same dose of insulin morning and evening) If different blood glucose concentrations are suspected during day

versus night (e.g., good BGC and control of clinical signs during the day but presence of PU/PD during the night), a 24-hour BGC or use of a continuous blood glucose monitoring device should be considered. When performing a BGC, the insulin and feeding schedules followed by the owner should be maintained. Poor appetite can strongly affect the results of a BGC. Food and insulin can be administered at the clinic after the first blood glucose measurement. If the animal refuses to eat in the clinic, the BGC should be abandoned. The evaluation of the BGC allows the clinician to determine if the insulin administered is effective and identify the glucose nadir, time of peak insulin effect, duration of insulin effect, and degree of fluctuation in blood glucose concentrations. In well-controlled DM, glucose concentrations should stay between 80 and 250-300 mg/dL. Insulin efficacy is evaluated, in part, by determining the difference between highest and lowest glucose concentrations. A small difference (e.g., 50 mg/dL) is acceptable if the highest blood glucose level recorded is <220 mg/dL but not acceptable if it is >300 mg/dL. The most important parameters are the glucose nadir and the duration of the insulin effect. The glucose nadir should, ideally, be between 80 and 150 mg/dL. A lower nadir can be caused by insulin overdose, excessive overlap of the insulin action (common if long-acting insulin analogues are used), prolonged periods without food (the cat refused to eat in-hospital), or strenuous exercise. A glucose nadir >160 mg/dL can be caused by an insufficient insulin dose, insulin resistance, and technical problems attributable to the owners. In a cat already treated with high dosages (e.g., >1.5 U/kg per injection), owner error and insulin resistance are the main differential diagnoses. Duration of insulin action can be determined if the glucose nadir falls within the desired range. Duration is defined as the time from injection through the glucose nadir until the glucose concentration exceeds 250 mg/dL. When duration is too brief (e.g., <8 hours), signs of DM are usually exhibited. When duration is too long (e.g., >14 hours), risk of hypoglycemia is higher. Duration of action may be altered with changes in diet. One may change to an insulin product with a different action profile. Performing BGCs on consecutive days is not recommended. BGCs should never be assumed to be reproducible. Day-to-day variables and the diabetic condition itself are rarely static. Variables include the amount of insulin drawn into the syringe each time, the amount of insulin absorbed after each injection, and the interactions between insulin, diet, exercise, stress, excitement, presence of concurrent disorders, gastric emptying, and secretion of the counterregulatory hormones (e.g., glucagon, epinephrine, cortisol, growth hormone). All these factors change with time and alter the chances of reproducible BGCs. Lack of consistency in BGC results can create frustration unless expected. Lack of consistency is common and reflects any variable that could alter glucose concentrations. When dose change appears appropriate, it should not exceed 10% to 25%. However, in documented or suspected hypoglycemia, the dose should be decreased by about 50%. Insulin doses should not be modified more frequently than every 5 to 7 days, except in hypoglycemia.

Continuous glucose monitoring systems and the flash glucose monitoring system

Continuous glucose monitoring systems (CGMSs) are routinely used to monitor glucose concentrations in diabetic human patients and are also currently used in diabetic dogs and cats. These systems allow glucose concentrations to be monitored without the need for repeated blood sampling. The CGMS measures interstitial glucose (IG) rather than blood glucose concentrations. Interstitial fluid is easily accessible, has quite rapid equilibration with the blood and has a good correlation with blood glucose. Several CGMSs are currently available; the use of iPro® (Medtronic), Guardian Real Time® (Medtronic) MiniMed Gold®(Medtronic), GlucoDay® (Menarini diagnostic) and FreeStyle Libre® (Abbott) has been reported in dogs and cats. The Guardian REAL-Time One is a frequently used CGMS which measures interstitial glucose using a small, flexible sensor inserted through the skin into the subcutaneous space and secured to the skin with tape. The sensor is connected to a transmitter which is also fixed to the patient with tape and sends data in a wireless fashion over a maximal distance of 3m to a pager-sized monitor. Data are collected every 10 seconds, and a mean glucose value is

computed every 5 minutes. The data can be downloaded to a computer for analysis. Currently, CGMS devices present some defects. They need to be calibrated two-three times a day, which requires blood sampling, and the sensor is quite expensive and can be used for only a few days. Furthermore, the monitor displays glucose concentrations from 2.2 to 22.2 mmol/l; concentrations outside this range are correctly recorded but need to be downloaded to be visualised. A new CGMS (Freestyle Libre (Abbott), produced for humans, consists of a small, round, disposable, water-resistant sensor which continuously measures glucose in the interstitial fluid by means of a small (5 mm long × 0.4 mm wide) filament inserted SC.

The FGMS generates information every minute, and the readings are automatically stored in 15-minute intervals for up to 14 days. Interstitial glucose concentrations are displayed when the sensor is wirelessly scanned (or "flashed") with a smartphone on demand. The smartphone then displays the past 8 hours of glucose information, including current glucose, a trend graph and a trend arrow which indicates the direction of the patient's current glucose concentration with respect to the previous results. In cats, the application and the use of the FGMS is apparently painless, easy to usw and well-tolerated (Figure 1). Mild erythema at the site of the application can be observed at the end of the wearing period.

With the FGMS the glucose data are stored in the cloud and easily viewable by the clinician through LibreView (the FreeStyle Libre website). This allows for optimal patient monitoring.

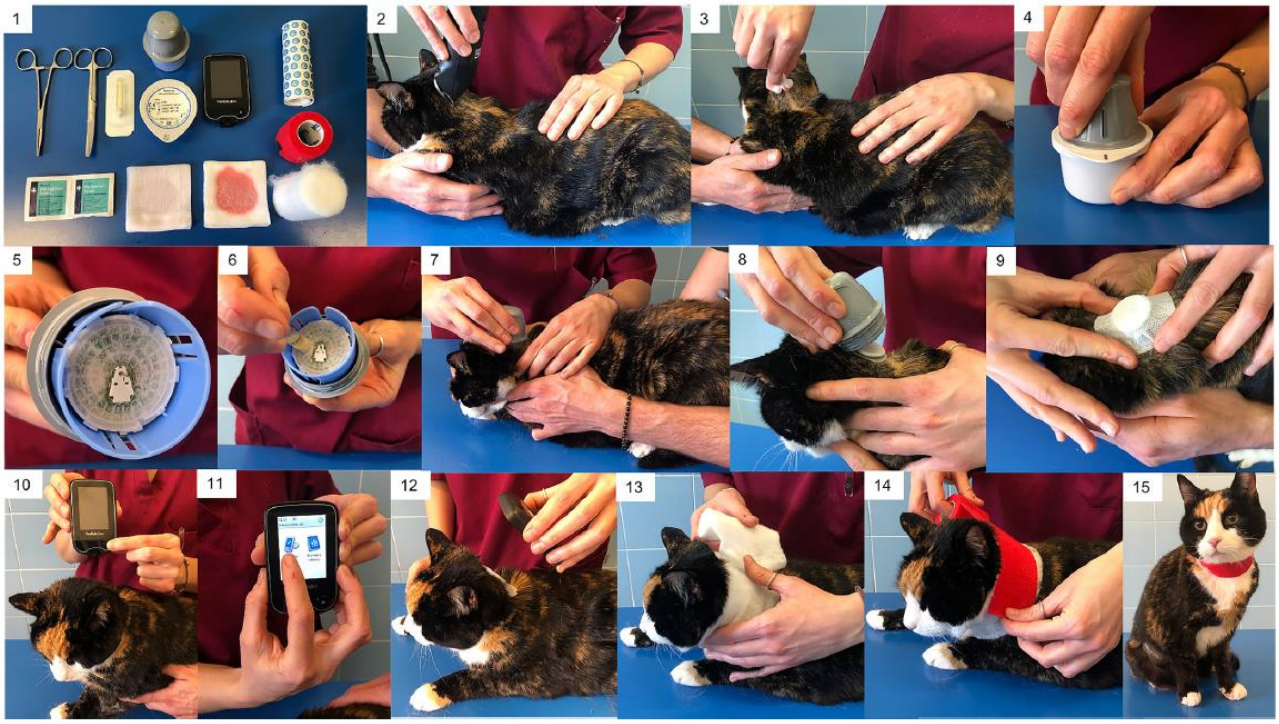

FIGURE 1 FreeStyle Libre application in a diabetic cat. (1) Freestyle libre sensor pack, applicator and reader with the necessary equipment:
alcoholic wipes supplied by the Freestyle libre manufacturer, gauze (3 with chlorhexidine and 3 with alcohol), scissors and forceps, tissue glue,
tape, cotton and elastic bandage; (2) the dorsal aspect of the neck is trichotomized; (3) the skin is cleaned with chlorhexidine and alcoholic wipes;
(4) the dark mark on the sensor applicator is lined up with the dark mark on the sensor pack and, on a hard surface, is pressed down firmly on the
sensor applicator until it comes to a stop; (5) lifting the sensor applicator out of sensor pack, the sensor applicator is ready; (6) a drop of tissue

glue is added on the skin-surface of the sensor; (7) the sensor applicator is placed over the site and pushed down firmly in order to apply the
sensor; (8) it is ensured that the sensor is secure (if necessary, the forceps can be used to avoid the detachment of the sensor); (9) the sensor is
additionally secured by covering it with a patch; (10) the reader is turned on by pressing the home button; (11) touching "start new sensor" and
(12) holding the reader within 1.5 in. (4 cm) the sensor is scanned and is ready to measure the glucose concentration after 60 minutes; (13) the
sensor is secured with a cotton bandage and (14) with an elastic bandage, and (15) the cat is ready to go home

Inter-day and intra-day glycemic variability

In addition to the inter-day glycemic variability (GV), an intra-day day GV exists. This is defined as intra-day glycemic excursions, including episodes of hypoglycemia and hyperglycemia.

Somogyi

Nowadays, it is believed that the Somogyi phenomenon is not a special entity, but part of the GV complex. Indeed, contrary to a historic veterinary dogma, in recent years, overwhelming evidence accumulated contradicting the existence of the "Somogyi effect". The Somogyi effect is defined as a rebound hyperglycemia following a hypoglycemic episode or a rapid decrease of BG concentration that evokes the release of diabetogenic hormones, especially epinephrine and glucagon, and direct hypoglycemia-induced stimulation of hepatic glycogenolysis. However, up to date, there is no evidence in cats or other species that DM counterregulatory hormones are released excessively in response to hypoglycemia. Instead, the opposite is true: hypoglycemia counterregulatory responses are impaired in DM.

Glycemic variability

In people, GV is an indicator of glycemic control.14 A high GV is considered to be a risk factor for hypoglycemia, microvascular complications, neuropathy, nephropathy, retinopathy, stroke, and all-cause mortality. In cats, GV has not been studied yet. However, because the mechanisms leading to impaired counterregulatory responses in cats are largely the same as in people, it would be reasonable to hypothesize that, as in people, increased GV in cats would also lead to increased frequency of hypoglycemia in the long run.

In cats with high intra-day or inter-day GV, as a first step, it is recommended to check for compliance with insulin and dietary therapy as well as technical issues related to insulin (e.g., syringe size, outdated insulin). After that, the cat should be evaluated for the presence of concurrent disorders/conditions. If no reason is identified, the insulin dose should be set to a level that avoids hypoglycemia as much as possible, even if it means experiencing phases of hyperglycemia. Another option is switching to an insulin formulation associated with a lower GV (e.g., degludec or glargine 300U/ml).

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TREATMENT OF FELINE HYPERTHYROIDISM

Thursday 12 September | 11:00 - 13:00 | Amphitheater N. Skalkotas - Room A

Federico Fracassi

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Spontaneous hyperthyroidism (thyrotoxicosis) is a clinical condition resulting from an excessive production and secretion of thyroxine (T_4) and *triiodothyronine* (T_3) by the thyroid gland.

In 98% of cases feline hyperthyroidism is a disorder due to a benign neoplasm; although benign, if not properly treated it may result in a severe and progressive impairment of the animal, as a result of the state of thryrotoxicosis. The aetiopathogenetic mechanisms capable of causing the disease in cats are still unknown, and thus treatment is aimed at directly controlling excessive hormone production by the thyroid neoplasia. To this end, three therapeutic options are available, each of which presenting advantages and disadvantages that should be carefully evaluated for each individual patient.

- Destruction of the neoplastic tissue with radioactive iodine
- Surgical thyroidectomy
- Inhibition of hormone secretion with antithyroid drugs
- Limited-iodine food

Treatment with radioactive iodine: In view of its high therapeutic efficacy and the relative absence of complications, radioactive iodine therapy is considered the treatment of choice for feline hyperthyroidism. However, due to the radioactive potential of the agent used, this treatment can only be carried out in authorised facilities, which explains why its use is still limited. The β radiations of I^{131} selectively destroy hyperfunctioning thyroid cells, sparing normal thyroid tissue. The radioactive agent may be administered orally, intravenously or subcutaneously and a single administration is usually sufficient to attain the therapeutic effect (a second treatment is needed in only 5% of cases). The treatment requires hospitalisation and isolation of the cat for at least one week after the administration of I^{131} because of the high degree of elimination of radiation through faeces and urine. Radioactive therapy is especially advantageous in cats with bilateral thyroid lobe involvement, in the presence of pathological ectopic thyroid tissue, or in the rare cases of carcinoma of the thyroid gland. The possible complications associated with the use of this treatment are related to the possible onset of a nephropathy, not caused by the treatment itself but by the return to a euthyroid state in subjects in whom the hyperthyroidism present before treatment was masking the presence of the disease. Before implementing this treatment it is therefore advisable to first check, with the aid of medical antithyroid treatment, whether the concentration of T_4 can be reduced safely without causing renal failure.

Surgical treatment: Uni- or bilateral thyroidectomy is a quick, effective and relatively easy procedure, and is often the preferred treatment approach for the disease in clinical practice. In 70% of cases adenomatous hyperplasia involves both thyroid lobes, even though bilateral involvement is not always recognized in view of the small size of the neoformations. In these cases, if a unilateral thyroidectomy is performed, a recurrence of the disease can be observed

months later. Once the need for surgery has been established and the correct thyroid lobes have been identified (ideally a nuclear medicine scan should be performed before surgery), the next step is to stabilize the cat for surgery. Most hyperthyroid cats are elderly and have heart disease resulting from their thyroid condition. To set the patient on the road to recovery, the thyroid level is brought into the normal range with two to four weeks of oral medication (usually methimazole). Alternatively, certain heart medications (propranolol or other beta-blockers) are often used to compensate for the heart disease associated with hyperthyroidism, especially in cats with resting heart rates greater than 220 beats per minute. After thyroid levels have normalized, it is important to watch for an exacerbation of renal disease that may be unmasked by the treatment of hyperthyroidism. Concurrent kidney problems complicates anesthesia and may even preclude the surgery. Thyroidectomy can be performed using extra- or intracapsular techniques; however, the latter technique is preferable, as it reduces the risk of impairment (damage or removal) of the adjacent parathyroid gland. If a bilateral thyroidectomy is performed the main postoperative complication is the onset of iatrogenic hypoparathyroidism, which is generally temporary; for this reason, after this type of operation serum calcium concentrations should be monitored for at least one week. Hypocalcaemia should only be treated if clinical signs are present or if serum calcium concentrations are below 6.5 mg/dl, even in the absence of clinical symptoms. Sings of hypocalcaemia include anorexia, lethardy, anxiety, irritability, cramps or muscle pain, muscle tremor, especially in the face and ears, tetany and seizures. In all cases of bilateral thyroid surgery the plasma Calcium levels should be monitored by measuring preoperatively and at about 20 h after surgery. In cases with severe hypocalcemia and clinical symptoms (tremors, tetany, convulsions) IV administration of 0.5 mmol Ca^{2+}/kg as calciumgluconate is given under close ECG monitoring. The same dose that was needed to control tetany and tremors is diluted with at least an equal volume of saline 0.9% and administered subcutaneously, 2–4 times a day. In cases without clinical symptoms of hypocalcemia the following protocol is used: if plasma calcium is < 1.0 mmol/l or more than 10% below the preoperative value, calcium(boro)gluconate (1–2 ml/kg) is administered subcutaneously, 2–4 times a day, diluted with at least the same volume of 0.9% saline. As soon as the cat is eating oral supplementation is started. Calcium carbonate powder (15–20 mg/kg) is added to each meal and dihydrotachysterol is provided at a starting dose of 0.05 mg per cat once a day during the first 3 days, and then decreased to 0.025 mg once a day.Supplementation may be needed for only a few days or for life depending on the damage to the parathyroids. Some surgeons prefer to perform thyroidectomy in stages, removing one thyroid lobe and transplanting the associated parathyroid gland into a local muscle belly to preserve its blood supply. The same procedure is performed on the other thyroid lobe two to three weeks later. The staged procedure reduces the risk of hypocalcemia but does involve two anesthetic procedures on the senior feline patient who is already somewhat debilitated by the hyperthyroid situation.

Hypocalcemia is not a concern for cats requiring removal of only one thyroid lobe. Usually levothyroxine supplementation is not needed if only one lobe is removed. After bilateral thyroidectomy oral substitution with L-thyroxine is provided (50 µg per cat twice daily, starting on the fourth day after surgery). Plasma T4 levels are measured after one month and then every six months. The dosage of L-thyroxine is adjusted if necessary to maintain plasma T_4 within the normal range.

Medical treatment: Medical treatment is a practical option that does not require the use of special equipment and, at least initially, is not expensive. With the exception of the rare cases of thyroid gland carcinomas, medical treatment has few contraindications, mostly connected above all with the onset of side effects. The more commonly used drugs in both human and veterinary medicine for the long-term control of hyperthyroidism are the *thiouracil derivatives*: **carbimazole and methimazole (thiamazole).** These drugs inhibit the action of the thyroid peroxidase enzyme and consequently block the synthesis of thyroid hormones. When hormone production is inhibited a rapid return to a condition of euthyroidism is generally observed, in

around 2-4 weeks after the start of treatment. Compared to the treatment with radioactive iodine and to thyroidectomy, these drugs allow a reversible control of the disease: 24-72 hours after discontinuation of the drug, the cat returns to a state of hyperthyroidism. Although this is considered a negative aspect, in some situations this result may be considered advantageous: it can be used to test whether with the return of euthyroidism the cat develops an overt renal failure or before thyroidectomy to stabilise the patient. Carbimazole after oral administration is metabolised and converted into methimazole, the molecule with antithyroid properties. A 5 mg dose of carbimazole is equivalent to approx. 3 mg of methimazole. The initial dosage of carbimazole is 2.5 mg/cat twice daily and the initial starting dose of carbimazole is 10-15 mg/cat once a day. Methimazole, like carbimazole, is a drug that, if well tolerated by the subject, has an efficacy greater than 90% in the treatment of hyperthyroidism. The most common side effects of methimazole are anorexia, vomiting and lethargy. These symptoms generally arise within the first 4 weeks from the beginning of treatment and they can be resolved by reducing the dosage or by using the transdermal formulation of methimazole. In some cases more severe adverse reactions to the drug have been reported, including: blood dyscrasia (thrombocytopenia, leukopenia), facial excoriations from self-trauma and liver disease. In these cases the administration of the drug should be discontinued. **Transdermal methimazole:** in the cat, methimazole may be more easily administered transdermally, using a pharmaceutical preparation expressly formulated with PLO (pluronic lecithin organogel). The owner, wearing gloves, should apply the ointment 2 times a day, to the inner pinna. The starting dose is 2-2.5 mg/cat every 12 hours. The bioavailability of the drug is inferior compared to that of the formulation for oral administration, and hence the efficacy is lower. Nevertheless, this formulation is especially advantageous for those cats in whom tablets are difficult to administer, and especially if tablets are associated to the appearance of gastrointestinal effects. **Therapeutic monitoring**: The first control after the beginning of treatment is at 2-4 weeks, to test the concentration of T_4, to exclude the onset of possible drug adverse reactions and to monitor renal function. It is important to evaluate renal function and T_4 concentration simultaneously during treatment, to make sure that the latter is maintained even with GFR values associated with a state of euthyroidism. Hormonal monitoring may be carried out independently from the moment of drug administration but is inportant that in the day ofr monitoring the medication has been administrated; concentrations of T_4 within the lower half of the reference range are generally associated with a good control of the disease. Is it common to see an increase of creatinine (also above the reference range) during treatment, this is for the normalization of GFR (that before treatment is abnormally high). In such cases a reduction of the a methimazole/carmimazole is not usually indicated. However, if with the recovery of euthyroidism the cat becomes azotaemic and symptomatic, the drug dosage may be reduced to ensure that the concentration of T_4 remains within the upper half of the reference range.

Limited-iodine food: Production of thyroid hormone requires uptake by the thyroid gland of sufficient amounts of iodine, which is provided by dietary intake. The only function for ingested iodine is for thyroid hormone synthesis. This observation led to the hypothesis that limiting dietary iodine intake could be used to control thyroid hormone production and potentially manage hyperthyroidism in cats. After more than a decade of research and development, a limited-iodine therapeutic food (Hill's® Prescription Diet® y/dTM Feline) containing < 0.3 ppm (mg/kg) iodine on a dry matter basis (DMB), is now available as an option for managing cats with hyperthyroidism. Results from few recent studies suggest that an iodine-restricted food may be effective in reducing serum total thyroxine concentration in hyperthyroid cats. The main problem is the palatability and many cats after a while refuse the dete. Compared to oral or transdermal methimazole, the dietetic treatment did not cause any increase in serum creatinine, but was less effective in improving bodyweight, liver parameters and general control of the disease.

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FELINE CALCIUM HOMEOSTASIS DISORDERS

Thursday 12 September | 11:00 - 13:00 | Amphitheater N. Skalkotas - Room A

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HIPERCALCEMIA IN CATS

Hypercalcemia is a condition that, independently of the underlying cause, can be considered an endocrine problem. Any cause of hypercalcemia involves the alteration of the hormones that regulate calcium homeostasis.

DIFFERENTIAL DIAGNOSIS OF HYPERCALCEMIA

Idiopathic Hypercalcemia

Pathophysiology

Idiopathic hypercalcemia is considered a common diagnosis in hypercalcemic cats and the cause remains unknown.

There may be genetic factors or possibly dietary factors involved. Some studies have reported hypercalcemia associated with the feeding of an acidifying diet or use of urinary acidifiers, which resolved after dietary change or discontinuation of the urinary acidifying therapy.

Age, breed

Cats with idiopathic hypercalcemia can be of any age. It is likely, however, that breed plays a role because 40 % of the cats reported having idiopathic hypercalcemia were long-haired breeds including Domestic Longhair, Himalayan, Persian, and Maine Coon.

Diagnosis

Idiopathic hypercalcemia is a diagnosis of exclusion, and other causes must be ruled out before a diagnosis is made and treatment began.

Dietary and/or medical management

Dietary management may be successful in many cases. Considering that cases of idiopathic hypercalcemia have been reported in cats fed with acidifying diets, the first line of treatment should probably involve the use of a non-acidifying diet, but this has not been well defined.
Feeding a high fiber diet, or feeding a wet diet is recommended as an initial first step, particularly in cats with only mild or moderate hypercalcemia. In cats for which dietary modification fails to normalize serum concentrations of Ca2+, medical management can be considered.

The orally administered bisphosphonate, alendronate has emerged as the first-line drug treatment for idiopathic hypercalcemia.
Orally administered alendronate has been associated with esophagitis and esophageal stricture in humans, and for these reasons, strategies to decrease the transit time through the esophagus are used. A small amount of butter can be helpful.

Chronic Kidney Disease (CKD)

In cats with CKD, hypercalcemia is reported with a frequency of 10% to 32%.
The severity of hypercalcemia in these animals is usually mild. Regardless of the underlying pathophysiology of hypercalcemia in CKD, specific treatment of hypercalcemia is usually not necessary.

Primary Hyperparathyroidism

Pathophysiology
Primary hyperparathyroidism is an uncommon cause of hypercalcemia in cats. Primary hyperparathyroidism is usually caused by an autonomous hyperfunctional adenoma of a single parathyroid gland.

Laboratory Testing and Diagnostic Imaging
Serum biochemistry results are often irrelevant (except TCa concentration). The phosphate concentration is often normal, although hypophosphatemia is expected due to the increase in PTH.
Results of measuring intact PTH concentrations, while essential in confirming a diagnosis of primary hyperparathyroidism, can be misleading. The finding of a PTH concentration above the reference range confirms the diagnosis of primary hyperparathyroidism if concurrent CKD has been ruled out.

Treatment
Surgery is the treatment of choice since in most cases of primary hyperparathyroidism the cause is a single hyperfunctional adenoma of a parathyroid gland.
The postoperative complications reported in cats were a unilateral Horner syndrome, which reportedly resolved, and a permanent change of voice, presumably caused by damage to the recurrent laryngeal nerve, whereas in dogs the postoperative complication most serious is hypocalcemia. This is because the presence of a hyperactive parathyroid nodule involves the atrophy of the other parathyroid glands, consequently, its removal can lead to transient hypoparathyroidism and postoperative hypocalcemia. Post-parathyroidectomy hypocalcemia has been documented in the cat, but the need for treatment has not been determined. Serum Ca (Ca2+ if available) should be monitored at least twice a day after parathyroidectomy and if hypocalcemia develops, especially if it is associated with clinical signs, it should be treated.

Vitamin D Toxicosis
Intake of excessive exogenous vitamin D can lead to toxicity. This type of intoxication derives mainly from the accidental intake of rodenticides and in small part from an excessive presence of vitamin D in the diet.

Hypercalcemia of Malignancy

Hypercalcemia caused by malignant cancers has been well-demonstrated in the cat.. Hypercalcemia of malignancy may or may not be associated with increased serum concentrations of PTHrP in cats. In addition to pulmonary neoplasia, hypercalcemia of malignancy has been reported in cats with squamous cell carcinoma, renal carcinoma, thyroid carcinoma, multiple myeloma, alimentary lymphoma, and FELV-associated leukemia.

Hypoadrenocorticism
Hypoadrenocorticism is an uncommon endocrinopathy in cats. Although there is little reported in the literature, it is believed that hypercalcemia occurs in about 10% of cats suffering from this disease.

Granulomatous Disease

Macrophages within granulomatous tissue can produce calcitriol leading to overt hypercalcemia. This phenomenon is well-established in human patients and has been reported in single case reports in cats.

GENERAL MANAGEMENT OF HYPERCALCEMIA

In asymptomatic patients with mild hypercalcemia (ionized calcium <0.25 mmol/L above the reference interval) and who present a calcium x phosphate product not altered, they do not require immediate treatment, whereas for patients who show an increasingly severe and acute calcium concentration, may require immediate and more aggressive treatment.
No single treatment is recommended for managing all cases of hypercalcemia and, therefore, therapy should be set based on the underlying disease.
Supportive therapy is aimed at enhancing renal excretion of calcium and preventing calcium resorption from bone.

Drugs and their doses, which can be used in the management of hypercalcemia:

Drug	Dose	Route of administration	Frequency of administration
Furosemide	1-2 mg/kg	IV, SC, PO	q8-12h
Prednisolone	0.5-1 mg/kg	SC, PO	q12-24h
Dexamethasone	0.1-0.2 mg/kg	IV, SC	q24h
Pamidronate	1.0-2.0 mg/kg	Slow IV infusion (about 4h) 0.9% NaCl	May be repeated after 7-14 days
Alendronate	5-20 mg/cat	PO	q7 days
Calcitonin	4-6 IU/kg	SC	q 8-12h

HYPOCALCEMIA

Differential Diagnosis for feline hypocalcaemia

The following list includes the more important causes of hypocalcemia in cats:

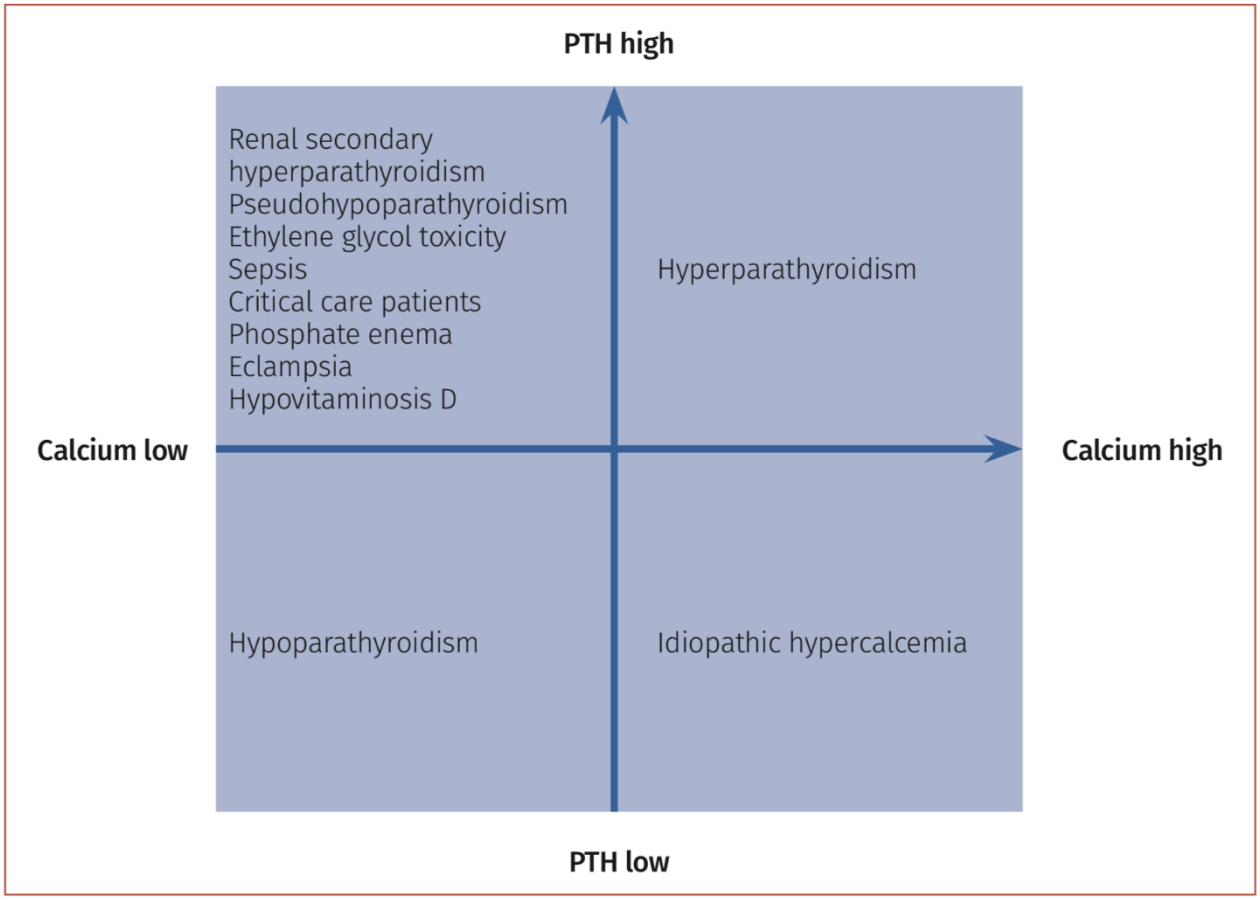
- Hypoalbuminemia
- Acute and chronic renal failure
- Acute pancreatitis
- Hypovitaminosis D
- Urinary tract obstruction
- Ethylene glycol toxicity
- Sepsis and critical care patients
- Hyperthyroidism

- Hypoparathyroidism is a rare condition in people and dogs but is even less commonly encountered in cats.
- Hyperthyroidism is the most common endocrinopathy reported in cats. In the past, surgical thyroidectomy was used more frequently and accidental removal or damage to parathyroid tissue did occasionally occur.
- Permanent hypoparathyroidism in cats can be caused by sterile inflammatory-mediated destruction of the parathyroid glands, presumably due to an immune-mediated mechanism.
- Severe hypomagnesemia can cause functional hypoparathyroidism.

Diagnostic Evaluation

Ca2+ is the best parameter to investigate the calcium concentrations in the feline patient. Ca2+ should be always evaluated when hypocalcemia is suspected. Full serum biochemistry, urinalysis and CBC can identify most of the cause of hypocalcemia. If the cause of hypocalcemia is not identified, the measurement of serum PTH can be helpful.

Below is reported the differential diagnosis of calcium disorder in the cat categorized by PTH and calcium concentrations (From **Skelly BJ "Feline primary hypoparathyroidism and hypocalcemia" In Feline Endocrinology. Ed. Feldman EC, Fracassi F, Peterson ME, Edra 2019**):



Treatment

Acute hypocalcemia

Intravenous Ca salts are the initial treatment of choice. Ca gluconate (e.g. 10% calcium gluconate 0.5-1.5 ml/kg over 20-30 minutes) or borogluconate are the most frequently recommended.

The use of subcutaneous calcium supplementation is controversial. Sterile abscess formation and skin sloughing has been reported when calcium salts were used SQ in some dogs.

Chronic hypocalcemia

Early calcium supplementation is helpful to ensure high intestinal luminal calcium concentrations that will encourage passive calcium absorption over the period of time it takes for vitamin D to begin to work. Once vitamin D is working effectively, calcium can usually be decreased or stopped completely as the amount of calcium present in cat food is sufficient.

Calcitriol is the active form of vitamin D and therefore does not require metabolism to become active. It has a rapid onset of action (1-4 days) and a short half-life.

Dihydrotachysterol is a useful vitamin D supplement because it comes in a liquid formulation as a 0.25 mg/ml solution. Dihydrotachysterol requires hydroxylation by the liver to reach its active form but does not need to be hydroxylated again by the kidney.

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SURGICAL MANAGEMENT OF SQUAMOUS CELL CARCINOMA OF THE EXTERNAL GENITALIA IN DOGS

Thursday 12 September | 14:30 - 16:30 | Amphitheater N. Skalkotas - Room A

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Squamous cell carcinoma (SCC) is a malignant epithelial tumor in dogs that uncommonly affects canine external genitalia in the male and only a few case reports appeared in the literature.

A large case series of 15 male dogs with SCC of the prepuce, scrotum, or penis was recently published. [1] The Pitt bull breed was overrepresented. Median age was 8 years (range: 5 to 13 years) and the median weight was 28 kg (range: 9.6 to 49 kg). Six dogs had white coat color and nine dogs had nonwhite color. Tumors may be single or multiple. Most dogs showed ulcerations and had tumors located at the prepuce and a few had tumors situated in the scrotum the prepuce and scrotum, penis, or prepuce and penis. Cytologic examination from samples obtained from the lesions indicated SCC in most dogs. Surgeries performed with 2 cm lateral margins included penile amputation and scrotal urethrostomy, scrotal ablation, and orchiectomy, partial penile amputation or partial penile amputation and partial preputial ablation. Postoperative complications included hemorrhage, bruising at the urethrostomy site, and urethrostomy dehiscence. The median duration of postoperative hemorrhage was 2 days (range: 1 to 4 days). The median duration of hemorrhage following penile amputation and scrotal urethrostomy was 2 days (range: 1 to 4 days) and the median duration of hemorrhage following partial penile amputation was 1 day. Most SCCs were moderately or poorly differentiated and a few were well differentiated. Inguinal lymph node metastasis was detected in a few dogs. Recurrence of SCC was recorded in almost half of the dogs. The median recurrence time was 13 months (range: 8-30 months). Most dogs with recurrence were euthanized as their clients declined further surgery or other treatment. No distant metastasis was identified at necropsy in any of the dogs that died or were euthanized. After a median follow up of 23 months (range: 8 to 72 months), eight dogs were alive, five were euthanized and two dogs died from unrelated causes. The median survival time for the five dogs with poorly differentiated SCC was 14 months (range: 8 to 30 months). The median survival time for the 10 dogs with moderate and well-differentiated SCC was 24 months (range: 8 to 72 months). The overall mean survival time was 48.132 months (95% CI 31.633 to 64.630 months). [1]

For dogs with SCC of the external genitalia, surgical excision appears to be a viable treatment option overall. [1] Treatment options for squamous cell carcinoma of the penis, prepuce, and scrotum include scrotal and preputial ablation, penile amputation, and scrotal urethrostomy. The most frequent complications following surgery were hemorrhage and tumor recurrence. In comparison to dogs with well- and moderately differentiated SCC, those with poorly differentiated tumors that recurred had a lower survival rate and a worse prognosis. The majority of dogs had a favorable outcome. To provide local control of the tumor, wide surgical excision was carried out in the current case series; however, using 2 cm lateral margins only resulted in

complete margins in 60% of the dogs and incomplete margins in 40%. Tumors that are well or moderately differentiated might only require 2 cm of lateral margins, whereas those that are poorly differentiated might require larger margins. [1]

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FLUORESCENCE-GUIDED SURGERY IN DOGS WITH CANCER: NEW DEVELOPMENTS AND POTENTIAL

Thursday 12 September | 14:30 - 16:30 | Amphitheater N. Skalkotas - Room A

Hilde De Rooster

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Despite the emergence of multimodal approaches to cancer, surgery remains the most important modality for several tumor types. Unfortunately, obtaining clean resection margins can be challenging for oncologic surgeons, in particular for tumor types with invasive growth and high local recurrence rate. Any tumoral tissue left after surgery may lead to tumor recurrence, negatively impacting the patient's quality of life and overall survival.

Traditionally, tissue palpation, visual inspection, and real-time frozen section analyses were the only means used by surgeons to identify tumour margins during resection, and to assess the presence of residual disease. Over the past decades, several imaging modalities have been evaluated to facilitate full resection of solid tumors through the enhanced visualization of malignant tissue during surgery. Among these emerging technologies, real-time optical imaging stands out for its ability to directly visualize certain anatomical structures in vivo. Notably, Near-Infrared Fluorescence imaging shows great promise among potential optical imaging technologies. This technique utilizes near-infrared fluorescence probes composed of a fluorophore that becomes optically active under near-infrared excitation wavelengths.
Within the visible light spectrum, the human eye can detect various wavelengths and tissue depths, but it cannot differentiate between spectra with minor wavelength differences. Consequently, objects with nearly identical colors can be challenging to impossible to distinguish. This is one of the reasons why it may be difficult to differentiate between benign and malignant tissue during oncologic surgery, a very important differentiation affecting clinical outcome. The near-infrared spectrum lies between the visible light and infrared spectra. Using the NIR spectrum in a clinical setting has several advantages compared to the visible light spectrum. Inherent autofluorescence, caused by the presence of physiological biomolecules such as hemoglobulin, amongst others, is avoided. In addition, scattering is significantly lower than in the visible light spectrum. These properties will result in a far better image resolution during surgery. Another important difference between near-infrared light and visible light is that the former can penetrate soft tissues for up to 15 mm whereas visible light only has a penetration depth of 2 mm.

Over the last decade, fluorescence-guided interventions have gained interest as a method to assist surgeons in real-time by demarcating cancerous tissues for precise and complete resection. With the aid of fluorescence-guided surgery, the incidence of positive tumor margins can be reduced. Additionally, there is an increasing demand for specific methods to visualize different tissue types as well as healthy tissues that should be preserved. Furthermore, due to the rising use of minimally invasive surgical techniques, such as laparoscopic surgery, palpation

cannot be used to distinguish between malignant and benign tissues and the need for extra tools is pressing.

The non-targeted fluorescent contrast agent Indocyanine Green (ICG) was the first to be registered and become commercially available, albeit for many other indications than oncology. Fluorescence-guided surgery using ICG is feasible but provides only limited added value to standard-of-care tumour resection. Theoretically, tumor-specific ligands, coupled with a fluorescent substance, should more accurately stain tumor cells by binding to their target proteins, thereby increasing the likelihood of complete surgical removal of the tumor. Currently, some translational veterinary trials testing targeted fluorophores are ongoing. Whereas veterinary oncology lags, compared to human medicine, (novel) techniques such as ICG-based fluorescence-guided surgery introduced in human cancer patients is evaluated in dogs. Alternatively, (pre)clinical trials in canine cancer patients with novel targeted contrast agents will reveal translational information to the benefit of men.
At Ghent University, Belgium, exciting translational studies are currently performed, that do not only study fluorescence-guided surgery based on fluorescent intensity after injection of novel targeted near-infrared fluorescent contrast agents but also study the fluorescence lifetime differences in the different tissues.

Suggested reading

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SPONTANEOUS CANCER MODELS IN COMPANION ANIMALS IN SEARCH OF NOVEL THERAPEUTIC ALTERNATIVES IN HUMANS

Thursday 12 September | 14:30 - 16:30 | Amphitheater N. Skalkotas - Room A

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EBVS® European Specialist in Small Animal Surgery, Veterinary Teaching Hospital, Soft Tissue Surgery

The likelihood that a dog develops cancer at some stage in its life is thought to be approximately 1 in 4 dogs whereas almost 1 in 2 dogs over the age of 10 will do so. In cats, the incidence of cancer is less well described, but, also in this species, 1 in 5 animals in an older population is likely to become affected. Fortunately, for more and more of these patients, the cancer diagnosis is no longer an immediate death sentence. As in humans, there is a ceaseless striving to improve diagnostics and therapeutics, which requires a lot of research efforts.

All cancer research initially starts with fundamental research, including the use of patient-derived cell lines. Successful studies will then lead to investigations in laboratory animals. There is a very long history of using rodent models, in particular mice, in cancer research. Rodent cancer models are considered the standard model in cancer research and provide a well-known first basis for testing the toxicity, potency, and therapeutic efficacy of new cancer therapeutics. Although translating those research findings to humans is far from ideal, rodents remain popular cancer models for very many reasons. Since they are used for decennia, most research equipment and research methods are extremely focused on rodents. It is relatively easy and cheap to house and maintain rather large groups of mice and inbred lines offer excellent standardization, allowing for easy study designs and the availability of a matched control group. The fact that human tumor cells are experimentally implanted in mice, most often in tissues that are of different tissue origin than the tumor cells, is one of the major reasons to lead to results that have little predictive potential in human oncology patients. An extremely small minority of successful preclinical rodent trials will ultimately lead to a successful outcome in subsequent human clinical studies.

Initiating clinical trials in humans is a lengthy, expensive and ethically challenging process. It is therefore of utmost importance to try to carefully identify only the truly promising preclinical trials before moving forwards to a trial in human cancer patients.

Companion animals, in particular pet dogs but also cats, have greater access to clinical trials than humans, in which access to clinical trials is only allowed in refractory cases. And, not unimportantly, participation in clinical studies also benefits the tumor-bearing animal itself, by providing an additional treatment option and, consequently, an additional chance of being cured.

For almost 50 years, (pre)clinical trials have been conducted in dogs with spontaneous cancer as they seem excellent candidates in many respects. Dogs share a histologic, biologic, and genetic cancer background that is significantly closer to humans than that of rodents. Besides, the tumors develop in the presence of a functioning immune system, and interaction between the tumor, host, and tumor microenvironment in dogs is comparable to humans. In various

tumors, there are compelling similarities between cancers in dogs and humans. Furthermore, diagnostic and treatment options are available and similar to identical for both dogs and humans, and the progression of cancer in dogs is rapid enough to yield results within a reasonable timeframe. These similarities suggest that results obtained in companion animals should have a very high predictive value and successful (pre)clinical trials in dogs or cats will ultimately lead to a much higher rate of successful outcome in subsequent human clinical studies.

At Ghent University, Belgium, there are exciting and fruitful collaborations and interaction between veterinary and human research initiatives has already led to promising outcomes in various domains, in particular in oncology. Of course, clinical research in dogs and cats with cancer is not only beneficial for the development of new cancer treatments; it also contributes to the research of environmental risk factors, cancer biology and progression, and the identification of cancer-associated genes.

Suggested reading

Abma et al. A single dose of intravenous combretastatin A4-phosphate is reasonably well tolerated and significantly reduces tumour vascularization in canine spontaneous cancers. Vet Comp Oncol 2018 Dec;16(4):467-477. doi: 10.1111/vco.12402.

Do Valle et al. Safety assessment of fluorescently labeled anti-EGFR Nanobodies in healthy dogs. Front Pharmacol 2023 Sep 14:14:1266288. doi: 10.3389/fphar.2023.1266288. eCollection 2023.

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RECONSTRUCTION OF FELINE SKIN WOUNDS. WHAT'S HOT AND WHAT'S NOT

Thursday 12 September | 17:00 - 19:00 | Amphitheater N. Skalkotas – Room A

Lysimachos G. Papazoglou

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Skin wounds in cats are often a result of traumatic injuries, oncologic surgeries, or infectious conditions and their management can be challenging for the small animal surgeon. Feline skin wounds can be closed primarily or by second intention. Contaminated wounds should be lavaged, surgically debrided, dressed, and allowed to heal by second intention until the formation of granulation tissue; then primary closure should be considered.

Topical wound agents have been recently evaluated in full-thickness surgical wounds in experimental cats. Hydrocolloid dressings accelerate healing in feline full-thickness surgical wounds. [1,2] Platelet-rich plasma (PRP) injection promoted quicker granulation tissue formation, and wound contraction, increased total wound healing percentage, and showed better perfusion. [3] In contrast, medical-grade honey or hypericum ointment application did not show to accelerate healing. [4]

Surgical options for primary wound closure in cats included subdermal plexus skin flaps, axial pattern flaps, and free skin grafts. Subdermal plexus flaps including advancement, transposition, rotation, [5] or fold flaps are simple to perform and can be used as a first-line reconstruction for the coverage of acute or chronic wounds. [6] Subdermal plexus flaps used to cover skin wounds in cats had an 83% good or excellent outcome. [6] Seroma formation, dehiscence, and failure were the most commonly recorded complications in cats observed a mean of 1 week post-surgery.

Axial pattern flaps are used to reconstruct bigger wounds in cats. Axial flaps commonly used in cats included caudal superficial epigastric, omocervical, thoracodorsal, caudal auricular, deep circumflex iliac, and lateral caudal flaps. [7,8,9] Thoracodorsal flaps combined with omental pedicle flaps were used for the reconstruction of chronic nonhealing wounds in cats. [7, 10] Axial pattern flaps used to reconstruct skin wounds showed a 58% good or excellent outcome. [7] Flap dehiscence, swelling, necrosis, discharge, infection, and seroma formation were the most common complications observed. [7,8]

Free skin grafts are segments of full-thickness skin that are transferred from one location to another. [11,12] They are commonly used for the reconstruction of wounds in the limbs. [9] Success rates are significantly higher in grafts used in cats (77%) than in dogs (38%). Graft failure and donor site dehiscence are the most common complications reported. [11]

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WHAT TO EXPECT AFTER EXTRAHEPATIC PORTOSYSTEMIC SHUNT SURGERY IN DOGS AND CATS?

Thursday 12 September | 17:00 - 19:00 | Amphitheater N. Skalkotas - Room A

Hilde de Rooster

EBVS® European Specialist in Small Animal Surgery, Veterinary Teaching Hospital, Soft Tissue Surgery

Portosystemic shunts are the most prevalent congenital disorders of the hepatobiliary system in dogs. A portosystemic shunt (PSS) is an abnormal blood vessel that links the portal vein to the systemic circulation, allowing blood from the stomach, intestines, pancreas, and spleen to bypass the liver. An extrahepatic PSS (EHPSS) connects a vessel, typically contributing to the extrahepatic portal vein.

The initial study on managing congenital extrahepatic portosystemic shunt (cEHPSS) in dogs was published in 1976. Medical management focuses on reducing the entry of toxins from the gastrointestinal tract into the systemic circulation. This is achieved through a diet moderate in high-quality proteins and medications that decrease ammonia absorption from the intestines such as lactulose and/or antimicrobials.

Surgical management is considered the best treatment option for dogs with clinical symptoms of congenital PSS since it may offer better QoL and extended survival. However, surgery carries the risk of serious perioperative complications.

Numerous medical, surgical, and interventional strategies have been proposed and implemented. In the past, complete ligation was the preferred treatment for dogs that could endure total cEHPSS occlusion during surgery. This method aimed to achieve maximum attenuation of a cEHPSS in one procedure, guided by portal pressure measurements and visual assessments during occlusion. Recently, gradual occlusion techniques—such as thin film banding, ameroid constrictors, and coil embolization—have gained popularity to reduce the risk of perioperative complications, life-threatening portal hypertension, and to manage the high percentage of dogs that cannot tolerate sudden shunt occlusion. Although the goal of surgical attenuation is the complete closure of the congenital PSS, the shunt may remain partially patent, or multiple acquired portosystemic shunts (MAPSS) may develop.

The success of surgical attenuation of congenital PSS can be evaluated based on clinical outcomes, medical imaging, and liver function tests. Although clinical outcome assessment might seem straightforward and cost-effective, it often does not accurately reflect the presence or absence of persistent shunting. Complete closure of the congenital PSS yields more successful and sustained positive outcomes compared to cases with persistent shunting. Nevertheless, clinical improvement is also reported following partial surgical attenuation, despite persistent shunting.

Recent research aimed to determine whether the plasma amino acid profile and vitazmines normalise in dogs with surgically attenuated extrahepatic PSS (EHPSS) after complete EHPSS closure. This information is important because surgical treatment is not always successful, and, consequently, a number of dogs with congenital PSS need life-long medical treatment. After

successful EHPSS closure, the BCAA-to-AAA ratio and the concentrations of vitamin A, 25-hydroxyvitamin D and folic acid significantly increased; yet the results were still indicative of moderate to severe hepatic dysfunction.

Suggested reading

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Devriendt et al. Persistent hypercobalaminemia three months after successful gradual attenuation of extrahepatic shunts in dogs: a prospective cohort study. BMC Vet Res 2022 Jan 6;18(1):18 doi: 10.1186/s12917-021-03123-1.

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Serrano et al. Treatment of congenital extrahepatic portosystemic shunts in dogs: A systematic review and meta-analysis. J Vet Intern Med 2019 Sep;33(5):1865-1879. doi: 10.1111/jvim.15607.

SURGICAL TREATMENT OF SOFT TISSUE SARCOMAS OF THE SKIN AND SUBCUTANEOUS TISSUES IN DOGS

Thursday 12 September | 17:00 - 19:00 | Amphitheater N. Skalkotas - Room A

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Soft tissue sarcomas (STS) are a histologically heterogeneous group of mesenchymal tumours. STS may arise from any anatomical site. In dogs they usually develop in a subcutaneous location and are very common accounting for 9 - 15% of all cutaneous or subcutaneous tumours.[1,2]
STS have been grouped based on similar histological features and biological behaviour that are common to all of them and include: fibrosarcoma, perivascular wall tumours (previously called haemangiopericytoma), liposarcoma, infiltrative lipoma, malignant fibrous histiocytoma, mesenchymoma, myxosarcoma, non-plexus derived peripheral nerve sheath tumours (previously called neurofibrosarcoma or schwannoma) and undifferentiated sarcoma.[1,3-4]
Medium – to large-breed and middle-aged to older dogs are more commonly affected. Median age at diagnosis is reported between 10 and 11 years.[1-4]
Dogs with STS are usually presented with a palpable, firm, subcutaneous mass free or firmly attached to the underlying tissues although, sometimes they can be soft and lobulated.[1,4-6] The mass may be present for many months although, some large masses may arise and grow quickly and then remain in a stable size. They are usually slowly growing. Large masses may become ulcerated. In most cases no other clinical signs are detected.[1-4,6]
STS are most commonly found on the limbs 60%, the trunk 35% and the head 5%.[1,4]
Diagnosis is supported by cytology on fine needle aspirated samples, and it is confirmed by histopathologic examination of tissue samples.[1-2] Biopsy methods include incisional biopsies, punches and needle core instruments.[1,5] When Tru-cut needles or trephines are used multiple samples (minimum of six cores) should be obtained from different locations. To avoid seeding of neoplastic cells during biopsy the selected site is one that can be completely removed when tumour excision is performed. Fascial planes around the circumference of the tumour should also not be disrupted.
Diagnostic imaging is used for staging and surgical planning. Three-view thoracic radiographs or computed tomography (CT) and abdominal ultrasound are employed to check for pulmonary metastasis.[1] CT provides the surgeon valuable information for surgical planning as it denotes whether the STS is anatomically well confined or has infiltrated deeper fascial planes.
Treatment options for STS include surgery alone, surgery followed with radiotherapy, and surgery followed by chemotherapy. Adjuvant therapies may be employed either before (neoadjuvant) or after (adjuvant) surgery.[5-7]
Surgical excision is the treatment of choice for most STS. It provides local control of the disease. First surgery has better possibilities of cure. It is important to recognize that resection of STS requires knowing the surgical limitations and the regional anatomy, been familiar with the disease process and tumour biology and have the necessary surgical skills.
STS are enclosed by a pseudocapsule with poorly defined margins. Neoplastic cells can penetrate this pseudocapsule thus, surgical resection that passes through this plane can leave tumour cells, resulting in recurrence. Therefore, wide or radical excision is proposed for STS.
Wide excision with surgical margins of 2 to 3 cm and one deep fascial plane should be considered an optimal goal when surgery is the sole treatment.[4-5] Nevertheless, recent studies report good outcomes with narrow-margin excision for low grade STS.[3] Defects following wide excision can be closed primarily by simple apposition or reconstructed by using a local or an

axial pattern flap. The entire specimen should be submitted for histologic assessment with the margins marked to aid the pathologist in determining completeness of excision.
Tumours located on the distal limb present challenges because of the potential for compromised limb function, lack of deep fascial barriers and the need for reconstruction of the resultant defect.[6]
Revision surgery with re-excision, after inadequate resection of STS, has an increased difficulty, especially when tumours are located on the limbs. Nevertheless, it is reported that a favourable prognosis can be achieved without the need for radiation therapy or amputation.[8] Recurrence of STS after surgical resection is reported 1–3 years after surgery. Thus, a follow-up of at least 2 years is recommended.
Histologically STS are characterized as low (grade I), intermediate (grade II) and high (grade III) based on the differentiation score (well-differentiated, poorly differentiated, undifferentiated), the mitotic score (1-3) and the tumour necrosis score (0-2). Higher grades are associated with higher rates of local recurrence, distant metastasis and shorter disease-free intervals.[2] They metastasize through hematogenous route to the lungs and rarely to the regional lymph nodes.[2,5]
Prognostic factors for STS include the histological characteristics (i.e. grade, histologic type, mitotic count etc.), physical characteristics (i.e. size >5-cm, location, palpable features), as well as completeness of the excision margins, patient age and co-morbidities. Rates of recurrence increase with grade and metastasis may develop in 1.7 - 41% of cases.[2,3,4,6,9,10]
Results of many studies indicate that STS biology determines the outcome rather than the extent of resection.[3-5]

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OVERVIEW OF ZOONOTIC DISEASES OF COMPANION ANIMALS

Thursday 12 September | 08:30 - 10:30 | MC 3 - Room B

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Introduction
Zoonotic diseases are defined as being common to, shared by, or naturally transmitted between humans and other vertebrate animals. Humans are infected with zoonotic agents from direct contact with an infected animal, contact via contaminated food or water, from shared vectors, and from the shared environment.

Zoonoses can classified as either an anthropozoonosis or a zooanthroponosis; the former maintained in nature by non-human animals that is transmissible to humans such as rabies and brucellosis; whereas the latter maintained by humans that can also infect animals (reverse zoonosis) such as protozoal infections, tuberculosis in cattle, and some instances of methicillin-resistant *Staphylococcus aureus* (MRSA).

Zoonotic diseases can generally be more prevalent or more severe in immune-compromised individuals, people with HIV/AIDS, very old or very young, people treated for immune-mediated disease or organ transplant recipients ; and those on chemotherapy.

Incidence
The full incidence of companion animal zoonoses is not well understood as few diseases are reportable, resulting in sporadic data that is biased towards unusual populations, outbreaks or case reports. An important exception is rabies as it is a well-tracked disease, in terms of the incidence of infection, identification of sources and complete data availability.

The overall burden of companion animal zoonoses is hard to discern as it can involve various factors such as morbidity, mortality, economic impacts of disease, economic impacts of disease prevention and social, psychological and emotional impacts. The spectrum of zoonotic diseases varies from rare and devastating (rabies), common but with potential sources beyond companion animals (campylobacteriosis); or common and problematic but of limited direct health impact (dermatophytosis). Zoonotic diseases can also be regional (plague, coccidioidomycosis, blastomycosis, brucellosis).

Zoonotic Disease Risk
All animals harbour potentially multiple zoonotic pathogens; however, the risk of zoonotic disease risk is highly variable between animal species, individual animals, households and circumstances. Animal, human and exposure factors all play major roles.

As there is increased awareness of zoonotic risks by high-risk groups, veterinarians may more often be asked about risk and prevention. They may be at increased risk of disease from pathogens that rarely cause disease in immunocompetent individuals (*Capnocytophaga canimorsus*) or at risk of more severe disease than typically encountered by otherwise healthy individuals (salmonellosis). Unfortunately "immunocompromised individuals" do not belong to one clear and distinct group, as the degree of compromise can be highly variable between individuals, as well as within the same individual over time. Nonetheless, people with suboptimal

immune systems have some elevated degree of infectious disease risk compared to the general population but may also have the greatest benefits from pet interaction.

Contracting Zoonotic Diseases

Direct contact with animal faeces (enteric zoonoses), respiratory secretions, urogenital secretions, or infected skin and exudates, as well as bites and scratches can all result in human infections. Some zoonotic agents are transmitted between animals and people by shared vectors such as fleas, ticks and mosquitoes.

Zoonotic agents are often contracted via the faecal-oral route associated with poor hand hygiene and/or inadequate personal protective equipment. Appropriate hand-washing before and after handling animals or their associated items is essential to reduce the risk of transmission. Transmission can also occur via contact with wounds or mucous membranes, or inhalation. Humans that are immune compromised, due to chemotherapy, chronic illness, or extremes in age, are at increased risk for contracting zoonoses. Finally, a risk for zoonotic disease that each veterinarian and owner face is the increased exposure to animals.

Enteric Zoonoses

There are multiple infectious agents of the gastrointestinal tract that potentially can be shared between animals and humans. A large number of enteric zoonotic agents are infectious when passed with faeces (*Campylobacter* spp., *Salmonella* spp., *Giardia* spp., *Cryptosporidium* spp. and others) and thus direct contact with infected animals can result in human infections. A more important route of infection is, however, from the
ingestion of the infectious agent in contaminated food, water, or other environmental sources. *Giardia* spp., *Cryptosporidium* spp., *Toxocara* spp., *Ancylostoma* spp and *Toxoplasma gondii* all require a period outside the host prior to becoming infectious.

While on the zoonoses list, *Giardia* and *Cryptosporidium* spp. of dogs and cats are rarely detected in people and human strains have not been associated with illness in pets. Prevalence rates for enteric zoonoses have been reported multiple studies of dogs and cats and generally are generally greater in those with diarrhoea. These findings emphasize that diagnostic workups for enteric infections are indicated due to potential human health risks. The minimal diagnostic plan to assess for enteric zoonoses in pets with diarrhoea includes a faecal flotation, *Giardia* spp., screening procedure, and faecal wet mount. Faecal culture should be considered if *Salmonella* spp. or *Campylobacter* spp. are on the list of differential diagnoses. Dogs and cats with normal faeces are not considered human health risks.

Bite, Scratch, or Exudate Exposure Zoonoses

People bitten by animals can be common. In the USA approximately 300,000 emergency room visits per year are made by people bitten by animals has been reported. However, the precise number of bite wounds in the is difficult to determine because many animal bites are never reported. In generally dog and cat bites account for the majority of bite wounds encountered in the emergency room. In one publication, the average annual incidence of dog bites was highest in children aged < 10 years and males, while that of cat bites was highest in adults aged ≥ 80 years and females. Bites were more likely to occur in rural settings, in private residences, and during the summer. Both dog and cat bite injuries were more likely to occur to upper limbs. Bacteria were isolated from 3% of dog bite injuries and 21.5% of cat bite injuries at initial presentation.

Most of the aerobic and anaerobic bacteria associated with bite or scratch wounds only cause local infection in immunocompetent individuals. However, 28–80% of cat bites become infected and severe sequelae including meningitis, endocarditis, septic arthritis, osteoarthritis, and septic shock can occur.

Immunodeficient people or people exposed to *Pasteurella* spp., *Capnocytophaga canimorsus* or *C. cynodegmi* more consistently develop systemic clinical illness. Splenectomised people are at increased risk of developing bacteraemia. *Mycoplasma* spp. and L-form bacterial infections of people has been associated secondary to dog or cat bites.

Although *Bartonella* spp., *Yersinia pestis*, and *Francisella tularensis* infections of people can be associated with bites and scratches these agents are also vector-associated zoonoses.

Of the many fungal agents that infect both humans and animals, only *Sporothrix* spp., and the dermatophytes have been shown to infect humans upon direct exposure. *Histoplasma*, *Blastomyces*, *Coccidioides*, *Aspergillus* and *Cryptococcus* infections of people and animals can occur in the same household, but infection of people generally results from a common environmental exposure rather than by direct contact with an infected animal.

Rabies can be considered the only significant small animal viral zoonosis worldwide. Pseudorabies is a herpesvirus that infects pigs; dogs and humans can develop self-limiting pruritic skin disease following exposure. Feline retroviruses are not zoonotic.

Respiratory and Ocular Zoonoses

Bordetella bronchiseptica and *Chlamydia felis* cause mild respiratory disease and *C. felis* has been associated with conjunctivitis in people. Most people with *Bordetella* infections are infected by *B. pertussis* but some immunocompromised people develop infection by *B. bronchiseptica*. People are the principal natural hosts for *Streptococcus* group A bacteria, *S. pyogenes* and *S. pneumoniae*, which cause "strep throat" in people. Dogs or cats in close contact with infected humans on rarely develop transient, subclinical colonization of pharyngeal tissues and so theoretically can transmit the infection to other humans. *Yersinia pestis* and *F. tularensis* can be transmitted from cats or dogs to people in respiratory secretions.

Genital and Urinary Tract Zoonoses

Leptospira spp. (dogs more than cats), *Brucella canis* (dogs), and *Coxiella burnetii* (cats more than dogs) are the most common zoonotic agents in this group. Whether *Leptospira* spp. of cats are associated with illness in people has not been studied extensively. *Coxiella burnetii* is a rickettsial agent found throughout the world.

Many ticks, including *Rhipicephalus sanguineus*, are naturally infected with *C. burnetii* and so this agent is also a shared vector zoonoses. It is most commonly associated with respiratory disease in infected people that come in contact by inhaling the organism that is shed in high numbers in some cats during parturition.

Vector-borne Zoonoses

Examples of vector borne zoonoses would be *Rickettsia rickettsii* (ticks), *Ehrlichia* spp. (ticks), *Borrelia burgdorferi* (ticks), *Rickettsia felis* (fleas), *Bartonella* spp. (fleas, ticks), *Anaplasma phagocytophilum* (ticks), and *Dirofilaria immitis* and West Nile virus (mosquitoes). Either the animal brings the vector of the organism into the environment or the person is in the same environment as the vector, both of which will result in human exposure.

Raw Diets and Zoonoses

The main concern with feeding raw diets is that there may be a high risk of pets shedding of *Salmonella* and multidrug-resistant *E. coli*. Raw animal product based pet treats such as rawhides and pig ears have been implicated as causes of outbreaks of salmonellosis in people. Raw meat or eggs should not be fed to pets of immunocompromised individuals because of the risk of exposure to pathogens from faeces (or faecal-contaminated surfaces), food bowls, water bowls or from the mouth of the animal after eating.

Conclusion

While veterinarians rightly must refrain from direct involvement in human health issues, they must recognize the potential role of zoonotic diseases and their role in the management of such diseases. Increased awareness of zoonotic diseases, infection control and increased communication between human and veterinary medicine in the One Health approach should be the way forward.

TOXOPLASMOSIS

Thursday 12 September | 08:30 - 10:30 | MC 3 - Room B

M. Bisia, A. Ligdas, P. Ligda, B. Venardou, G. Balatsos, V. Karras, E. Zavitsanou, N. Tegos, **S. Sotiraki**, A. Michaelakis, E. Patsoula

Dirofilaria spp a vector-borne parasite transmitted by mosquitoes, poses significant threat to both animal and human health. Our study aimed to expore the transmission dynamics of *Dirofilaria* spp in the Attica region, where clinical observations suggested that the parasite was not circulating. Over a two-year period, we conducted comprehensive surveillance targeting both mosquito vectors and canine populations, to assess the risk of *Dirofilaria* spp transmission in the region.

During the first study year, blood fed *Culex pipiens* mosquitoes were collected from an already established and operating extensive mosquito trap network across Attica. Poolled mosquito samples were molecularly analysed for the presence and genotyping of parasites' DNA. In addition, serological analyses (i.e., ELISA) were performed on samples from stray dogs of this region, for the presence of parasites' antibodies. This initial phase provided crucial insights into the prevalence of *Dirofilaria* infection in both vector and canine populations. Thus, in the subsequent year, our study focused to specific locations where positive mosquito or/and canine samples were identified, to gain a deeper understanding of local transmission patterns. For this, blood fed mosquitoes collected all year and serum samples from domestic dogs were analysed as previously described.

Our findings revealed a low prevalence (10%) of Dirofilaria positive mosquitoes during the first year, which slightly decreased to 4.6% in the second year. Similarly, serological analysis of stray dogs showed very low prevalence of circulating antibodies against *Dirofilaria.* For the domestic dogs, only one was found positive.

Although these results suggest a minor risk of *Dirofilaria* transmission in the study area, our study underscores the importance of ongoing surveillance and vigilance. Climate change and other environmental factors may alter the dynamics of mosquito-borne diseases, potentially leading to a *Dirofilaria* transmission emergence in this region in the future. Therefore, continued monitoring and preventive measures are essential to safeguard both animal and human health in the Attica region.

LEPTOSPIROSIS

Thursday 12 September | 08:30 - 10:30 | MC 3 - Room B

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Introduction
Leptospirosis is a bacterial zoonotic disease of worldwide significance in many animals and humans caused by infection with antigenically distinct serovars of *Leptospira interrogans sensu lato*. There is some confusion about the classification of leptospires as the serogrouping used in the past overlaps with newer classifications based on genetic methodologies. In addition, classification of leptospirosis has moved from predominantly serovar- based classification to that based on genetic typing (genotype-based classification).

Aetiology
Leptospira organisms are thin, flexible, filamentous bacteria made up of fine spirals with hook-shaped ends. More than 200 different serovars have been identified in the *Leptospira interrogans* complex. Each serovar has a primary host that maintains the organism and contributes to its dissemination in the environment. Although all mammals are susceptible to infection, clinical signs are most severe with non-host adapted serovars.

There are over 200 pathogenic serovars, which are grouped into antigenically related serogroups. Serovars known to infect and cause disease in dogs include *canicola, icterohaemorrhagiae, grippotyphosa, portlandvere, copenhageni, hebdomadis, dadas, pomona, ballum, bratislava, autumnalis, bataviae, australis,* and *hardjo*; others are also being recognized. In addition, classification of leptospires is gradually moving from predominantly serovar-based classification to that based on genetic typing (genotype-based classification).

Each serovar (and more accurately, each genotype) is adapted to one or more mammalian host species (maintenance hosts). Other hosts act as incidental hosts. Disease in incidental hosts tends to be more severe and the duration of shedding is generally shorter. Maintenance hosts include dogs (*canicola*); rats (*icterohaemorrhagiae*); small wildlife mammalian species such as voles, skunks, and raccoons (*grippotyphosa*); cattle and pigs (*pomona*); pigs (*bratislava*); cattle (*hardjo*); and mice (*ballum*). The separation between maintenance and incidental host may, however, not be clearly defined, as factors such as host immune response and degree of exposure may influence whether disease or subclinical infection occur.

Pathogenesis
Leptospires can penetrate mucosa or broken skin and can be directly transmitted by contact through urine, venereal routes, placenta, bites, or ingestion of infected tissues. Shedding by infected animals usually occurs via urine. The more common way of transmission is indirect transmission, which occurs through exposure of susceptible animals to a contaminated environment (e.g., soil, food, or bedding). Water contact is the most common means of spread, and habitats with stagnant or slow-moving, warm water favour organism survival.

Once in the host, leptospires begin to multiply entering the circulatory system and organs such as kidneys, liver, spleen, central nervous system, eyes, and genital tract. Organ damage is

caused by the replicating leptospires as well as the host's inflammatory response. The extent of damage depends on the virulence of the leptospires and host susceptibility. As serum antibodies increase, the organism is cleared from most tissues, except for the kidneys. Renal colonization occurs in most infected animals, and the organism usually persists in renal tubular epithelial cells for years. Recovered dogs can excrete organisms in their urine intermittently for up to 4 years after infection.

Clinical Signs

The severity of clinical signs depends on the age and immune competence of the animal, serovar involved, and the virulence and quantity of the acquired bacteria. Dogs under 6 months of age are more susceptible and often show marked hepatic dysfunction.

The majority of leptospiral infections in dogs are sub-clinical. Per-acute leptospiral infections can occur and are characterized by massive leptospiraemia, resulting in shock and often death with few clinical signs. Less severe infections are characterized by fever, anorexia, vomiting, dehydration, and polyuria. Other clinical signs include meningitis, uveitis, abortion, and infertility. Pulmonary changes are associated with pulmonary haemorrhage, most likely due to endothelial damage and vasculitis.

Acute renal failure is common as renal colonisation occurs in most infected animals because the organism replicates and persists in renal tubular epithelial cells, even in the presence of neutralizing antibodies. Renal function in some dogs that survive acute infections may return to normal within several weeks or may develop chronic compensated polyuric renal failure.

Leptospirosis can cause profound hepatic dysfunction without major histological changes. The degree of icterus in both canine and human leptospirosis usually corresponds to the severity of hepatic necrosis. In dogs, icterus can also be associated with haemolysis. Chronic active hepatitis and hepatic fibrosis have occasionally been demonstrated as sequelae to serovar *grippotyphosa* infection in dogs. The initial hepato-cellular injury and the persistence of the organism in the liver results in altered hepatic circulation and immunologic disturbances that perpetuate the chronic inflammatory response. This process may result in extensive hepatic fibrosis, cirrhosis, and finally hepatic failure.

Disseminated intravascular coagulation may occur rapidly and result in acute endothelial injury and haemorrhagic manifestations. Leptospira lipopolysaccharides stimulate neutrophil adherence and platelet activation, which may be involved in inflammatory and coagulatory abnormalities.

Clinical Pathology

On urine analysis, isosthenuria, bilirubinuria, proteinuria, sometimes glucosuria, and increased numbers of granular casts, leukocytes, and erythrocytes in the sediment may be evident.

Laboratory abnormalities include leukocytosis, thrombocytopenia, azotaemia, electrolyte disturbances, bilirubinaemia, hypoalbuminaemia, and mild-moderate elevated liver enzyme activity. Coagulation parameters may be altered in severely affected animals. Although hyperkalemia has been reported, normokalemia or hypokalemia are more common because of the effect of Leptospira on the renal medullary ascending tubule electrolyte cotransporter mechanism.

Diagnostic Imaging

Thoracic radiography may reveal a focal or diffuse interstitial to broncho-interstitial pattern. An alveolar pattern may represent pulmonary haemorrhage. Occasionally mild pleural effusion is also evident.

Abdominal radiography may show hepatomegaly, splenomegaly, renomegaly and/or ascites.

Hyperechoic renal cortices and mild pyelectasia can be evident on abdominal ultrasound.

Diagnosis

The diagnosis of leptospirosis requires a high clinical suspicion for the disease based on knowledge of the range of clinical presentations that suggest leptospirosis Establishment of a diagnosis is important, as animals can serve as reservoirs and thus pose potential zoonotic risks. The diagnosis is based on a combination of clinical signs, clinical pathology changes, and use of diagnostic tests such as PCR, microscopic agglutination test (MAT), and in-clinic serologic assays.

Serology

Serological tests using MAT, immunofluorescent assays, or enzyme-linked immunosorbent assay (ELISA). In-clinic serologic assays that detect antibodies (IgG/IgM, SNAP Lepto, IDEXX Laboratories and IgM, WITNESS Lepto, Zoetis) are available. With the MAT test, titres are provided for several different serovars to increase the chance of antibody detection. Studies in humans and dogs have shown that the serovar with the highest titre can vary over time and that paradoxical cross-reactivity to multiple serovars occurs after exposure to a single serovar. Thus, the MAT test does not reliably predict the infecting serovar, and therefore should not be used for this purpose.

Titres with any serologic test may be negative in the first week of illness because of the short incubation period and delay in antibody production. Low positive or negative titres after at least one week of illness suggest leptospirosis is not present. Overdiagnosis results from misinterpretation of positive serologic test results. Positive titres early in the course of an illness may reflect residual post-vaccination titres or prior subclinical infection and are not diagnostic for the disease. Demonstration of a 4-fold rise in titre is required over a 1–2-week interval to demonstrate true infection. Post-vaccinal titres against *icterohaemorrhagiae, canicola, grippotyphosa* and *pomona* occasionally rise as high as 1:6400 for a few months after vaccination, and these will interfere with interpretation. Serology results can also vary dramatically between laboratories.

Direct visualization

Visualisation of leptospires can be done in fresh urine by dark-field microscopy, tissue sections, air-dried smears, and immunofluorescence and immunohistochemical staining techniques.

Culture

Leptospira can be cultured from blood, urine, or CSF using special liquid, semisolid, or solid culture media and as they are fastidious organisms sampling should always be done prior to any antimicrobial therapy. Culture, however, is difficult because of the fastidious growth requirements and the need for specialized media and darkfield microscopy. Recent advancements in methods that accelerate growth of leptospires may overcome these hurdles in the future.

PCR

PCR not only allows a diagnosis but also identification of specific serovars. PCR can be used to detect leptospires in blood, CSF, aqueous humor, and urine. PCR assays are best performed on

blood and urine concurrently because urinary shedding begins 10 days after the onset of infection.

Treatment

Antimicrobial therapy is essential to terminate the bacteraemia with treatment being divided into two stages: the first stage is to inhibit multiplication of the organism and reduce fatal complications of infection, whereas the second stage is to eliminate the carrier state.

Penicillin (such as ampicillin or amoxicillin) and its derivatives are the antibiotics of choice for terminating leptospiraemia. These drugs prevent shedding and transmission of the organism within 24 hours of therapy. They do not, however, clear renal infections or eliminate the carrier state and chronic shedding.

Drugs that are effective in eliminating the carrier state include doxycycline, tetracyclines, aminoglycosides, or the newer erythromycin derivatives. In animals with only mild clinical signs, doxycycline can be used for both initial and elimination therapy.

Supportive therapy depends on the severity of the clinical signs, whether renal or hepatic dysfunction is present, and presence of other complicating factors.

Prevention

Leptospira vaccines are generally safe and efficacious, and studies suggest they provide a minimum of a 1-year duration of immunity with vaccination reducing the prevalence of highly virulent forms of illness. Although it was prevalent when bivalent (*Canicola* and *Icterohaemorrhagiae*) vaccines were in widespread use, vaccine failure appears to be uncommon with the current quadrivalent vaccines (*Canicola, icterohaemorrhagiae, grippotyphosa*, and *pomona*. Reaction rates of newer vaccines appear to be approaching those of distemper-hepatitis-parvovirus vaccines, even in small breed dogs

As wild animal reservoirs and sub-clinically affected domestic animals continue to harbour and shed organisms, control of rodents in kennels, maintenance of environmental conditions to discourage bacterial survival, and isolation of infected animals are important steps in preventing the spread of disease. Minimizing access to potential maintenance hosts may also help to prevent infection. As complete control of shedding by wild animal reservoirs is impossible, vaccination of all dogs in endemic areas is essential.

Leptospirosis in Cats

The prevalence of clinical illness is low in cats, despite the presence of leptospiral antibodies in the feline population and the exposure of cats to leptospires excreted by wildlife. Serovars *canicola*, *grippotyphosa*, and *pomona* have been isolated from cats. Outdoor cats have the highest antibody titres and transmission from rodents is most likely. Although cats develop antibodies after exposure, they appear to be less susceptible than dogs to both spontaneous and experimental infection. Clinical signs are usually mild or not apparent, despite the presence of leptospiraemia and leptospiuria and histological evidence of renal and hepatic inflammation.

Public Health Considerations

Leptospirosis remains an important zoonosis, although most documented human leptospirosis results from exposure to rodents or other reservoir hosts like cattle, or recreational activities that involve water, rather than contact with dogs.

Urine from infected dogs can cause disease in humans when it encounters mucosal surfaces or a break in the epidermal barrier. Latex gloves are necessary when urine or urine-contaminated items are handled, and face masks and goggles should be worn when contaminated kennel areas are hosed down. Urine-contaminated areas should be cleaned with dry paper first to avoid dilution of urine, then washed with bleach or iodine-based disinfectants. All dogs known to be or suspected of shedding should be treated with doxycycline.

TREATING DOGS AGAINST ECHINOCOCCUS GRANULOSUS: INNOVATIVE TOOLS FOR INTEGRATED CONTROL

Thursday 12 September | 11:00 - 13:00 | MC 3 - Room B

Laura Rinaldi[1], Antonio Bosco[1], Paola Pepe[1], Elena Ciccone[1], Martina Nocerino[1], Nicola Lattero[1], Maria Paola Maurelli[1]

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Cystic echinococcosis (CE), caused by the larval stage of the cestode Echinococcus granulosus, is one of the most widespread zoonoses in Mediterranean countries. CE is now included in the list of the 20 neglected tropical diseases (NTDs) for which control measures are recommended by the World Health Organization. The life cycle of E. granulosus involves a variety of wild and domestic ungulates as intermediate hosts as well as canids as definitive hosts. In pastoral farming of the Mediterranean areas (e.g. Greece and Italy) the disease is still highly prevalent in animals and humans, and primarily affects sheep and dogs. Control programmes against E. granulosus are considered long-term public health measures that require an integrated approach, including various actions for animals and humans in terms of surveillance, prevention, treatment and education. In this framework, new innovative actions and research projects (i.e. PRIMA Echino-Safe-Med) to control CE have been implemented in the Mediterranean region to improve surveillance and control strategies against E. granulosus in definitive and intermediate hosts. As non-owned dogs play a key role in the maintenance of CE transmission, baiting with praziquantel currently appears to be the most effective method to limit the transmission of CE and an important aspect in the control of this parasitic disease. In endemic areas, traditional measures to control CE are still ineffective, as surveillance and treatment strategies do not reach inaccessible grazing areas (accessible to stray canids) and are usually designed for large geographical areas, without considering that the prevalence of CE can vary greatly in different locations in the same region. Geographic information systems (GIS) show great potential to support control strategies against CE in highly endemic areas. In addition, the use of GPS devices makes it possible to track the movements of animals (sheep and dogs) and identify the most frequented locations within grazing areas. Other innovative devices include drones and camera traps for the capillary and automatic distribution of baits (laced with praziquantel) to stray dogs in remote areas.

DIROFILARIA IMMITIS AND DIROFILARIA REPENS: INSIGHTS INTO EPIDEMIOLOGY, DIAGNOSIS AND ZOONOTIC RISK

Thursday 12 September | 11:00 - 13:00 | MC 3 - Room B

Laura Rinaldi[1], Maria Paola Maurelli[1], Antonio Bosco[1], Ortensia Montella[1], Lavinia Ciuca[1]

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Heartworm disease and subcutaneous dirofilariosis caused by Dirofilaria immitis and D. repens (Spirurida, Onchocercidae), respectively, are important vector-borne diseases, especially for dogs and cats. In addition, zoonotic infections, mostly due to D. repens, are a major public health problem. The epidemiological situation of canine dirofilariosis based on data reported from recent studies has shown that the prevalence of both D. immitis and D. repens is increasing in Europe and especially in the Mediterranean areas (e.g. Greece and Italy). However, changes in the prevalence of both D. immitis and D. repens are continuously reported, identifying non-endemic areas with increased prevalence and previously endemic/hyper-endemic areas with decreasing prevalence.There are many factors related to vectors (presence of competent mosquito species) and hosts (compliance with chemoprophylaxis by owners, presence of wild canids as reservoirs) that may influence the prevalence of Dirofilaria infections in the Mediterranean countries. The correct management of these infections should be based on an effective and correct approach to diagnosis and up-to-date control, as well as practical prophylactic measures to protect animals and humans. Advances in epidemiology (using geospatial tools and modelling), diagnosis (improving traditional and validating innovative techniques) and control will be discussed to protect animals and humans from D. immitis and D. repens in a One Health perspective

FELINE HEPATOZOONOSIS – FROM SUBCLINICAL INFECTION TO SEVERE DISEASE

Thursday 12 September | 11:00 - 13:00 | MC 3 - Room B

Gad Baneth
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Introduction

Hepatozoonosis is a vector-borne infection caused by apicomplexan protozoa (Baneth, 2011). *Hepatozoon* species infect a wide variety of amphibians, reptiles, birds, marsupials and mammals. In contrast to most tick-borne pathogens which are transmitted via the tick salivary glands, *Hepatozoon* species infect vertebrates by ingestion of arthropod hosts containing infective sporozoites. Two different species of *Hepatozoon* infect dogs and three species are known to infect cats (Baneth and Allen, 2022).

Feline hepatozoonosis

Hepatozoonosis of domestic cats has been reported from several countries in Asia, Europe, Africa and America (Baneth, 2011; Baneth and Allen, 2022). Most reported cases of feline hepatozoonosis were caused by *Hepatozoon felis*, However, *Hepatozoon silvestris*, originally reported from wild cats (*Felis silvestris*), has also been reported to be associated with severe disease in some cases of domestic cats in Europe, and it has been shown that *H. canis* also infects cats, but with no apparent clinical manifestations described so far (Baneth et al., 2013; Giannelli et al., 2017). The vectors of all feline *Hepatozoon* spp. are currently unknown. Transplacental transmission from the queen to its offspring during pregnancy and also transmission by preying on other possible mammal hosts have been suspected as modes of transmission for *H. felis* (Baneth et al., 2013).

Hepatozoon felis and *H. silvestris* infections are associated with infection of muscle tissue and their meronts have been identified in the myocardium, skeletal muscles and intestine of cats with hepatozoonosis (Baneth et al., 2013; Kegler et al., 2018, Simonato et al., 2022). Elevated activities of the muscle enzyme creatinine kinase were reported in cats with hepatozoonosis in a retrospective study of this disease. The level of parasitaemia is usually low in cats with less than 1% of the neutrophils containing gamonts (Baneth et al., 1998).

Epidemiology

In a study that evaluated the occurrence of *Hepatozoon* spp. in domestic cats from insular and continental Greece (Crete, Mykonos, Skopelos, Attica and Thessaloniki) by light microscopy and PCR, of 282 cats examined, 72 (25.5 %) were positive by PCR for *Hepatozoon* spp. and of them, 9 (12.5 %) harbored *H. felis* gamonts detected in the blood by blood smear microscopic examination. DNA sequences obtained from 35 cats were all positive for *H. felis*. (Morelli et al., 2021)

In another study of feline hepatozoonosis in the Mediterranean region, blood and serum samples from 600 cats from France, Portugal, Greece, Spain, Italy and Israel were collected as well as data on the tested cats including: age, sex, breed, housing conditions, geographical origin, clinical signs and laboratory blood test parameters (Carbonara et al., 2023). Blood

samples were tested for *Hepatozoon* spp by conventional PCR targeting the 18S rRNA gene. The overall prevalence of *Hepatozoon* spp. infection was 14.5%. Prevalence was significantly higher in cats from Greece (30%) and Portugal (23%), followed by Spain (15%), Israel (15%) and France (4%). Cats from Italy were negative. *Hepatozoon felis* was identified in 86 cats and *H. silvestris* was detected in one shelter cat from Portugal (Carbonara et al., 2023).

Treatment of feline hepatozoonosis

No controlled experiments have been published on the treatment of feline hepatozoonosis and the drugs used in some published cases of *Hepatozoon* spp. infection were used off-label. Imidocarb dipropionate at 6 mg/kg injected subcutaneously twice with an interval of 14 days in combination with doxycycline at 5 mg/kg orally for four weeks has been reported to be effective in a cat that recovered from *H. felis* infection (Basso et al., 2019). Another cat which recovered clinically was treated with primaquine, an anti-malarial drug, at 2 mg/kg orally once, and oxytetracycline at 50 mg/kg every 12 hours for 7 days (Van Amstel, 1979).

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GETTING THE BEST OUT OF THE BIOCHEMICAL PANEL IN RENAL PATIENTS

Thursday 12 September | 14:30 - 16:30 | MC 3 - Room B

Prof. Habil. Dr. Alexandru Bogdan VIȚĂLARU

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Definition of CKD: presence of structural or functional abnormalities of one or both kidneys for 3 months or longer.

Blood markers	Urine markers
Elevated BUN	Impaired urine concentrating ability
Elevated serum creatinine	Proteinuria
Hyperphosphatemia	Cylindruria
Hyperkalemia or hypokalemia	Renal hematuria
Metabolic acidosis	Inappropriate urine pH level
Renal hypoalbuminemia	Inappropriate glucosuria
Imaging markers (e.g., size, shape, number)	Cystinuria

Renal disease is a prevalent condition in veterinary patients, particularly in older animals. Accurate and comprehensive diagnosis and management of renal disease rely heavily on the biochemical panel, a fundamental diagnostic tool in veterinary medicine. This presentation explores the significance of maximizing the utility of the biochemical panel in renal patients to ensure effective diagnosis, monitoring, and treatment.

Comprehensive Diagnosis

The biochemical panel provides a snapshot of the patient's metabolic status, which is crucial for diagnosing renal disease. Key parameters include blood urea nitrogen (BUN), creatinine, and electrolyte levels. Elevated BUN and creatinine levels are primary indicators of renal insufficiency, reflecting the kidneys' reduced ability to filter waste products. Electrolyte imbalances, such as hyperkalemia or hypokalemia, often accompany renal dysfunction and can have serious consequences if not promptly identified and corrected.

By thoroughly interpreting these values, veterinarians can determine the severity of the renal disease and distinguish it from other conditions with similar clinical signs. For instance, dehydration can also cause elevated BUN and creatinine levels. Therefore, understanding the context of the biochemical panel results is essential for accurate diagnosis.

Creatinine and urea limitations:

They only increase when 75% of the nephrons are compromised!
They are also impacted by other non-renal factors!
More useful Biochemistry tests are SDMA, NGAL snd FSF23.
IRIS has an useful algorithm for AKI.

Stage	Blood creatinine* µmol/l mg/dl SDMA# µg/dl		Comments
	Dogs	Cats	
1	<125 <1.4 <18	<140 <1.6 <18	Normal blood creatinine or normal or mild increase blood SDMA. Some other renal abnormality present (such as, inadequate urinary concentrating ability without identifiable non-renal cause (in cats not dogs), abnormal renal palpation or renal imaging findings, proteinuria of renal origin, abnormal renal biopsy results, increasing blood creatinine or SDMA concentrations in samples collected serially). Persistently elevated blood SDMA concentration (>14 µg/dl) may be used to diagnose early CKD
2	125 –250 1.4 – 2.8 18 - 35	140 – 250 1.6 – 2.8 18 - 25	Normal or mildly increased creatinine, mild renal azotemia (lower end of the range lies within reference ranges for creatinine for many laboratories, but the insensitivity of creatinine concentration as a screening test means that patients with creatinine values close to the upper reference limit often have excretory failure). Mildly increased SDMA.Clinical signs usually mild or absent.
3	251 – 440 2.9 – 5.0 36 - 54	251 – 440 2.9 – 5.0 26 - 38	Moderate renal azotemia. Many extrarenal signs may be present, but their extent and severity may vary. If signs are absent, the case could be considered as early Stage 3, while presence of many or marked systemic signs might justify classification as late Stage 3.
4	>440 >5.0 >54	>440 >5.0 >38	Increasing risk of systemic clinical signs and uremic crises

Monitoring Disease Progression

Renal disease is often a progressive condition, necessitating regular monitoring to assess disease progression and adjust treatment plans. Serial biochemical panels allow veterinarians to track changes in renal function over time. For example, a gradual increase in creatinine levels may indicate a slow decline in renal function, while a sudden spike might suggest an acute exacerbation or a secondary condition affecting the kidneys.

Moreover, monitoring electrolyte levels helps manage complications associated with renal disease. Hyperphosphatemia, a common issue in renal patients, can lead to further renal

damage and other systemic effects if not controlled. Regular biochemical panels enable timely intervention to correct such imbalances, thus improving patient outcomes.

Guiding Treatment Decisions

The biochemical panel is instrumental in guiding therapeutic decisions for renal patients. Treatment strategies, including fluid therapy, dietary modifications, and medications, are often tailored based on the biochemical panel results. For instance, the presence of significant azotemia might prompt the initiation of intravenous fluids to help flush out toxins and support renal function. Concurrently, identifying and managing electrolyte imbalances can prevent potentially life-threatening complications.

Furthermore, the panel can reveal underlying conditions that may complicate renal disease management. For example, elevated liver enzymes might indicate concurrent hepatic disease, necessitating a comprehensive approach to treatment that addresses both renal and hepatic dysfunction.

In summary, the biochemical panel is a critical tool in the diagnosis, monitoring, and management of renal disease in veterinary patients. By thoroughly understanding and utilizing the information provided by the biochemical panel, veterinarians can make more accurate diagnoses, effectively monitor disease progression, guide treatment decisions, and enhance communication with pet owners. As such, maximizing the utility of the biochemical panel is vital for improving outcomes in renal patients and ensuring the best possible care in veterinary medicine.

"Reading" the urine: what can we find out from the "liquid gold"?

Thursday 12 September | 14:30 - 16:30 | MC 3 - Room B

Prof. Habil. Dr. Alexandru Bogdan VIȚĂLARU

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Urinalysis is a cornerstone diagnostic tool in veterinary medicine, providing essential information about a patient's health, particularly regarding the urinary tract, kidneys, and metabolic status. This essay delves into the significance of urinalysis, highlighting its role in diagnosis, monitoring, and guiding treatment in veterinary practice.

Diagnostic Significance

Urinalysis offers critical insights into the health of the urinary system, enabling the detection of various disorders. Key components of urinalysis include physical examination, chemical analysis, and microscopic examination of the urine. Each of these components provides valuable diagnostic information:

1. Physical Examination: Evaluating the color, clarity, and odor of urine can provide initial clues. For example, hematuria (blood in urine) may indicate trauma, infection, or urinary tract neoplasia, while changes in urine color can suggest hemoglobinuria or bilirubinuria, pointing to hemolysis or liver disease, respectively.

2. Chemical Analysis: Testing for the presence of proteins, glucose, ketones, bilirubin, and other substances can reveal metabolic and systemic conditions. Proteinuria, for instance, may indicate glomerular disease, while glucosuria is a hallmark of diabetes mellitus. The urine pH and specific gravity also provide insights into renal concentrating ability and potential systemic acid-base disorders.

3. Microscopic Examination: Identifying cells, crystals, bacteria, and casts under the microscope can pinpoint infections, inflammatory processes, or crystal-induced conditions like urolithiasis. For example, bacteriuria and pyuria (pus in urine) are indicative of urinary tract infections (UTIs).

Monitoring Health and Disease Progression

Urinalysis is invaluable for monitoring the progression of diseases and the response to treatment. In patients with chronic kidney disease (CKD), regular urinalysis helps assess renal function and detect complications such as proteinuria or urinary tract infections. Additionally, in diabetic animals, monitoring for glucosuria and ketonuria can guide insulin therapy and dietary management.

For patients prone to urinary stones, periodic urinalysis can help detect and manage crystal formation before it progresses to urolithiasis. Regular checks can prevent the recurrence of stones, ensuring better long-term health outcomes.

Guiding Treatment Decisions

Urinalysis results directly influence treatment strategies. In cases of urinary tract infections, identifying the presence and type of bacteria through urine culture and sensitivity testing can guide the selection of appropriate antibiotics, ensuring effective treatment. For patients with urinary crystals or stones, identifying the crystal type (e.g., struvite, calcium oxalate) informs

dietary modifications and therapeutic approaches to dissolve existing stones or prevent new ones from forming.

Moreover, the detection of conditions such as proteinuria or hematuria may prompt further diagnostic investigations, including imaging studies or more specific renal function tests, leading to more precise and targeted treatments.

Enhancing Preventive Care

Routine urinalysis as part of annual health check-ups is crucial for early detection and prevention of diseases. Early identification of abnormalities, even in asymptomatic patients, allows for timely intervention and management. For instance, detecting early signs of renal disease through mild proteinuria or alterations in urine concentration can lead to interventions that slow disease progression and improve quality of life.

In conclusion, urinalysis is an indispensable diagnostic tool in veterinary medicine, offering comprehensive insights into the health of the urinary tract, kidneys, and overall metabolic status of animals. Its ability to diagnose, monitor, and guide treatment decisions makes it a vital component of veterinary care. Regular urinalysis contributes to early detection of diseases, effective management of ongoing conditions, and enhancement of preventive care, ultimately leading to improved health outcomes for veterinary patients.

MEDICAL MANAGEMENT OF THE ANEMIA OF CHRONIC KIDNEY DISEASE

Thursday 12 September | 14:30 - 16:30 | MC 3 - Room B

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Anemia associated with chronic kidney disease (ACKD) occurs in 30-65% of the affected dogs and cats. The prevalence and severity of the anemia increase as CKD progresses, being more common and severe in the advanced International Renal Interest Society (IRIS) stages (III and IV). Anemia in canine and feline patients with CKD adversely affects quality of life, has the potential to exacerbate the progression of CKD, and some studies identify anemia as a negative predictor of survival in CKD, similar to humans with CKD.

Pathogenesis of the ACKD is clearly multifactorial. The major component is the *reduced production of erythropoietin* (EPO) by the peritubular fibroblast cells of the inner cortex and outer medulla of the kidneys. In normally functioning kidneys, under hypoxic conditions, the intracellular transcription factor hypoxia inducible factor (HIF), binds to the EPO gene (in the fibroblasts), activating its expression, with resultant increased EPO production. Under normoxic conditions, HIF is degraded by the HIF prolyl-hydroxylase (HIF-PH) enzymes. Uremic patients have a dysregulated feedback loop, leading in relative rather than absolute EPO deficiency, as indicated by the fact that EPO concentration is usually within or slightly below or above the reference ranges, but it is disproportionally low for the severity of the anemia, when compared to anemic cats and dogs without uremic syndrome. *Anemia of inflammation* is an important determinant of the ACKD (CKD is a proinflammatory state per se, upregulating hepcidin synthesis, which further accumulates due to impaired renal clearance), leading to functional iron deficiency (sequestration in the iron stores). In addition, *blood loss* associated with uremic syndrome-induced gastrointestinal tract bleeding and impaired platelet function, along with the frequent in-clinic blood sampling procedures (may end up in absolute iron deficiency), *reduced red blood cell lifespan* (uremic toxins), and *secondary hyperparathyroidism* which promotes myelofibrosis and diminishes bone marrow erythropoiesis, may further worsen anemia in CKD.

The diagnosis of the ACKD is relatively straightforward in the clinical setting, provided that other causes of anemia have been reasonably excluded. The documentation of a normocytic, normochromic, nonregenerative anemia (may be microcytic and hypochromic in absolute iron deficiency), without white blood cell or platelet abnormalities, in the context of a serum biochemistry panel suggestive of advanced CKD, is consistent with ACKD. Measurement of EPO is not usually necessary, because it is time-consuming, expensive, does not reflect the severity of relative EPO insufficiency (may overlap with non-renal diseases), and is not thought to be of prognostic value.

Treatment objectives in the ACKD include 1) the cessation of blood loss (if present) and 2) the increase of the erythrocyte mass via blood transfusion and/or the administration of erythropoiesis stimulating agents (ESAs).

Blood loss in CKD is minimized by treating clinically relevant intestinal parasitic infections, and by alleviating overt uremia-induced bleeding by rationally using gastroprotectants (e.g., omeprazole, 1 mg/kg, PO/IV, BID). Blood collection for diagnostic purposes should be kept to a minimum in cats and small dogs, to avoid hospital-acquired anemia. Blood transfusion should be considered for the emergency treatment of severe acute or chronic anemia, in the context of unavailable ESAs or while awaiting response after their administration. Blood-typed and cross-matched whole blood (20 ml/kg) or preferably packed red blood cells for normovolemic patients (10-15 ml/kg) may be given. Limited blood product availability and high cost, reduced erythrocyte life span when transfused in a uremic animal and transfusion-related complications, call for treatment alternatives for the long-term management of the ACKD.

The most effective treatment option in ACKD is the use of ESAs, including human recombinant EPO (rHuEPO) for dogs and cats and the recently available HIF-PH inhibitors (e.g., molidustat) for cats. Canine and feline erythropoietin share an 81-83% homology with the amino acid sequence of human erythropoietin, explaining the affinity of human products to bind to and interact with erythropoietin receptors of dogs and cats. Based on the current IRIS guidelines, administration of ESAs is considered when the anemia is severe enough to compromise the animal's quality of life (usually when hematocrit drops below 20%), typically in late IRIS stages; however, accumulating evidence indicates that earlier medical intervention, before the severe reduction of hematocrit, might be of additional benefit to the animals by slowing the progression of CKD (Elliott 2023). Several rHuEPO products are commercially available, including epoetin alfa and beta (rarely epoetin zeta) or darbepoetin alfa, which differ in their degree of glycosylation, but have similar clinical efficacy (i.e., equally effective in increasing hematocrit and improving quality of life). Darbepoetin is a highly glycosylated product, with 3-fold longer half-life, allowing for less frequent administrations, while it is thought to be less antigenic (less likely to trigger the formation of anti-EPO neutralizing antibodies) compared to the less glycosylated EPO products. Induction dose for epoetin alfa and beta is 100-150 U/Kg, SC, three times weekly, while the starting dose for darbepoetin is 1-1.5 μg/kg (dogs, cats) or 6.25 μg/cat, SC, on weekly intervals (1 μg of darbepoetin equals to 200 U of epoetin). The increase rate of hematocrit is proportional to the dose of epoetin/darbepoetin, thus, in severe anemia, the highest end of the dose range may be indicated, followed by weekly hematological examinations. Once the target hematocrit (30-35% and 25-30% in the dog and cat, respectively) is achieved, typically in 3-4 weeks or longer, maintenance dosing should be individualized, giving usually the same or slightly lower dose per injection once or twice weekly (epoetin) or every 2-3 weeks (darbepoetin). Although current guidelines suggest that iron supplements should be given to all cats and dogs treated with EPO products, regardless of the iron status, the optimal way to supplement iron in these patients remains to be determined. Oral iron sulphate (100-300 mg/dog, 50-100 mg/cat, daily) or injectable iron dextran (50 mg, IM, [cat], or 20 mg/Kg, IM, [dog], every 3-4 weeks) can be considered for the duration of the EPO treatment. Parenteral iron may be more effective in restoring the functional iron deficiency, alleviating the problem of hepcidin-mediated iron malabsorption from the gastrointestinal tract. Oral iron supplementation may cause abdominal pain, vomiting and diarrhea, while parenteral iron may cause injection site pain and potentially iron overload.

Similar to human experience, approximately 30-35% of dogs and cats with ACKD given EPO products fail to respond. Potential reasons for the treatment failures include underdosing (e.g., cats treated with less than 1 μg/kg darbepoetin weekly), the inappropriate storage-

inactivation of the drug, the suboptimal iron replenishment, the continuous occult blood loss, and the development of anti-EPO antibodies. The latter is a major adverse event associated with the use of EPO, occurring in 20-70% of dogs and cats receiving traditional EPO products for several months, and less frequently in darbepoetin-treated animals. Reasonable suspicion for the development of anti-EPO antibodies emerges when the hematocrit is declining, in the context of a sufficient or increasing dose of EPO and a profound erythroid hypoplasia (myeloid-to-erythroid lineages ratio >8) in the bone marrow cytology, which might culminate in pure red cell aplasia. This immunologic reaction may also affect the endogenous EPO, rendering the animal transfusion-dependent for several months, prompting the definitive discontinuation of treatment. After cessation of EPO, anti-EPO antibodies may progressively decline, but immunologic memory precludes restart of treatment. At this time, it is not clear if immunomodulatory treatment (e.g., glucocorticoids) may prevent the immunologic rejection of EPO or hasten hematologic recovery. A range of other potential complications associated with the use of rHuEPO include arterial hypertension, seizures, local reaction at the injection site, erythrocytosis (polycythemia), fever, joint pain and vomiting. Unlike humans, EPO-induced thromboembolic disease has yet to be substantiated in dogs and cats.

Molidustat, an HIF-PH inhibitor, has been FDA-conditionally approved for the treatment of ACKD in cats, representing a promising novel alternative in the therapeutics of ACKD. Molidustat upregulates the production of endogenous (rather than supplementing exogenous) EPO, increases iron absorption in the gastrointestinal tract (by reducing hepcidin levels) and enhances iron uptake into the erythropoietic cells. Safety and efficacy were recently assessed in healthy cats and cats with ACKD (Charles et al. 2024, Boegel et al. 2024). Molidustat-treated cats with ACKD (5 mg/kg, PO, SID, for 28 days) had significantly higher hematocrit values compared to their baseline values or placebo-treated cats. Vomiting was the most common side effect in the treated cats. Several healthy-treated cats experienced erythrocytosis, but this was very uncommon in cats with ACKD. HIF-PH inhibitors may represent a more physiological way of upregulating EPO production and improving iron bioavailability, potentially allowing for earlier therapeutic intervention in cats (and likely dogs) with ACKD (Elliott 2023). It is currently unclear if (and by which route) iron supplements should be given along with molidustat, as that was not examined in the studies contacted in cats. Furthermore, the long-term administration strategy of molidustat in sick cats awaits refinement.

As a future perspective, recombinant adeno-associated viral vectors (rAAVs) with tropism for muscle tissue, such as SB-001, may confer long-term expression of feline EPO and enhance erythropoiesis. In a recent clinical trial, the safety, efficacy and optimal dose of SB-001 were evaluated in 23 client-owned cats with ACKD (IRIS stage 2-4), with an overall dose-depended response rate of 86% (cats with hematocrit increase). It was generally well tolerated, although hypertension developed in a few cats (Vaden et al. 2023).

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NEW AND OLD TREATMENT OPTIONS FOR FELINE INFECTIOUS PERITONITIS: INDIVIDUALISING TREATMENT

Thursday 12 September | 17:00 - 19:00 | MC 3 - Room B

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Feline coronavirus (FCoV) is the causative agent of the serious disease of feline infectious peritonitis (FIP). FCoV has a cell tropism for the enterocytes and usually causes clinical signs of enteritis or no clinical signs at all. Being an RNA virus though, FCoV has a high level of genetic variation due to frequent errors (mutations) during RNA replication. The hypothesis is that these mutations can occasionally facilitate the switching of cell tropism from a mostly mild enteric (less-virulent) FCoV pathotype to an FIP-associated FCoV pathotype1.
When FIP develops, the replicating FCoV in monocytes causes damage to the blood vessel walls, allowing plasma to leak out of the vessels; this can appear clinically as an effusion in the abdominal, thoracic and/or pericardial cavities (wet FIP form). In more chronic forms of FIP, granulomas result on affected organs (dry FIP form). Dry FIP can involve any organ, including nervous system (neurological form) and eyes (ocular form).
Feline infectious peritonitis (FIP) is considered fatal unless treated promptly with the appropriate antiviral treatment. Various antiviral drugs have shown promising results in vitro2. The mainstay of treatment at present is the nucleoside analogue GS-441524 and its prodrug remdesivir with multiple studies showing clinical efficacy ranging from 81.3-88.6%3-5 and no relapse for the responders up to one year after treatment6. The nucleoside analogue molnupiravir has also been used with success7,8. The protease inhibitor GC376 also appears effective in the injectable form, although oral effectiveness appears to be inferior to GS-4415249. These antiviral treatments act quickly, with fever and other clinical signs often improving markedly within a few days, allowing the clinician to attempt trial treatment of cats in which FIP is very likely but cannot be confirmed. Most studies have used 84-day treatment courses, but evidence has now been published that shorter courses of 42 days may be equally effective for cats with effusions; such shorter courses will enable improved access to treatment for cost and/or compliance reasons10.
Despite the significant progress in treatment that has happened over the last few years, FIP remains a challenging disease for the clinicians for several reasons:
1. It is often difficult to obtain a definitive diagnosis. Although effusive and non-effusive forms of FIP are described, there is much overlap between these forms and the clinical signs of FIP can change over time. Invasive diagnostic tests are often needed to secure diagnosis, but they carry a risk of the patient deteriorating.
2. The antiviral treatment is often expensive, not licensed and not available legally in many countries. Some countries have access to veterinary compounded antiviral products whereas others have access to antivirals developed for humans such as remdesivir or molnupiravir. In others, owners source antivirals themselves online, but the quality, purity, and concentration of

active ingredients in these preparations is usually unknown, and can be variable11, although they are often effective.

3. The ideal drug dose and duration of treatment is not certain yet. It is commonly believed that the neurological and ocular cases may need higher dosages due to the blood-brain and blood-ocular barriers.

4. Acute phase proteins are an integral part of treatment monitoring. Nevertheless, they are not specific for FIP and clear guidelines as to how they can guide treatment decisions are lacking.

5. Since the outbreak of feline infectious peritonitis (FIP) in Cyprus, caused by FCoV-23, a new combination of cat and dog coronaviruses, there is urgent need to understand modes of transmission and treatment options for 'traditional' FIP versus FCoV-23 as new or similar outbreaks may occur world-wide.

Considering the challenges above, the upcoming lecture will further focus on clinical FIP case scenarios. The cases that will be presented will serve as a practical guide to diagnosis, treatment and monitoring that can help individualising drug dose and treatment duration on a case-basis. Furthermore, the attendant will gain an insight into novel monitoring tools that are expected to revolutionize FIP treatment soon, such as Therapeutic Drug Monitoring (TDM) and viral load assessment.

TDM involves measuring blood concentrations of the active metabolite of the antiviral drug, such as EIDD-1931 and GS-441524. This will allow for a greater understanding of how individual cats metabolise these drugs to avoid underdosing as a reason of treatment failure (because of poor absorption and/or rapid excretion in urine). Furthermore, certain antiviral drugs such as molnupiravir have been associated with dose-dependent toxicity and TDM will ensure that overdose is avoided. Optimising drug treatment should improve the prognosis for individual cats.

Viral load assessment involves measuring FCoV load by PCR with quantification in blood, faeces, fluid or tissue before, during and after treatment. This will show how quickly these drugs clear FCoV from blood and stools, helping to reduce new infections and to tailor the duration of treatment for the individual patient.

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THE EPIDEMIOLOGICAL PRESENTATION AND SURVEILLANCE OF FCOV- 23, FELINE INFECTIOUS PERITONITIS OUTBREAK IN CYPRUS

Thursday 12 September | 17:00 - 19:00 | MC 3 - Room B

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Introduction.

Feline coronavirus (FCoV) is a common feline viral disease which is present globally[1]. FCoV presents itself in two biotypes. The first biotype, which is the most frequently found in naturally occurred infections, is the feline enteric coronavirus (FECV). The FECV is characterized by low virulence and mild clinical signs, typically limited to mild enteritis. The second biotype, is proposed to originate each time from a mutation in an FECV-infected cat, is known as feline infectious peritonitis virus (FIPV)[2]. FIPV is the causative agent of feline infectious peritonitis (FIP), a fatal disease if left untreated. The different disease presentation of the two biotypes is due to changes in the virus's tropism from cells in the enteric tract to macrophages. This change in primary tropism also impacts the virus's ability to transmit from cat to cat, with the main transmission pathway of FECV being faecal-oral route, while FIPV typically has relatively poor transmission potential[3]. Outbreaks of FIP have been previously documented in the UK[4] , the USA[5] and Taiwan[6] and were restricted to catteries and rehoming centers. Our team was the first to report a recent alarming outbreak of FIP in Cyprus since June 2023[7]. The number of FIP PCR-confirmed cases in samples from cavity fluids, abdominal lymph nodes, or tissue biopsies from

[1] Horzinek and Osterhaus, 1979
[2] Jaimes *et al* 2020
[3] Gao et al, 2023
[4] Barker EN *et al.*, 2022
[5] Healey EA *et al.*, 2022
[6] Wang Y-T *et al.*, 2013
[7] Attipa C *et al.*, 2023

patients with a FIP compatible clinical appearance, has increased more than 20-fold compared to the previous year (2022). It is estimated that the outbreak has affected more than 8000 cats in Cyprus in the first six months of 2023. We described the emergence of a new feline corona virus (FCoV) recombinant affecting both owned and unowned cats in Cyprus[8]. The virus, named FCoV-23, was found to spread quickly across the island causing clinical signs of FIP.

Materials and Methods.

Following the discussion of increased FIP cases amongst clinicians, our team initiated an outbreak investigation which was followed by the establishment of a surveillance system. Two methods were used to collect data both for the outbreak investigation and the surveillance: (a) laboratory results, (b) epidemiological outbreak investigation and surveillance through online questionnaires administered by the Pancyprian Veterinary Association (PVA).

A. Initial laboratory investigation was performed with data collected from FIPV PCR positive cases. These data were gathered through samples submitted for routine diagnosis of suspected FIP cases[i], by licenced veterinarians in Cyprus. The veterinarians submitted samples from abdominal/thoracic or pericardial effusions or cerebrospinal fluid to the Vet Dia Gnosis laboratory, from where the samples were sent to Laboklin laboratories in Germany, for a FCoV PCR test. A monitoring surveillance system of the PCR positive cases that documents the PCR positive cases throughout time and with a frequent update on the data, was established this way.

B. The second method consisted of three online questionnaires, administered by the Pancyprian Veterinary Association (PVA) via a social media group and via email. The first questionnaire was delivered in March 2023, with the objective to investigate the existance of an outbreak and capture a crude number of suspected FIP cases for the first trimester of 2023. A second questionnaire was delivered in July 2023, aiming to capture the evolution of the outbreak for the first six months of 2023. The last questionnaire was delivered in December 2023 and was answered by 40 veterinary practices. The aim of this questionnaire was to capture the crude number of cases per trimester for 2022 and 2023.

Results

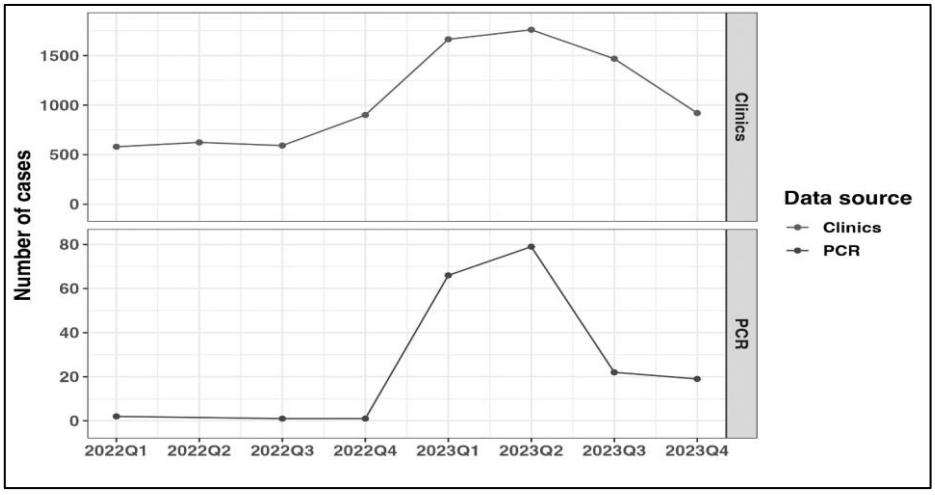
A. Laboratory process: The total number of PCR-positive cases that were submitted to the Vet Dia Gnosis laboratory between December 2022 and March 2024, was two hundred and two (202) in total. These samples were collected in real time and are the only data-source of confirmed cases from individual cats. According to the data, the outbreak peaked in spring 2023 (N=37 in March) and even though the cases started decreasing after May, they remained high during the summer. During the winter 2023-2024, cases appear reduced, nevertheless PCR confirmed cases continued being present in all districts with a new increase described in March 2024.

B. Questionnaire Process. The first online questionnaire that was administered by the PVA was answered by 23 veterinary practices out of 150 (15% of the total number of veterinary practices in Cyprus). In this first questionnaire there was documentation of an increase in suspected by nearly 9 times and confirmed cases by 4 times in comparison to 2022. The second online

[8] Attipa C *et al.*, 2023b

questionnaire that was administered by the PVA was answered by 40 veterinary practices (out of 150 in total in Cyprus). This represents 26% of the clinics in Cyprus. In this questionnaire, there was documentation of the number of cases from January 2022 until December 2023 divided into trimesters. The result of the questionnaire agrees with the data collected from the Vet Dia Gnosis laboratory and suggests that the peak of the outbreak was recorded in Spring of 2023, also agreeing that, even though the number of cases dropped in numbers following the spring period of 2023, the total number of cases remains increased compared to 2022. We have compared the results on the total number of cases from the two processes (A and B), divided in trimesters from January 2022 until December of 2023 (Figure 1. Upper graph "Clinics").

Figure 1. Number of suspected FIP cases from January 2022 until December 2023 divided in trimesters, according to the laboratory investigation ("PCR") and the epidemiological investigation using a questionnaire filled in by veterinary practitioners ("Clinics"). Data from the two processes show that the peak of the FCoV23 outbreak took place in spring 2023 and, besides, the decrease of cases that followed, it did not fade out.



Discussion

In this study, we presented the results of an FIP outbreak investigation and surveillance due to a newly emerging FCoV variant, the FCov23, that was reported in Cyprus early in 2023. Unlike previous outbreaks which were restricted to catteries and rehoming centers [9, 10, 11], the one in Cyprus has spread very quickly throughout all the island districts and wasn't controlled or limited to a single cattery/rehoming center or geographical area. The surveillance system used to monitor and act upon this outbreak (PCR and questionnaire-based processes), which was performed with limited resources, indicated the first ever reported outbreak of FIP recorded in the literature with such long duration as it continues to cause disease in several cats (as of 06/2024). The data collected through the two processes indicates that the FCoV23 induced FIP possesses different characteristics from previously reported FIP outbreaks. Despite their limitations the two processes can be used to facilitate the detection and monitoring of future viral outbreaks in Cyprus or used as model to detect and surveillance of other viral outbreaks in general.

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PROGNOSTIC FACTORS FOR CANINE MAST CELL TUMOURS: SOME HELP TO UNTANGLE THE KNOT

Thursday 12 September | 08:30 - 10:30 | MC 2 - Room C

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In human medicine, a prognostic factor influences a patient's outcome independently of treatment, and a predictive factor is one with a relationship to the response to a particular therapy.
The definition of prognostic factors in veterinary medicine is often a mix of the two definitions, as historically considered negative prognostic factors might 64haracteri their impact when the correct therapy is applied.

Mast cell tumours are a great example of how clinical and pathological negative prognostic factors change patients' prognoses and how we must change our approach to them when we encounter some of them. For this reason, historical MST times will not be described here, as they might change depending on the type of therapy proposed, unless they truly change the outcome independently of treatment.

This lecture will classify canine negative prognostic factors into two categories: clinical and clinical pathological or histological.

CLINICAL PROGNOSTIC FACTORS FOR CANINE MAST CELL TUMOURS:

The **age and breed** of a dog significantly influence the prognosis of canine mast cell tumours (MCTs). Older dogs typically exhibit a worse prognosis compared to their younger counterparts. Additionally, breed predispositions play a critical role. While breeds such as Boxers, Boston Terriers, and Bulldogs tend to develop less aggressive forms of MCTs, other breeds like the Chinese Shar-Pei are more susceptible to aggressive and high-grade tumours. These breed-related tendencies suggest that genetic factors inherent to these breeds may influence the biological behavior of the tumours, affecting their progression and response to treatment.

The **anatomical location and size** of the tumours also serve as crucial prognostic indicators. MCTs in high-risk areas such as the muzzle, inguinal, and perineal regions are associated with a poorer prognosis. This is likely due to these areas' dense vascular and lymphatic networks, which facilitate metastasis. Furthermore, larger tumours, typically those exceeding 3 cm in diameter, are more prone to metastasis and local recurrence, indicating a more aggressive clinical course. The size of the tumour is directly correlated with its ability to infiltrate surrounding tissues and spread to distant sites. Median survival times (MST) for dogs with high-risk anatomical locations and large tumours are generally reduced.

Another negative prognostic factor is the **recurrence** of MCTs after initial treatment. Recurrent tumours often display more aggressive behaviour and resistance to standard treatments, complicating clinical management and reducing the likelihood of long-term remission.
Stage, meaning metastasis to regional lymph nodes, liver, spleen, or other organs, significantly worsens the prognosis. The presence of metastasis indicates systemic spread of the disease,

which is associated with a lower survival rate and increased morbidity. Median progression-free survival (PFS) for dogs with metastasis to distant organs, aka stage 4, is notably shorter, often less than 6 months.

Systemic symptoms such as vomiting, diarrhoea, and gastrointestinal ulceration, often resulting from the release of histamine and other vasoactive substances by the neoplastic mast cells, further contribute to a poor prognosis. These symptoms not only indicate the systemic impact of the tumour but also complicate clinical management, requiring additional therapeutic interventions to manage these paraneoplastic effects. Dogs presenting with systemic symptoms have historically a reduced MST, frequently less than 4 months, as usually these are correlated with advanced disease.

CYTOLOGICAL AND HISTOLOGICAL PROGNOSTIC FACTORS

Cytological examination of MCTs provides valuable prognostic information, particularly regarding cell morphology. Poorly differentiated cells, 65haracterized by irregular nuclear shapes, high mitotic figures, and multinucleation, indicate a more aggressive tumor phenotype. These **morphological features** suggest a higher degree of malignancy and are associated with rapid tumor growth and a higher likelihood of metastasis. High granularity within the cells is also a sign of aggressive behavior and correlates with a poorer clinical outcome.

Histopathological analysis remains the cornerstone of prognostication for canine MCTs. Histologic grading systems, such as the Patnaik and Kiupel grading systems, are employed to predict clinical outcomes. High-grade tumors, corresponding to Grade III in the Patnaik system or high-grade in the Kiupel system, are associated with significantly worse prognoses. These grading systems take into account various histological features, including **cellular differentiation, mitotic activity, and the presence of necrosis**, to provide a comprehensive assessment of tumor aggressiveness. Dogs with high-grade MCTs according to these grading systems have a significantly reduced MST, often less than 4 months for Grade III tumors and less than 6 months for high-grade Kiupel tumors.

The mitotic index, defined as the number of mitoses per high-power field, is a critical pathological parameter. A high mitotic index is strongly associated with a worse prognosis, as it reflects rapid cellular proliferation and tumor growth. Specifically, a mitotic index greater than 5 is considered a significant indicator of a more aggressive tumor, predicting a higher potential for local invasion and distant metastasis. Median survival times for dogs with a high mitotic index (>5) are significantly reduced, often to less than 6 months, compared to those with a low mitotic index.

The **Ki-67 index**, another marker of cellular proliferation, is determined through immunohistochemical staining. A high Ki-67 index indicates a high rate of cell division, which correlates with a more aggressive tumor and poorer prognosis. This index is particularly useful in distinguishing between low-grade and high-grade MCTs, providing additional prognostic information that complements histological grading. High Ki-67 index values are associated with an MST of around 6 months, compared to over 2 years for tumors with low Ki-67 indices.

Vascular and lymphatic invasion by tumor cells is another strong prognostic indicator. The presence of neoplastic cells within blood vessels or lymphatics signifies a higher potential for metastasis, as these pathways facilitate the spread of cancer cells to distant sites. This histological feature is associated with a poorer prognosis and necessitates more aggressive therapeutic interventions to manage the disseminated disease.

Genetic mutations in the c-KIT gene, play a pivotal role in the pathogenesis and progression of MCTs. Mutations in exons 8, 9, and 11 of the c-KIT gene are linked to more aggressive tumour behaviour and poorer clinical outcomes. These mutations lead to constitutive activation of the KIT receptor tyrosine kinase, promoting uncontrolled cell growth and survival. The presence of these mutations indicates a more aggressive tumor phenotype and, when treated just with surgery, dogs with c-KIT mutations typically have a reduced MST, around 4-6 months, compared to those without such mutations.

Subcutaneous MCTs generally have a better prognosis compared to their cutaneous counterparts. However, this prognostic advantage diminishes if the subcutaneous tumours are high-grade or exhibit a high mitotic index. The depth of the tumour and its histological characteristics are, therefore, critical factors in determining the prognosis of subcutaneous MCTs. Median survival times for high-grade subcutaneous MCTs are significantly shorter, often less than 6 months, compared to low-grade subcutaneous tumours, which can exceed 2 years.

In conclusion, the prognosis of canine mast cell tumours is influenced by a multitude of factors spanning clinical presentation, cytological characteristics, and histopathological features. A comprehensive assessment that integrates these diverse prognostic indicators is essential for accurately predicting clinical outcomes and guiding therapeutic decision-making. Advances in molecular diagnostics and targeted therapies promise to improve the prognosis and quality of life for dogs affected by these complex and heterogeneous tumours. By understanding the interplay between various prognostic factors, veterinarians can better tailor treatment plans to each patient's individual needs, ultimately improving clinical outcomes and advancing the field of veterinary oncology.

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NOW THE KNOT IS UNTANGLED: HOW DO WE TREAT MAST CELL TUMORS?

Thursday 12 September | 08:30 - 10:30 | MC 2 - Room C

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The complexity of MCTs necessitates a multifaceted therapeutic approach tailored to individual cases based on various prognostic factors. This summary outlines the current therapeutic strategies for canine MCTs, emphasizing the integration of clinical, cytological, and histopathological prognostic factors into treatment algorithms.

Surgical Management
Treatment strategies for mast cell tumours (MCTs) depend on the tumour's clinical stage and the presence of negative prognostic factors. Surgical excision is typically the preferred treatment for tumours localised to the skin, provided the tumour is in an area where wide excision is feasible. Historically, it was recommended to excise MCTs with a 2-3-cm margin of surrounding normal tissue. However, this recommendation was based on anecdotal evidence.

Recent studies have refined the approach to surgical margins. Two main strategies are now used for excising low- and intermediate-grade MCTs less than 5 cm in diameter: **the metric approach and the proportional approach**. The metric approach involves using fixed lateral margins of 1 cm for low-grade and 2 cm for intermediate-grade MCTs. In contrast, the proportional approach bases the lateral margins on the maximum dimension of the tumour. Regardless of the approach, deep margins should include the removal of one uninvolved fascial plane and, if necessary, deeper muscle layers.

For MCTs in locations where wide excision might be challenging due to size, anatomical constraints, or owner concerns, a biopsy to determine histologic grade can guide whether narrower margins might suffice. For instance, 1-cm margins may be adequate for low-grade MCTs in some cases.

Management becomes more complex for MCTs located on distal extremities where primary closure is difficult. Treatment options include wide excision with subsequent defect reconstruction, limb amputation, or marginal excision followed by radiotherapy (RT) or chemotherapy. Preoperative biopsies can determine histologic grade, which helps set the required lateral margins for complete excision. If primary closure is unfeasible, wide excision followed by reconstruction or secondary intention healing is a viable option. Studies show that wounds healing by second intention after wide excision with 2-cm margins have a high healing rate.

Marginal excision followed by RT can also be an acceptable approach for low- to intermediate-grade MCTs if the tumor is excised without visible residual disease and the wound is closed primarily. Two-year control rates of 85% to 95% are achievable with RT. When RT is unavailable, postoperative chemotherapy can be considered, though the evidence is limited, and results should be interpreted cautiously.

If initial surgical excision is incomplete, additional local therapy is usually required, however low-grade MCTs have been proven to have low recurrence rate, despite dirty margins. A second wide excision or adjuvant RT might be employed. Studies indicate that while not all MCTs with incomplete margins will recur, some might have higher recurrence rates in intermediate-to high-grade tumors.

Alternative local therapies, such as hyperthermia, intralesional brachytherapy, photodynamic therapy, and cryotherapy, have been explored but are not as well-established or practical as surgery or RT. Adjuvant corticosteroid therapy, despite its common use, lacks substantial evidence of benefit for intermediate-grade MCTs.

Conversely, high-grade tumours (Patnaik grade III, Kiupel high grade) or tumours with incomplete surgical margins require more aggressive management. Following surgery, adjunctive treatments such as radiation therapy or systemic therapy are recommended to control residual disease and prevent recurrence.
Treatment of anaplastic or undifferentiated MCTs, which include high-grade tumours and those with metastasis, remains challenging. These tumours generally have a poorer prognosis. Systemic adjuvant therapies must be offered.

Radiation Therapy
Radiation therapy (RT) serves several critical roles in managing MCTs. As an adjuvant therapy, postoperative RT is indicated for tumours with incomplete margins, particularly when re-excision is not feasible. RT can achieve local control rates exceeding 90% for incompletely excised tumours. In cases where tumours are surgically inoperable due to location (e.g., distal limbs, head) or size, definitive RT is a primary treatment modality.

Systemic Therapy
Systemic therapy is essential for managing metastatic MCTs or high-grade tumours with a high risk of systemic spread. Therapeutic options include chemotherapy, tyrosine kinase inhibitors (TKIs), and corticosteroids.

Various chemotherapeutic agents, including vinblastine, lomustine (CCNU), and doxorubicin, are used either as monotherapy or in combination protocols. Chemotherapy is indicated for high-grade tumors, those with confirmed metastasis, or in cases where surgery and RT are inadequate. Median survival times (MST) for dogs receiving chemotherapy range from 6 to 12 months for high-grade tumors.

Tyrosine kinase inhibitors (TKIs), such as toceranib and masitinib, target the products of c-KIT gene, which are implicated in the pathogenesis of MCTs. These drugs are particularly effective in tumors harboring c-KIT mutations, providing an MST of approximately 12 to 18 months in responsive cases, but they can be effective in non-mutated MCTs either. TKIs are used for unresectable tumors, metastatic disease, or as an adjuvant treatment post-surgery.

Corticosteroids, such as prednisone, are frequently used to reduce tumor burden and manage systemic symptoms. They can be used as part of combination therapy with chemotherapeutic agents or TKIs. Prednisone alone may induce partial responses but is typically less effective than other systemic therapies.

Therapeutic Algorithm Based on Prognostic Factors
The therapeutic approach for canine MCTs is guided by integrating clinical, cytological, and histopathological prognostic factors. The following algorithm outlines the decision-making process:

Initial Diagnosis and Staging: Perform thorough clinical examination, cytology, and biopsy. Stage the tumour using imaging modalities (e.g., ultrasound, CT, MRI) and aspirate regional lymph nodes.

Prognostic Factor Assessment: Evaluate age, breed, tumour location, size, and systemic symptoms. Assess cytological features such as mitotic index and Ki-67 index. Histopathological grading (Patnaik and Kiupel systems) and margin status are crucial for prognostic evaluation.

Localised, Low-Risk MCTs: Surgical excision with wide margins is the treatment of choice for low-risk MCTs. Follow-up includes regular physical examinations and monitoring.

Localised, High-Risk MCTs: High-risk MCTs necessitate surgical excision followed by adjuvant RT if margins are incomplete or high-grade features are present. Based on individual risk assessment, systemic therapy, including chemotherapy or TKIs, should be considered. Follow-up involves frequent monitoring and additional imaging as needed.

Non-Resectable or High-Risk Tumors: Definitive RT is the primary modality for non-resectable tumors. Systemic therapy, including chemotherapy or TKIs, is indicated for high-grade tumours or those with c-KIT mutations. Intensive monitoring for treatment response and side effects is essential.

Metastatic Disease: Systemic chemotherapy or TKIs are the primary treatments for metastatic disease. Supportive care includes managing systemic symptoms with corticosteroids and other palliative measures. Regular imaging and clinical assessments are necessary to monitor disease progression.

Conclusion
The management of canine mast cell tumours requires a tailored approach that considers individual prognostic factors to optimise therapeutic outcomes. Surgery remains the primary treatment for localised MCTs, with radiation therapy and systemic therapies playing critical roles in managing high-risk, non-resectable, or metastatic tumours. Advances in molecular diagnostics and targeted therapies, particularly TKIs, have improved the prognosis for dogs with aggressive MCTs. An integrative therapeutic algorithm, informed by clinical, cytological, and histopathological evaluations, is essential for guiding treatment decisions and enhancing the quality of life for affected dogs. Continued research into immunotherapy and novel treatment modalities holds promise for further advancements in managing this complex disease.

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CYTOLOGICAL GRADING OF CANINE MAST CELL TUMOURS

Thursday 12 September | 11:00 - 13:00 | MC 2 - Room C

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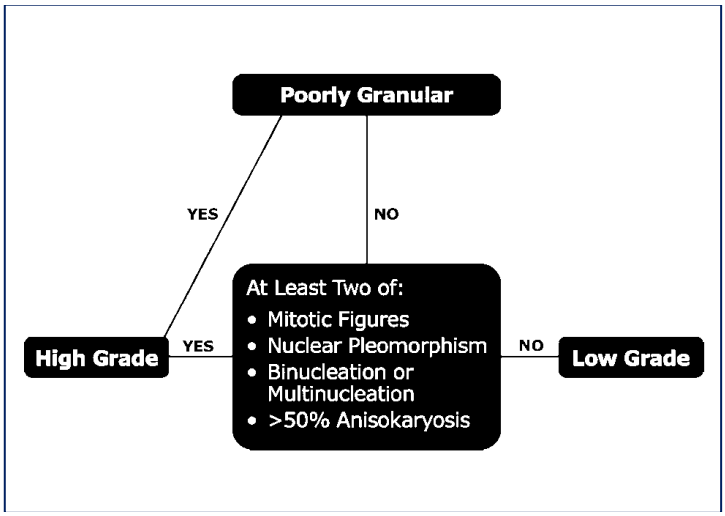
Mast cell tumour (MCT) is a common condition in dogs accounting for 16-21% all skin neoplasms. It usually presents a solitary solid mass, though a significant proportions of dogs with multiple tumours may occur. MCT usually occurs in older dogs (mean age 9 years), but has been reported in dogs under 1 year of age also. There is no gender predilection. Boxers, Retrievers, Pugs, Boston terriers and Pit-Bull terriers are at a higher risk of developing MCTs.

Definitive diagnosis can be achieved via cytology in a large percentage of cases (>90%). Aspirates from MCTs usually contain frequent mast cells with variable degree of granulation and signs of atypia. They may be accompanied by eosinophils, fibroblasts and collagen fibres.

Histopathology is useful to confirm the diagnosis, its exact location (cutaneous vs subcutaneous), establish surgical margins (if excision was complete) and to provide histopathological grading system.



Recently, several studies have been conducted to establish a cytological grading system for canine cutaneous MCTs. Such a system could aid in clinical staging and determining the most appropriate treatment, including surgery. Currently, there are four publications investigating this matter. Two studies directly applied the Kiupel two-tier histopathological grading system to cytology samples, while the other two developed new cytological grading systems inspired by the Kiupel system. Of these four publications, the one by Camus and colleagues is the one most commonly clinical pathologists referred too also because it is one of the few that compared cytology grading results with survival data. Based on this publication, it has been shown that a canine cutaneous MCT can be considered being high grade when it displays low/decreased granularity and/or it shows at least two of the following criteria of atypia including mitotic figures, nuclear pleomorphism, binucleation/multinucleation, and/or >50% of anisokaryosis. Dogs with

cytologic high-grade MCT were shown to be 25 times more likely to die within the 2 years follow up period, than dogs with low-grade MCT. Based on these results, the cytological grading system showed a Se and Sp of 88.2% and 94.8% respectively. Both false positive and false negative results can still occur, therefore histopathological grading is still recommended after surgery. More recently, Paes and colleagues established a new cytological grading system, similar to Camus, which also correlated with patient survival. The study showed that the higher the number of fibroblasts and amount of collagen fibres, the longer the survival and the lower the histological grade.

Fig.1 Cytological grading system for canine cutaneous mast cell tumours by Camus et al. 2016

Potential pitfalls in MCT cytological grading include the inability to know the exact localization of the mass via cytology, the use of rapid stains and possibly also the use of digital cytology. All these cytological grading systems have been validated only for canine cutaneous MCTs and do not apply to subcutaneous forms, which exhibit a different clinical behaviour. Unfortunately, neither the macroscopic examination of the mass nor cytology allows for certain determination of whether the masses are cutaneous or subcutaneous. This ambiguity can potentially lead the operator to grade an MCT that later proves to be subcutaneous. A recent study has also shown that rapid stains may not highlight MCT granules as effectively as Wright-Giemsa stains. This represents a potential risk in terms of grading, as granularity is one of the most critical elements to be evaluated. Therefore, this should be considered when performing a grading, and the use of Giemsa-based stains is favored. Digital cytology has revolutionized the field over the past few years, allowing veterinarians to scan their slides in-house, which are then read by remote pathologists worldwide, often within a few hours. However, digital cytology also presents some limitations in terms of resolution. Visualization and identification of mast cells, their granules and nuclear features can be more challenging on digital images than on glass slides. Therefore, validation of these grading systems on digital platforms may be required.

Recommended readings:

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IS THERE ANYTHING "NEW" IN VETERINARY ONCOLOGY? UPDATES ON TREATMENT OPTIONS

Thursday 12 September | 11:00 - 13:00 | MC 2 - Room C

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This section will focus on the available new drugs that represent significant advancements in the treatment of canine cancers and associated conditions. Laverdia-CA1 offers a new approach for managing lymphoma, Canalevia-CA1 provides an effective solution for chemotherapy-induced diarrhea, and Stelfonta offers a non-surgical option for managing mast cell tumors.
This section will also offer an overview of interventional oncology in veterinary medicine

Laverdia-CA1 (Verdinexor)
Laverdia-CA1 is an oral drug for dogs with lymphoma and has shown efficacy as a single-agent treatment for various types of canine LSA. Conditionally approved by the FDA in 2021, verdinexor works as a selective inhibitor of nuclear transport (SINE) drug, targeting the exportin-1 (XPO1) protein. XPO1 is overexpressed in certain cancers and exports tumour suppressor proteins (TSPs) from cell nuclei, making cells vulnerable to uncontrolled growth. By inhibiting XPO1, verdinexor traps TSPs within the nucleus, inducing programmed cell death in LSA cells.
In a phase II study, verdinexor demonstrated an objective response rate of 34.5% (20/58 dogs) with a median time to progression of 36.5 days for treatment-naive patients and 22 days for relapsed patients. Adverse effects are typically mild, including lethargy, anorexia, weight loss, vomiting, diarrhea, and elevated liver enzymes. These can usually be managed with supportive care.

Canalevia-CA1 (Crofelemer Delayed-Release Tablets)
Canalevia-CA1 is the first conditionally approved oral drug for dogs with chemotherapy-induced diarrhea (CID). CID is a common side effect of chemotherapy, often managed with metronidazole despite concerns over its widespread use and potential side effects.
Crofelemer, derived from the sap of the South American Croton lechleri tree, inhibits chloride ion channels in the gastrointestinal tract, reducing fluid secretion and normalizing fluid flow into the GI lumen. Unlike traditional treatments, this mechanism addresses the underlying causes of CID.
In clinical trials, crofelemer showed a treatment success rate of 75% compared to 25% in control groups. It is well-tolerated with minimal absorption into the bloodstream, making it a safe option for managing CID.

Stelfonta (Tigilanol Tiglate Injection)
Stelfonta is a novel intratumoral therapy approved by the FDA for local control of non-metastatic cutaneous and subcutaneous mast cell tumors (MCT) in dogs. Derived from the seeds of the Australian blushwood tree (Fontainea picrosperma), tigilanol tiglate has a multifactorial mode of action. It induces direct oncolysis of tumour cells, activates protein kinase C, causing an acute inflammatory response and local tumour hypoxia, and results in vascular

necrosis by destroying tumour vasculature. Additionally, it promotes wound healing through re-epithelialization and provides antimicrobial effects at the tumor site.
In pivotal trials, a single treatment with Stelfonta resulted in a complete response rate of 75%, with an overall response rate of 88% following a second treatment. Most wounds healed within 28 to 42 days post-treatment. Adverse effects include wound formation, injection site pain, lameness, and transient gastrointestinal symptoms.

Interventional oncology (IO) has gained popularity alongside traditional cancer therapies like surgery, chemotherapy, and radiation therapy in veterinary medicine. This growing field focuses on minimally invasive techniques for both diagnosing and treating cancer. For instance, stenting for malignant obstructions has been implemented in veterinary practice for about 25 years. More recent developments, such as intra-arterial chemotherapy delivery, embolisation, and ablation, show highly promising early results.

Intra-arterial Chemotherapy
Intra-arterial chemotherapy offers potential advantages over traditional intravenous administration by delivering a higher localized drug concentration to the tumor, minimizing systemic side effects. This method involves placing a sheath in the chosen artery and using guidewires and catheters to access the vascular supply of the affected organ. Despite its benefits, intra-arterial chemotherapy is not universally adopted in human medicine but shows promise, especially in the head and neck regions.
In veterinary medicine, studies comparing intra-arterial and intravenous chemotherapy for lower urinary tract neoplasia in dogs showed a significantly greater tumor size reduction and fewer side effects in the intra-arterial group. Additionally, combining intra-arterial chemotherapy with radiation therapy has been explored in osteosarcoma and bladder cancer treatments in dogs, showing promising results with minimal side effects.

Embolization/Chemoembolization
Embolotherapy, an established treatment in human oncology, involves creating localized ischemia to induce tumor cell death. Chemoembolization combines this with chemotherapy to enhance cytotoxic effects. Techniques include transarterial embolization (TAE) and transarterial chemoembolization (TACE), using drug-eluting beads (DEB-TACE) loaded with chemotherapy agents like doxorubicin.
In veterinary practice, liver tumor embolization has been reported most frequently. Various chemoembolic mixtures have been used, showing survival times ranging from 28 to 137 days. Studies on bland embolization and DEB-TACE in dogs reported median survival times of 419 days and varied outcomes, with tumor volume reductions ranging from 13% to 51%.
Prostatic artery embolization (PAE) is an effective treatment for prostate neoplasia, causing permanent cessation of blood flow to the prostate. In a study of 20 dogs undergoing PAE, all showed decreased prostatic volume and significant clinical improvement without major complications.

Nasal Tumor Embolization
While radiation therapy is often preferred for nasal tumors, embolization is a viable alternative. The isolated blood supply to the nasal cavity allows for highly tolerated embolization procedures.

Ablation
Ablative techniques, although sparsely described in veterinary literature, hold potential based on their applications in human medicine. Chemical ablation involves injecting agents like ethanol directly into the tumor, while thermal ablation uses energy or freezing agents to incite

cell death. Thermal techniques include radiofrequency ablation (RFA), cryoablation, microwave ablation (MWA), laser ablation, and high-intensity focused ultrasound.
RFA, cryoablation, and MWA are introduced percutaneously or through natural orifices, guided by imaging modalities like fluoroscopy, CT, MRI, or ultrasound. These techniques are common in treating hepatic, prostate, kidney, and bone tumors in humans, with potential applications in veterinary oncology. MWA, in particular, offers advantages over RFA, such as higher intratumoral temperatures and faster ablations.

Stenting of Malignant Obstructions
Stents are tube-like devices that recanalize luminal obstructions, allowing the excretion of body fluids or passage of substances. Urethral stenting is common in veterinary IO, providing life-saving relief from urinary tract obstructions. Clinical studies show successful urethral stent placements in dogs and cats, with complications like incontinence being the most common.
Ureteral stenting addresses obstructions caused by lower urinary tract neoplasia, improving conditions like hydronephrosis and hydroureter. In a study of 12 dogs with ureteral obstruction, stents were successfully placed, and complications were rare. For colonic, esophageal, and tracheal tumors, stents can be used when surgical resection is not feasible.
Vascular stents help palliate obstructions from large tumors or surgical complications, particularly in veins. Case series show successful stent placements restoring vascular patency in dogs with conditions like Budd-Chiari syndrome and heart-based tumors causing chylothorax.
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AI APPLICATIONS IN VETERINARY MEDICINE (PAST, PRESENT, FUTURE)

Thursday 12 September | 14:30 - 16:30 | MC 2 - Room C

Theodoros Petanidis
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Introduction

This exploration of the role of Artificial Intelligence in the veterinary field begins by tracing the brief history of AI, shedding light on key developments and transitions. Most importantly, it addresses the plethora of often confusing or weakly defined terms that inundate discussions around AI. Effort is taken to take a grounded, practical approach while avoiding hyperbole. In some cases, parallels are going to be drawn with human medicine, exploring potential crossovers. To help the reader stay abreast with recent advances, key areas where exciting development is taking place are mentioned along with figures whose insights and work offer valuable insights about the direction AI is moving to.

History and Terminology

Artificial Intelligence refers to the approximation of human intelligence processes by machines. These include learning (capturing information and rules from data), reasoning (applying these rules to reach conclusions) and self-correction (recursively analyzing outputs to improve performance). **Expert systems** were an early attempt in AI during the 1970s and 80s and while they are still used in certain domains (e.g., finance, engineering), they only rarely ended up being of use in medicine, despite concerted efforts to do so. The concept of an expert system involves implementing a well-structured, constantly curated knowledge base with domain-specific information and heuristics. An inference engine applies formal logical reasoning to this base to provide solutions or recommendations.

A fundamentally different approach in learning from data is what is known as **Statistical Learning**. This refers to a set of methods and techniques where models are trained on historical data to identify patterns, relationships, and structures within the data. These models use statistical algorithms to learn and make predictions without being explicitly programmed to perform the task. Examples include linear regression, logistic regression, support vector machines, decision trees and many more. Like with any other modeling technique the choice of algorithm depends on the nature of the underlying data and the type of prediction being made.

While **Machine Learning** is rooted in the field of statistics and is very closely related, it differs in focus and will include a wider array of approaches and other paradigms like neural networks, deep learning, reinforcement learning, and more, along with more advanced versions of classical models like random forests and boosted trees. ML practice will emphasize predictive accuracy, computational efficiency, and scalability much more than the statistical properties of data and model algorithms. More importantly, statistical models are designed to be interpretable, they focus on extracting insights and understanding relationships and interactions between variables. In contrast, machine learning models, especially deep learning models, will always prioritize predictive accuracy over interpretability, often becoming highly accurate yet opaque black boxes.

Many of the foundational statistical principles and theory behind machine learning were developed early in the second half of the 20th century. The limitations in computational power of the time did not allow for any real-world applications, however. Even the basic structure of neural networks and the methodology for training them (Rosenblatt's perceptron and backpropagation papers) was conceived in the 50s and 60s yet could not see real implementations until decades later. The wider field of AI saw slow advancement, failures, and reduced funding. This period, with its lowest point during the 90s is known as "AI winter". It ended

during the mid-2010s where we saw advances in designing and training neural networks, the introduction of deep learning methodologies, along with increased availability of computational power and large, good quality datasets.

A **neural network** is a computational model, consisting of interconnected nodes organized in layers. It processes information by receiving input, applying weights, and passing the result through an activation function to produce an output. Neural networks learn patterns in data through training, adjusting weights based on examples to improve performance. They are widely used in machine learning for tasks like image recognition and predictive analytics. **Deep Learning** is an ML methodology that involves building neural networks with many dense layers of neurons and often complex architectures.

In recent years, generative AI, a new subclass of increasingly powerful and versatile models capable of creating realistic and diverse content across various domains. Members of this subclass are **Large Language Models**, neural networks using the autoencoder / transformer paradigm with attention mechanisms. They have a high capacity to learn complex patterns and relationships within language, allowing them to generate coherent and contextually relevant text output and currently power highly capable chatbots and virtual assistants.

Veterinary Applications

Machine learning (ML) models are frequently utilized as the primary statistical tool in veterinary peer-reviewed literature, often replacing traditional modeling techniques. These models offer significant advantages: they handle highly multidimensional or multimodal datasets effectively, scale well with large data volumes, are computationally efficient, and can be seamlessly deployed in real-world applications beyond just research papers. Some examples are mentioned here, primarily representative of the different methodologies used. Boosted trees have been used to train a model that can be used as a diagnostic tool for Addiston's disease in dogs[1]. The resulting algorithm outperforms other screening tests based on routine laboratory blood work. Random forests were applied in the prediction of MMVD in canine electronic health data[2]. Bayesian networks were used to build a model of FCV on epidemiological data (electronic health records) with better performance compared to classic regression methods[3]. A shallow neural network demonstrated strong predictive accuracy in estimating the risk of CKD in cats[4]. These cases have one important thing in common data-wise. They are based on structured tabular data, invariably of low volume.

Without a doubt however, the biggest contribution of AI in veterinary medicine comes when applied to image data. In radiology / diagnostic imaging, the use of Deep Learning by way of training convolutional neural networks has allowed for applications in object detection and semantic segmentation (e.g., highlighting and classifying specific lesions in radiographs) in all imaging modalities. These models have proven repeatedly to be highly accurate[5,6] and they have been integrated into several commercial applications. Radiographs taken will be automatically annotated with suggested findings, allowing the veterinarian to accept or reject them and if needed escalate diagnosis to certified professionals. In cytology and most importantly, pathology, the early adoption of whole slide scanning has made available large datasets for training models of the same type. Advances in using AI in these fields, however, are lagging, possibly because of data quality and complexity issues. AI models have been extensively used in pathology research however, with only a few limited examples of commercial use in large laboratories. Image data has been used to train AI models using simple photographs for dermatologic diagnosis[7], and CNNs have been integrated in devices that can perform urine sediment and fecal sample analysis.

LLMs have been deployed already in many applications in everyday office software as assistants as well as customer support and education chatbots in many businesses. Huge investments are being made in developing and integrating this technology and this trend is bound to continue. In veterinary practice, they can be used as tools for quick information retrieval for veterinary staff as their capability to summarize and provide contextually correct information in unparalleled. They will assist with client communication, such as appointment

reminders, follow-up instructions, or educational materials on pet care. While these are often just implementations of generic LLMs, integrated in existing software, their impact on the quality of life of veterinary staff cannot be understated. In large scale applications, the usage of Retrieval Augmented Generation architecture can solve many of their limitations (hallucinations, unclear terminology, and others).

While note taking can be significantly facilitated using AI tools that convert text to speech, a significantly more important application could help codifying electronic health records, in a fashion much like what is used in human medicine (e.g., SNOMED-CT). Applying that at scale in large veterinary hospitals or groups can help with accessibility, coordination, efficiency and most importantly allow for better integration and analytics of large patient record datasets. Extracting codified information from clinical records will support queries and retrospective studies in the field of epidemiology and treatment efficacy. DeepTag[8] and VetTag[9] have shown there is potential in this area, by applying long short-term memory neural networks and transformers respectively but more work is needed.

Future

The field of AI and its applications are going to improve and develop with increasing speed and sophistication in the near future. Further integration of these models in existing software and some devices is going to generate more value for the veterinary practitioner and allow for previously intractable problems in research to be addressed. To fully leverage these technologies in both practice and research, it is essential to understand their limitations and how they can be mitigated. It is essential to incorporate in our everyday information diet the study of these advances in both human and veterinary medicine and to follow the opinion and insight of key figures in the field.

DEEP LEARNING IN VETERINARY IMAGE ANALYSIS (CHALLENGES AND OPPORTUNITIES)

Thursday 12 September | 14:30 - 16:30 | MC 2 - Room C

Theodoros Petanidis
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Introduction

This presentation dives deeper into the world of convolutional neural networks, describes their fundamental architecture and introduces the audience to the art of using large datasets to train them. It considers medical images as just grid data, irrespective of their source, be it diagnostic imaging, pathology, or cytology. In a discussion about the fundamentals of computation, data structures and feature extraction from the core techniques remain consistently powerful regardless of if they are applied on an X-ray or a scanned blood smear. Its objective is to provide a better understanding of how these models operate and how classical statistical principles are applied in evaluating their performance, ensuring that their predictions are both accurate and reliable. By the end of it, this presentation aims to have provided a robust foundational knowledge of deep learning and help creative thinking about the potential application and advancements in the field.

Anatomy of a convolutional neural network

CNNs constitute a specialized type of artificial neural network designed specifically for processing structured grid data, such as images. Their design consists of several key components, each playing a vital role in the network's ability to learn and make predictions. The **input layer** is the starting point of a CNN, where the raw pixel data of the image is received. This data is typically represented as a matrix of pixel values for grayscale images or a set of matrices for color images, with one matrix for each color channel (red, green, and blue). Computationally, what is taking place is basic matrix manipulation (linear algebra).[1] This makes certain types of hardware much more suitable for parallelizing such operations (GPUs vs CPUs)[2].
Convolutional layers are the core of these networks and apply learnable filters (kernels), or feature maps from previous layers. Kernels slide over the input, performing a convolution operation that produces a feature map. This map highlights features such as edges, corners, and textures. This process is inspired from observations of the primary visual cortex of animals (in particular, cats), specifically the simple cells that respond to basic visual stimuli patterns. The analogies with biological learning systems stop there, however. Following each convolution, **activation functions** like the Rectified Linear Unit (ReLU) are applied. This introduces non-linearity so the network can capture complex patterns including the intricate details in medical imagery[3].
Pooling layers reduce computational load and introduce feature refinement. They downsample the feature maps by summarizing the presence of features in local patches. This operation reduces the spatial dimensions of the data but preserves the most significant features, increasing robustness to input variation. The network's high-level reasoning is performed at the **fully connected layers**, where each neuron is connected to every neuron in the subsequent layer. The flattened output from the convolutional part of the network is processed into the final output (**output layer**). This is where the features learned from the convolutional section are synthesized into the final decision. A final SoftMax activation function is used to produce the final output, representing a probability distribution of different classes. All these components constitute a learnable hierarchical structure that starts from basic features and progressively builds complex representations[3].

Transfer Learning

It is important to note that in most applications in medical image analysis, these models are not trained from scratch. Most often, pre-trained models are used, initially developed on extensive datasets like ImageNet[4], to jumpstart the training process for new tasks related to medical image analysis[5]. These models can already extract key features from imagery (they can see edges, understand shapes) but they are usually trained on images of everyday scenes. In transfer learning, these models are further fine-tuned using data from the specific domain they are going to be deployed on. In simple terms, their last few layers are ablated and replaced by naive ones that are retrained. This process enhances performance, reduces training time, and accommodates scenarios where limited medical data may be available. This approach plays a pivotal role in accelerating the development of accurate and robust models tailored to medical imaging tasks, highlighting its importance in advancing healthcare technology.

Data Augmentation

By artificially expanding the size of the training dataset through various transformations, such as rotation, flipping, scaling, and adding noise, data augmentation helps expose the model to a more extensive range of variations and scenarios. Detailed awareness and curation of the distribution of available examples in the dataset becomes important as, at this stage, unwanted biases can be introduced. If adequate care is taken, this process not only boosts the model's ability to generalize well to unseen data but also aids in preventing overfitting, where the model memorizes the training data instead of learning meaningful patterns. In computer vision tasks, especially in medical imaging, where datasets may be limited or imbalanced, data augmentation serves as a valuable tool to enhance the diversity and representativeness of the training data, leading to more accurate and reliable model predictions.

Task characterisation

The most basic, foundational task for CNNs is image classification. The model receives an input image and predicts the most suitable class or label that represents the content of the entire image. This task is commonly used for applications such as identifying objects in images, recognizing scenes, and categorizing images into predefined classes. Image classification is a foundational task in computer vision and serves as the basis for more complex tasks like object detection and semantic segmentation. In object detection, the model is trained to identify multiple objects within an image and draw bounding boxes around them to pinpoint their locations. Object detection algorithms typically output both the class labels of the detected objects and their corresponding bounding boxes. Finally, semantic segmentation takes one step further and provides a more detailed understanding of the image by assigning a class label to every pixel. This fine-grained segmentation allows for semantic understanding of the picture and effectively goes from saying "there is legion of type X somewhere in this box" to saying, "this here is a legion of type X." Understandingly, the richness of data needed to train for these tasks is increasing. One needs one label per image for classification, one label per object for object detection and one label per set of pixels (mask mapping) for semantic segmentation.

Model Evaluation

Metrics used for model evaluation include accuracy, precision, recall, and F1 score. They will qualitatively assess the model's ability to correctly classify images, identify objects accurately, and delineate boundaries effectively. Techniques like confusion matrices and ROC curves help analyze classification errors and discriminative ability between classes. Furthermore, visual inspection and qualitative analysis play a vital role, particularly in tasks where interpretability and visual fidelity are crucial. Visualization techniques like heatmaps, activation maps, and class activation mapping help elucidate the model's decision-making process, highlighting regions of interest and providing insights into its internal workings, making it less of a black box[6]. This also fosters transparency and strengthens confidence that the model's reasoning is sound and matches expectations.

It's all about the data

At this point it becomes evident that while data scientists have quite some freedom in choosing or designing their own network to learn from medical imagery, data quality and volume are

equally (or even more) important. While digital imagery is available in large volumes these days, well curated and carefully labelled data is not, even though this is improving, especially in the field of radiology. While using natural language processing to extract features from the clinical records accompanying diagnostic images can provide reasonably accurate annotations this is not always possible or effective. The complexity and variability of medical conditions across different patients contribute to the need for diverse and well-curated datasets, further complicating the acquisition of labeled data for training robust computer vision models in medical imaging applications[7]. Addressing these challenges requires collaboration among healthcare institutions, data annotators, and technology developers to overcome data scarcity and ensure data quality. Understanding how best to manage good annotation efforts is key in extracting value from the immense amounts of data stored in the veterinary field that sits unexplored.

Model deployment

While developing an ML model itself will be the sole objective of a study where we need to summarize, understand, and describe a biological process beyond just describing our observations, that is not the type of exercise that is important in computer vision. Given a model that detects for example a specific type of cell in an FNA smear, we want to expose it to new smears and detect or count these cells. For that we need the model in a frozen state, where its weights and biases are not modified anymore. In that stage, CNNs are nothing more than a large matrix that contains none of the information used to train it but constitutes the distillation, the essence of what it has learned (in our example, an abstraction of how this specific cell looks like). It can be easily integrated into existing software or act as a standalone local or remote API itself. Executing inference from it is a computationally much easier task than training.

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ETHICAL DILEMMAS OF AI APPLICATIONS IN VETERINARY MEDICINE

Thursday 12 September | 14:30 - 16:30 | MC 2 - Room C

Michail Zavlaris

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AI is considered the fourth industrial revolution, predominantly because its applications in communication technologies, engineering, and medicine have profoundly changed these fields in the last ten years[1,2]. Although AI is applied in many veterinary medicine disciplines, e.g. oncology, radiology, and clinical or anatomic pathology, the ethical concerns are only discussed in small paragraphs of the papers published.

AI veterinary ethics rely on the unique bond between the client, the patient, and the vet, and are slightly differentiated from the ethical responsibilities and values that derive from the two-way relationship between the human patient and its practitioner[1]. Ethical dilemmas are occasionally listed in papers, with the main concern being the *transparency* of how data is used to build an AI model[3]. Vets may not be fully aware of how this data is processed by the technology developers and most importantly if the data used to treat an algorithm is trustworthy enough to justify their AI-guided decision-making process. In addition, the *security* of data used in algorithms' training and matters of ownership and handling this information, pose considerable dilemmas, as sensitive and private information may be leaked[1,3]. *Trust and distrust* in AI outcomes derive from concerns that vets or clients may have when opaque procedures are used to provide an outcome. When developers train algorithms, they use data processed by opaque methods (black box systems)[1,2]. Therefore, the final AI tool they create may suggest treatment approaches that cannot be fully evaluated for their accuracy by veterinary professionals[1,2,3,4]. As the quality of the input to treat algorithms has a considerable effect on the quality of the output, vets may be skeptical and may face dilemmas when assessing an AI-treated result[4]. Another concern is about the risk of *overdiagnosis* or the identification of harmless conditions by AI applications. The latter may lead to the unnecessary use of medications and might raise concerns about financial gain from AI firms or other stakeholders[3]. The *autonomy of clients* in making unbiased decisions on the treatment or euthanasia of their pet may be affected by the plethora of information available or not available, the lack of understanding of how AI tools make suggestions, and consequentially affecting their consent in surgical procedures or end-of-life decisions[2,3]. In addition, the extensive use of AI models in practice may prevent vet professionals from *losing their skills* as the demands of the high work volume may lead vets to rely more often on technology tools[3]. The *responsibility gap* is also a major ethical dilemma as poses liability questions when a wrong and harmful outcome for the animal arises if an AI tool is applied in diagnostic and/or treatment processes[3]. Liability may fall on many parties, such as engineers, firms, vets, regulatory bodies, and owners. However, the veterinary client and patient relationship is key in accountability and liability matters[3]. When

medical errors occur, a robust root-cause analysis should be applied to identify the liability of harming[1,4].

The establishment of a concrete, independent regulatory body or framework, with defined authorities in validating AI products and managing ethics, is an urgent need in the veterinary profession[1,4]. This uncertainty, and lack of guidelines, raise questions on how data can be shared or sold, who owns the data when an algorithm is developed, and if data owners have a share in any profits when an AI product is marketed[4,5]. The latter indicates that data holds immense value nowadays and resembles a new currency or a potential investment tool, if sellable. Veterinary ethics outline that vets should prioritize the welfare of animals, safeguard medical information, and continue to apply innovative knowledge and new skills for the animals' benefit, so logically, these rules could also be aligned with AI ethics[4]. In addition, tech innovators may be unfamiliar or insensitive to healthcare policies or ethics. Therefore vet professionals' input from the developmental stages to the deployment of any innovative product and participation in training should be strongly considered[1,2,3,5,6].

The establishment of a regulatory body in veterinary AI ethics is considered an emerging necessity[4,7]. The latter will require extensive consultations between veterinary associations, specialization colleges, veterinary market regulators, academia, government authorities, and veterinary corporations[4]. The rule of "do no harm" should influence vets' decisions, who should constructively challenge AI applications[4]. A lack of transparency in the use of data from AI firms may lead to a lack of trust, which will challenge the vets' and clients' relationship and could jeopardize the animals' health and welfare.

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VETERINARY SUSTAINABILITY SCAN: INSIGHTS FROM THE NETHERLANDS

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Summary

Introduction
The climate is changing, therefore we should take action. Carbon dioxide emissions are higher than ever and temperatures are rising as can be seen in figure 1 and 2 (1, 2). Besides temperature rising there is problems to tackle such as pharmaceuticals that are being released in our water and antibiotic resistance (3, 4).

Why we should not be afraid of the future
According to a survey conducted by The Lancet more than 50% of people aged 18-25 do think humanity is doomed (5). Dr Hannah Ritchie, senior researcher at University of Oxford and editor and lead researcher at Our World in Data, describes this as a problem. We should be optimistic and come into action. In The book Not the End of the World Hannah Ritchie describes the world problems we encounter and how we can be the first generation to build a sustainable planet (6). She uses statistics to explain how we are working towards solutions. We are on the right track, but the pace needs to increase drastically.

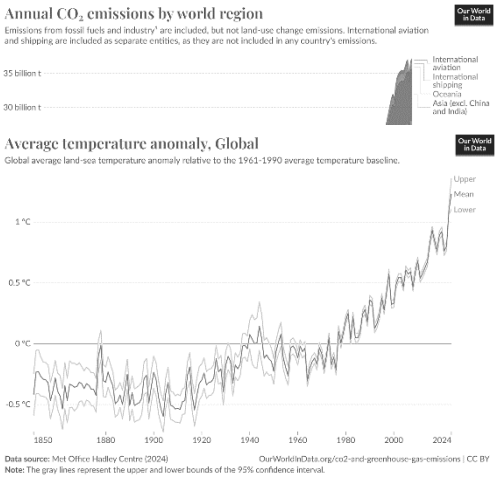

Figure 2. Average temperature anomaly, Global (2)

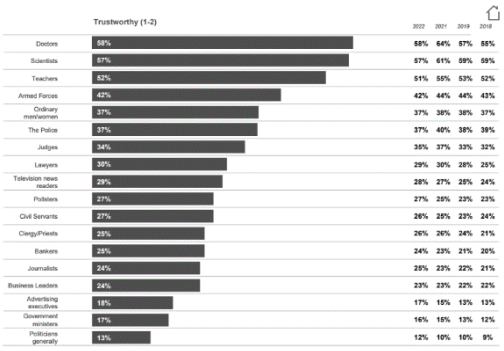

Figure 1. Trustworthiness of different professions (7)

Why veterinarians should get involved
Besides the impact a veterinarian can make on a personal level, veterinarians can also act as a trusted authority. According to the global trustworthiness index 2023 by Ipsos doctors and scientists are the most trusted professions, see figure 3 (7). For this reason it is important to speak out about sustainability and emphasize the urgency to change. Veterinarians can act as ambassadors for the one health principle, working towards a healthy planet for animals, people and society.

Sustainability scan from The Netherlands
Different organisations have been working on a sustainability scan for veterinary practice in The Netherlands. Stakeholders involved were Aeres University of applied sciences, The Dutch Green Veterinary Foundation and the Dutch Royal Veterinary Association.

Conditions of this project were:
The scan had to be fairly simple and quick to complete (30-60 minutes) for someone with practical knowledge.
The scan therefore could not and should not be complete.
The scan also had to immediately provide information and tools on how and with which improvements could be achieved.
The scan is intended for the individual practice. Particularly due to large differences between practices, mutual comparison (benchmarking) is not (yet) possible.

The first version was made in 2023 based on a bachelor thesis project (8). In 2024 a practical tool in excel was generated, which made it possible to download the tool and instantly use it. A pilot was conducted among about 15 practices to use and assess the scan in spring 2024. We also had a number of experts assess the scan on a number of individual components. The current version was created with the information we received in these ways and was launched in May 2024. The goal was to provide practitioners in the Netherlands with a useful tool with which they can use to monitor practice in terms of sustainability.

The scan is available in Dutch for free via The Dutch Green Veterinary Foundation (9). We are looking into the possibility to translate the tool to English to make it more accessible internationally. Usability of the tool outside the Netherlands should be evaluated and can be different in other countries. The organisations involved have not received any financial support from companies or organizations in the creation of this sustainability scan. Sometimes information links in the scan refer to companies or organisations. These links are solely because of the relevant information that can be found there.

Working together is key
At the Dutch national congress on sustainability in healthcare it became clear that we as veterinarians can learn a lot from what they have learned in human health care already. Why should we go and reinvent the wheel? It is important to work together on this topic and learn from each other. And besides, human doctors can learn a lot from veterinarians regarding sustainability. For instance, regarding reusing materials or the packaging of materials. In collaboration with different health care workers striving for sustainable health care in the Netherlands the book 'Groene planeet, groene zorg' is written, which translates to 'Green planet, green care' (10). Unfortunately, for people outside the Netherlands, the book is only available in Dutch. However, the authors intend to provide an English translation so that healthcare professionals in other countries can also be inspired.

Three take aways are highlighted by the authors at the end of 'Groene planeet, groene zorg'.

The most sustainable care is care not provided that does not need to be provided

The most sustainable way to go is not prescribing unnecessary treatments. Are the antibiotics we use always necessary? That is what we have to question every time we subscribe medication. And what are the limits of our treatments? Is it ethical for us to decide to do a hypophysectomy in a dog? Such limits are hard and difficult to determine, since nowadays animal healthcare is becoming increasingly advanced and more and more is possible. But should we do everything possible at the expense of the world? Where do we draw the line?

Making the planet more sustainable can be done at any level: weigh up impact and feasibility

In our daily life there are different types of settings where we can act more sustainable. For example in your private life you can choose to cycle instead of taking the car for short distances.

Or you can choose to eat more plant based proteins. At your workplace you can discuss sustainability and weigh options and try to convince others to make a change in working policies. Ofcourse we can try to change national laws, or even EU laws, but those changes will take a lot of time. 'Groene planeet, groene zorg' gives insight in what things you can do at each level to make an impact and gives away insights on impact and feasibility. Impact is different for all kind of actions, the same applies for feasibility. For example, feasibility of changes in our private life is easier than changes at the company we work at, or when we want to change EU laws.

Together we are strong

We need the system to change, from pharmaceuticals to pet owners. Every role in this system and the actions involved have an impact. We should work together to make the world more sustainable. If enough people are involved in this movement, then changes will accelerate. Besides the neccessity, such a movement connects, is fun and gives hope and energy.

In short: what can we do as veterinarians in terms of sustainability
Work together: together we are strong and can accomplish more than alone.
Take action: try to stay positive and take your responsibility where possible. Use tools provided by organisations such as Vetsustain or The Dutch Green Veterinary Foundation. Every small contribution will make a change and eventually will make the movement to sustainability more convenient.
Be optimistic: change takes time, be optimistic, spread positivity and try to change.

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Environmental Impact of Veterinary Medicine

Thursday 12 September | 17:00 - 19:00 | MC 2 - Room C

Dr ir Ivo Roessink

Wageningen Environmental Research, Wageningen, The Netherlands

Companion animals are regularly treated with antiparasitics and other pharmaceuticals. Once applied on the animal these compounds also find their way to the environment. As antiparasitics such as imidacloprid and fipronil also have a use in agriculture, much is known on their impact on populations and ecosystems. Lately, alarming reports have indicated that concentrations in surface water of these compounds are exceeding ecotoxicological standards and effects on populations can be expected. As these findings originate from waters heavily impacted by sewage treatment effluent, an agricultural origin is less likely and wash off from companion animals is regarded being the most likely source. This finding is corroborated by UK sales figures showing a decline in agricultural use after the ban in this sector but an increase in veterinary use of these compounds. Currently the use of izoxazolines is increasing and experiments have shown that, although less than imidacloprid and fipronil, these next generation antiparasitics can also transfer from companion animals to the environment. Having little to no information on their ecotoxicological profile does not necessarily make this an improvement in the context of environmental safety. As behavioral problems in companion animals are sometimes also treated with antidepressants, these pharmaceuticals are also excreted and reach environmental compartments. As these compounds are still biological active they still have impacts on non-target organisms in water and soil. Although companion animals have a huge benefit for human well-being, they have an unexpected detrimental impact on our environment via the chemicals they 'leak'. Although treatment of the animals is a necessity, better managing their waste, swimming behavior and discarded hairs can greatly reduce their environmental impact.

CREATING POSITIVE INTERACTION WITH ANIMALS IN THE PRACTICE

Thursday 12 September | 14:30 - 16:30 | MC 3.4 - Room D

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INTRODUCTION

Have you ever imagined what it would feel like to be grabbed while you were sleeping, put into a box and then driven to an unknown location where you could smell unpleasant smells and hear other humans screaming? Am I right to say that most people in this situation would be ready to attack anyone who approached or tried to restrain them? However, everyday, millions of companion animals are transported to unfamiliar and often unpleasant places, such as Veterinary Hospitals, Hotels or Shelters. If these animals are fearful and uncertain about the outcome of their ordeal is it realistic to expect them to be calm, quiet and co-operative with us as veterinary practices simply because we are working for their health and welfare! In a busy practice it is not unusual to have a "house full" of patients and feel under pressure to speed up our procedures and do our "good" work quickly, even if that results in us holding these animals in uncomfortable positions and using techniques that are motivated by the desire to get the job done! Some will say that friendly techniques take too long, but in reality respecting the emotional needs of out patients will lead to cooperation from the patient and make the process much faster in the future.

It can be argued that the handling techniques have been used for many years but that is not a reason to continue if the evidence is that these approaches can result in injury to practice staff and emotional trauma to the patients. Dog bites and cat bites and scratches are the most comnmonly reported injuries for veterinary staff and the majority of veterinarians and nurses are bitten or scratched when they are holding or handling their patients using the "old" techniques. I can remember seeing many nurses and vets being bitten because they were convinced that their physical strength was enough to keep the animal under control and used force rather than technique. When the hold failed and they got bitten these people would feel that it was their fault for not using enough force and would keep increasing the strength they used rather than question whether the technique was right.

Within the veterinary context the aim of handling patients is to deliver treatment which is intended to make the animal better, but when the animals are handled with force and speed this aim is compromised and even if the animal returns home in better physical health there is a risk of "behavioural damage". The memory of the "bad experience" can lead the animal to anticipate that it will be "threatened" the next time it comes to the practice and its resulting defensive behaviour can result in practice staff using more forceful techniques to handle it.The danger is that every visit will result in an escalation of the fear and resulting undesirable behaviour until the point is reached that the animal is unhandlable.There is also some evidennce that if the handling experience is particularly traumatising for the patient learning can become generalised such that the animal becomes defensively aggression toward humans in general and not just to practice staff. When we use appropriate techniques we will:

1. Reduce the animal's stress;
2. Reduce human stress (caregivers, veterinarians, nurses, staff);
3. Enhance animal welfare;
4. Avoid potentially dangerous responses (as aggression);
5. Guarantee the minimum interference of stress in the results of tests and examination (leading to an accurate diagnose);
6. Allow appropriate treatment;
7. Improve the relation between caregiver and veterinarian, increasing the level of confidence

FROM HOME TO THE VETERINARY CONSULTATION

The anxiety starts a long time before the arrival at the practice. For many cats, the panic starts when the carrier arrives from the garage. Often the carrier is kept in a place where the cat never sees it and it is only appearing when the cat is being removed from its comfort and safe territory. As a result the carrier is a sign that something very bad is going to happen. For this reason it is important to think ahead and take lots of care with the carrier. The carrier and the trip should be seen as a positive event associated with something pleasurable, such as food (counterconditioning – CC). Another option is that the carrier is kept in the household all the time and offered as an hiding place for the cat. In order to make the transportation more pleasant, a blanket with the cat's own scent should be placed inside and/or synthetic phermones should be sprayed. The application of the pheromones, as the spraying liquid has an alcohol carrier, should be made 15 to 30 minutes prior the cat going inside. Finally, remember that the driving style is an added factor for the cat that is inside the carrier (inside the driven car) and driving respectfully is important.

WAITING ROOM

When the client arrives at the veterinary practice his job has been done. Of course the practice has been actively involved in teaching the client how to minimise the stress for their pet during the process of getting it to the appointment but now that the cat has arrived it is the responsibility of the staff to create an inviting and secure environment from the cat's perspective. It is important to ask ourselves *"What does the animal see when arriving at the hospital?"*; *"Are there dogs barking or growling?"*; *"Are there cats vocalizing?"*. These questions apply particularly to the waiting room, but they should also be asked in every different area of the hospital including the consultation room and the hospitalisation ward. A first rule for every waiting room is: cats and dogs must be properly secured and/or restrained. Imagine the stress that can be induced if a dog, even one that is used to cats, walks freely into the waiting room and goes to sniff a cat inside its carrier, or if a cat that doesn't like to be kept inside the carrier and prefers to be on the caregiver's lap suddenly sees an excited dog abruptly approaching! To avoid these complicated situations, we must keep everything under control. If it is not a cat only clinic, than the waiting room should have a specific area for cats and another for dogs. If it is not possible to have two different rooms, at least visual barriers should be created so that the cats can feel more secure (also think about visual barriers between each carrier). A blanket, specially if it has the household scent, could cover the carier giving extra protection to the cat that is inside. The carrier should not be placed on the floor, because from the cat's point of view it is a much more vulnerable position in the presence of potential threats! Synthetic pheromone diffusers should also be plugged in (there can be one for dogs and one for cats, as they are specific for each species).

DURING THE CONSULTATION

Main rule: It is important for the veterinary staff to be seen as the animal's best friends during the consultation! So, let's give the animal what he likes most! Ask the caregivers not to give a big

meal before coming and tell them to bring the favorite treats to be given by ourselves. Some behaviourists recommend that food should be avoided when there is already fear existing, due emotional conflict with desire/seak and fear emotional motivation.

A rule that I recommend to those that work with cats is to have a number of clean towels available. Towels can be the veterinarian's best friend when handling cats. A clean towel should be used for each cat when he is anxious or requires difficult handling. The towel can be lightly heated in a microwave to have a more relaxing effect on the animal. Lifting the upper top of the carrier so it is slighty open enables you to slide a towel in over the bottom half so that the cat is totally covered by the towel. The majority of the cats hide below the towel and allow a complete examination without the need for hard restraint. That towel should not be used for another cat, as it is full of alarm pheromones and will cause distress for the cat that follows. Dr. Sophia Yin developed from this towelling technique her own specific handling style using a "wrap" – www.lowstresshandling.com. Using this restraint technique it is posible to completely avoid the (unfortunately) wellknown *scruffing* technique, which causes more stress and pain. The cat should be given time to get used to the new environment and should only be taken from the carrier when it is necessary. Taking the cat from the carrier must be done very gently and some cats should be examined in the bottom of the carrier, as it gives a greater feeling of safety. Some authors recommmend when the cat gets out of the carrier to a place it where is impossible to see or get in and if necessary let it explore the environment. However, when left to explore an environment very rich in scents, especially in multi-species clinics, many cats can present abrupt changes in emotional state and can respond to these with reactive behaviour. It is important to be aware of potentially "scary" noises that exist in the hospital setting. Water running or a disinfectant spray can be misinterpreted by the fearful cat as another cat hissing and motorised sounds of vaccum cleaners or clippers can be so stressful that the cat reacts with an immediate flight response, which if prevented can turn into a fight response. Unpleasant situations should always be minimized. For instance, always lubricate the thermometer. If the cat has had a previous bad experience it will often be more persistent in its attempts to avoid the procedure. The examination should always start with the less invasive techniques before the more invasive, and the same should be true for the restraint methods. Always start with minimal restraint. The necessary equipment (cotton, needles, syringes, vaccines, etc) should always be prepared and positioned in an easily accesible location before the consultation begins so that it can be easily accessed and used. Refrigerated drugs and vaccines should be taken from the fridge at the beginning of the consultation so that they can be close to environmental temperature before being injected. Treats should be given before and during the procedure. The carrier that was the worst enemy (for some cats) when the cat was at home has now become its best friend. Re-entering into the carrier can work as a positive or negative reinforcement!!! Between consultations the cleaning is very important as many alarm or attack pheromones could be present in the air. Ideally the room should be ventilated, cleaned and then synthetic pheromones should be sprayed on the examination table (in addition to the diffuser that should always be turned on) before the next consultation.

If, despite all our efforts, a fearful or panicking cat is imposible to relax and handle during the consultation, then chemical restraint should be considered. In fact, the sedatives should be given, for better results, before the animal gets more reactive, as their efficacy is higher the earlier they are administred and they should ideally be used before any behavioural changes. Sedation can be required not only to make the consultation easier for caregivers and staff and to avoid unnecessaary injury to them, but also for the health and wellbeing of the animal. Benzodiazepines can be given at home as a good solution (acepromazine should not be used in these cases!). It is important to give a trial dose of benzodiazepine before the consultation day to check the individual reaction of the animal (there are some paradoxic reactions described), and to enable the vet to determine the adequate dosage and time of duration.

Some authors also remind about the desinhibition effect of benzodiazepines that can increase the potential for aggressive behaviour. Gabapentines, Trazadone and Pregabaline (licensed for veterinary use in some countries) are currently some of the most comon drugs used in this cases as most of the side-effects seen in benzodiazepines will not be seen with its use. Also dexmedetomidine and some "cocktails" can be used via the transmucosal route with lots of success.

If we see that there is a behavioural problem during the visit, the caregiver should be informed and given advice as to how this could be improved. In just the same way as when a skin lesion is found we suggest a treatment, if there is a cat that shows signs of fear related to the veterinary consultation it is important to explain to the caregiver that specific treatment will be needed. Behaviour is not easily solved during the routine consultation and it is best to recommend a behavioural modification plan (DS/CC) adapted for each clinical case and supervised by a veterinarian working in behavioural medicine.

HOSPITALIZATION

Exactly the same concerns and recommendations related to the waiting or consultation room should be taken in account if the cat has to be hospitalized at the practice. Once an animal is sick and impaired, it will be more sensitive to the surrounding environment. Each cat should have access to a space for elimination which is separate from the resting or hiding locations. If this separation of resources is not acheived the cat will be distressed and may display unusual or unwanted behaviours such as hiding in the litter tray or eliminating in the dry food bowl. Environmental management which leads to cognitive stimulation is also a way to decrease stress and anxiety in all animals. Finally once the animal is better it will be returning home and once again it is important to prepare for this event. If there are any other cats in the household, a reintroduction plan should be given to the client. Contact between the cats should never be forced. The other cat(s) should be given time to get used to the scent of the arriving cat, before moving on to visual contact and finally direct contact. The returning cat should not be simply taken out from the carrier to go and greet the other(s) and it can help for it to stay inside the carrier for a while (the duration depending on the individual and varying from case to case) with a towel, which has the scent of the household group of cats on it, covering the carrier.

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UNLOCKING THE POTENTIAL: AN INTRODUCTION TO STEM CELL BIOLOGY AND REGENERATIVE MEDICINE

Thursday 12 September | 17:00 - 19:00 | MC 3.4 - Room D

Associate Professor Amir Kol, DVM, PhD, Dip ACVP (Clinical Pathology)

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Regenerative medicine is a rapidly evolving field focused on restoring normal organ and tissue function after injury. It distinguishes between tissue repair—where the injured tissue is replaced by non-functional scar tissue—and true tissue regeneration, which involves the replacement of damaged tissue with native-like tissue that restores normal function. This distinction is crucial for understanding the potential and limitations of current therapeutic approaches.
The field encompasses a variety of techniques, including cellular and gene therapies, tissue engineering, and nanotechnologies. These approaches aim to replace, engineer, or regenerate human and animal cells, tissues, or organs to restore normal function. In this lecture, we delve into the foundational aspects of stem cell biology, with a specific focus on its applications in veterinary medicine.
Learning Objectives:
Describe Defining Characteristics of Stem Cells:
Stem cells are characterized by two key properties: the ability to differentiate into specialized cell types and the capacity for self-renewal. These characteristics make them invaluable in regenerative medicine, as they can potentially replace damaged cells and tissues in the body.
Define Different Levels of 'Potency':
Stem cells vary in their differentiation potential, a property known as 'potency.' The primary levels of potency include:
Totipotent Stem Cells: These cells can differentiate into all possible cell types, including both the embryonic and extra-embryonic tissues. Totipotent cells are found only in the earliest stages of embryonic development (not discussed today).
Pluripotent Stem Cells: These cells can differentiate into all cell and tissue types of the adult organism. They do not give rise to extra-embryonic tissue such as the placenta. Pluripotent stem cells, such as embryonic stem cells (ESCs), can give rise to cells from all three germ layers: ectoderm, mesoderm, and endoderm.
Multipotent Stem Cells: These have a more restricted potential, typically differentiating into a limited range of cells within a particular tissue type or organ. Examples include hematopoietic stem cells, which can produce all the blood cells but not cells of other tissues.
Unipotent Stem Cells: These cells are specialized to produce only one cell type but retain the property of self-renewal, a characteristic feature of stem cells (not discussed today).
Identify Clinical and Research Applications of Various Stem Cells:
Pluripotent Stem Cells: These are crucial in early development and have significant research and therapeutic potential due to their ability to differentiate into any cell type of the adult organism. They are used in research to understand developmental processes and in regenerative medicine to develop treatments for a wide range of diseases, including neurodegenerative diseases, heart disease, and diabetes.
Hematopoietic Stem Cells (HSCs): These multipotent cells are responsible for the continuous production of blood cells throughout life. HSCs are used in treatments such as bone marrow transplants for leukemia and other blood disorders.
Intestinal Stem Cells: Located at the base of the crypts in the intestinal lining, these cells regenerate the gut's epithelial cells, making them crucial for maintaining the gut barrier and

function. They also hold potential in treating diseases like inflammatory bowel disease and other gut-related conditions.

Mesenchymal Stromal Cells (MSCs): MSCs can differentiate into various cell types, including osteoblasts, chondroblasts, and adipocytes, in vitro. They are widely studied for their regenerative properties, particularly their ability to modulate the immune response and promote tissue repair through the secretion of growth factors and cytokines.

Recognize the Current State of Stem Cell Research in Veterinary Medicine: Veterinary medicine has increasingly adopted stem cell research, although it lags behind human medicine in terms of clinical applications. For instance, MSC therapy is being explored for conditions such as osteoarthritis in dogs, equine musculoskeletal injuries, and feline chronic gingivostomatitis. However, standardization in protocols and further research are necessary to bring these therapies into routine clinical practice.

Detailed Exploration of Stem Cell Types and Applications:

Pluripotent Stem Cells: Pluripotent stem cells, such as embryonic stem cells, are derived from the inner cell mass of the blastocyst, a very early-stage embryo. These cells are capable of giving rise to every cell type in the body, making them a valuable resource for regenerative medicine and research. The primary assay used to demonstrate the pluripotency of these cells is the teratoma assay, where stem cells are introduced into an immunodeficient mouse. If the cells form a teratoma containing tissue types from all three germ layers, it confirms their pluripotent nature. Additionally, in animal models, the chimera assay, where stem cells are introduced into a developing embryo, can demonstrate their ability to contribute to all tissues in a regulated, physiologic, fashion.

The discovery of induced pluripotent stem cells (iPSCs), which are generated by reprogramming adult somatic cells to a pluripotent state, has been revolutionary. iPSCs hold the potential for patient-specific therapies, allowing for the development of personalized treatments that are less likely to be rejected by the immune system. However, challenges remain in ensuring the safety and efficacy of iPSCs, as the reprogramming process can sometimes lead to genetic abnormalities or incomplete reprogramming.

Multipotent Stem Cells: Multipotent stem cells are more specialized than pluripotent stem cells and are typically restricted to producing cell types within a specific tissue or organ. Hematopoietic stem cells (HSCs) are a well-known example, responsible for generating all blood cell types. The discovery of HSCs in the 1960s opened the door to bone marrow transplants, a life-saving treatment for various blood diseases.

Another critical group of multipotent cells is intestinal stem cells, which are essential for the continuous renewal of the gut lining. The development of organoid cultures from these cells has provided a powerful tool for studying intestinal diseases and testing new treatments. Organoids are three-dimensional structures that mimic the organization and function of real tissues, making them invaluable for research into gut physiology and pathology.

Mesenchymal Stromal Cells (MSCs): Initially identified for their ability to differentiate into bone, cartilage, and fat cells in vitro, MSCs are now understood to play a broader role in tissue repair. They do not directly replace damaged tissue but instead secrete a variety of bioactive molecules that promote tissue repair and modulate immune responses. This paracrine effect has been shown to enhance the survival and function of other cells, making MSCs a promising tool in regenerative medicine.

Despite their potential, MSC-based therapies face several challenges, including variability in cell quality and function depending on the source and preparation methods. There is also ongoing debate about the most effective delivery methods, tissue source, thawed vs fresh and dosages for achieving therapeutic effects.

Current State and Future Directions in Veterinary Medicine: In veterinary medicine, the use of stem cells, particularly MSCs, is being explored for a variety of

conditions. While promising results have been reported in the treatment of osteoarthritis, musculoskeletal injuries, and inflammatory diseases, there is a need for rigorous clinical trials and standardized protocols to ensure the safety and efficacy of these treatments.

iPSC technology is still in its infancy and standard protocols for cellular reprograming, cell maintenance in culture, differentiation protocols and characterization are inconsistent. While iPSC from the 3 major veterinary species (dogs, cats and horses) have been described, much more work is needed before clinical trials could be initiated.

As the field progresses, the development of better methods for isolating, characterizing, and delivering stem cells will be crucial. Advances in genetic and cellular engineering may also enhance the therapeutic potential of stem cells, leading to more effective and targeted treatments.

Conclusion:

Stem cell research holds immense potential for advancing regenerative medicine, both in human and veterinary contexts. By understanding the unique properties and capabilities of different stem cell types, researchers and clinicians can develop innovative therapies for a wide range of diseases and injuries. However, significant challenges remain, including ensuring the safety and consistency of stem cell therapies, understanding the mechanisms underlying their effects, and overcoming regulatory and ethical hurdles. Continued research and collaboration across disciplines will be essential in realizing the full potential of stem cell-based therapies.

POINT OF CARE MESENCHYMAL STROMAL CELL THERAPY IN VETERINARY MEDICINE

Thursday 12 September | 17:00 - 19:00 | MC 3.4 - Room D

Prof Dr Heiko von der Leyen, Maria Kontou, Marjon Gjika, Louiza Maria Gkouma, Emmanouil Simantirakis, Dr Chronis Fatouros

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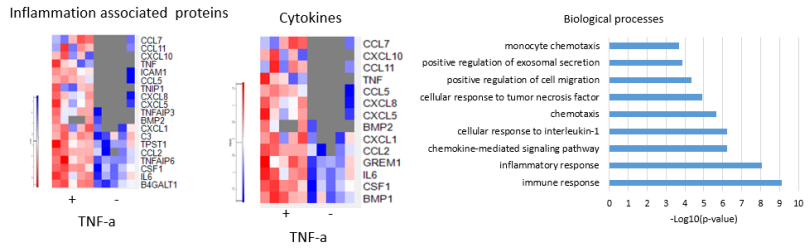
Mesenchymal stromal cells (MSCs) have been referred to as an "Injury Drugstore" [1]. This describes the fact that MSCs home in on sites of injury or disease and secrete bioactive factors that have immunomodulatory and regenerative capacity. MSCs are multipotent cells found in various tissues, including bone marrow, adipose tissue, and umbilical cord blood. They are known for their unique properties, including self-renewal and the ability to differentiate into different cell types such as osteocytes, chondrocytes, and adipocytes. Resident site-specific and tissue-specific stem cells construct new tissue when stimulated by bioactive factors secreted by the exogenously supplied MSCs. The multipotent potential of mesenchymal cells is best illustrated by various terms which were discussed in the past like "multipotent stromal cells" or "medicinal signaling cells", but also "magic signaling cells" [2]. MSCs employ some remarkable properties for therapeutic applications:

- Immunomodulation: MSCs possess potent immunomodulatory capabilities, making them invaluable in treating autoimmune disorders and inflammatory conditions. They can dampen excessive immune responses, reducing inflammation and tissue damage.
- Regeneration: MSCs can differentiate into various cell types, making them a valuable tool for regenerating damaged tissues and organs. This potential is particularly promising in treating injuries, degenerative diseases, and conditions like osteoarthritis.
- Low immunogenicity: MSCs exhibit low expression of major histocompatibility complex (MHC) molecules, reducing the risk of immune rejection when used in allogenic (from a different donor) transplantation. This makes them a feasible option for off-the-shelf therapies.
- Safety profile: clinical trials and research have shown a favorable safety profile for MSC therapy. Adverse events are relatively rare, making it a safer option compared to other cell-based therapies.
- Wide therapeutic range: MSC therapy has shown promise in treating a diverse range of clinical conditions including osteoarthritis and graft-versus-host disease (GVHD).

Cartil-S is an Orgenesis/Theracell Laboratories proprietary ATMP product for the treatment of osteoarthritis based on autologous MSC. Proteomics analysis of the secretome from Cartil-S indicates its mechanism of action to involve regulation of cellular responses to IL-1, modulation of pro-inflammatory response, and chemokine-mediated signaling (Fig 1).

Proteomics data supporting claimed mode of action for Cartil-S



theraCell Advanced Biotechnology

Fig 1

According to Article 2(1) of Regulation (EC) No 1394/2007 EMA/CAT designated MSC products as advanced therapy medicinal products (ATMP). MSC-based products have become one of the most clinically studied cell therapy candidates, in particular employing autologous applications. Clinical products include indications like limbal stem cell deficiency due to ocular burns, graft-versus-host disease, complex perianal fistulas in Crohn's disease or spinal cord injury.

Autologous MSCs cell therapy has been extensively used for the treatment of knee osteoarthritis and for localized cartilage damage. Reduction of pain associated with OA and improvement of the quality of life for patients receiving MSC therapies have been well documented in numerous clinical trials [3]. Cartil S has been administered to over 100 patients in the period 2015-2020. The collaborating health care providers (orthopedic surgeons) obtained the medicine directly from the manufacturer before marketing authorization, on an individual basis under their direct responsibility. A retrospective analysis of the treated patients showed at 12 months follow up that 98.5% of the joints pain score improved, 58.9% of the joints improved in extension range, and 73.9% of the joints improved in flexion range. Furthermore, 82.8% of the joints showed an overall improvement higher than 70%. The intra-articular injection of AD-MSCs was well tolerated.

In veterinary medicine the clinical application of MSC-based therapies has been focused mainly on clinical indications in dogs and horses, e.g., the treatment of the musculoskeletal system (tendons, ligaments, and joints) diseases and osteoarthritis. Additionally, MSCs are being used in recurrent airway obstruction in horses, while in cats and dogs, there are attempts to use them in digestive system disease (inflammatory bowel disease) and chronic kidney disease [4].

For therapeutic applications, MSC are manufactured from adipose tissue becoming the most common source of MSCs by surgical sampling. We have developed a minimally invasive collection of adipose tissue biopsy (~1gr) which allows an expansion of 50-90 million cells within ~2 weeks (2 passages lipoaspirate as starting material). The use of a minimally invasive process allows to obtain an arguably very small amount of starting material (less than 1g of tissue, intact adipose tissue, not fat lipoaspirate), the tissue architecture is preserved, and metabolic activity of source cells is optimal at time of MSC extraction. The process is not aggravating for the patient, carries a far lower risk of contamination than the liposuction process, and MSC are isolated and expanded in a short time (<10 days). The MSC product consists of 20 million cells with high purity supplied fresh for intra-articular injection within 24 h. Stability of the cells at 2-8 °C is established for up to 36 h post-filling of the syringe. The product has been developed and adapted to EU-GMP manufacturing standards.

MSC products are regulated as Advanced Therapy Medicinal Products (ATMP) like human cell therapies, because culturing of cells exceeds minimal manipulation. Good Manufacturing Practice (GMP) guidelines must be followed, QC tests and product release by a qualified person are mandatory. Thus, the production of MSCs for therapy can be expensive and time-consuming. Scalability and cost-effectiveness have been a challenge for widespread adoption of cell therapy, especially at point of care.

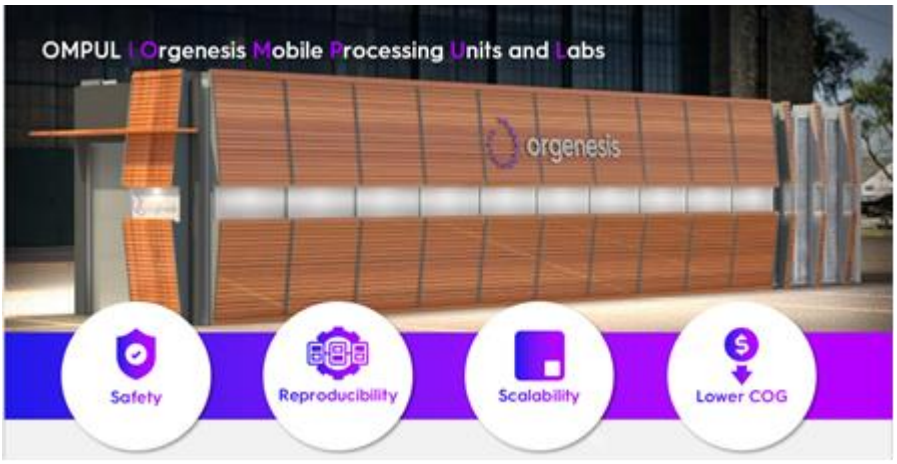
As a solution for this challenge, a deployable platform for point of care (POC) manufacturing and delivery can provide a high-quality, standard, efficient, and scalable pathway for production and distribution of advanced therapies, making them available to a large number of patients quickly and at reasonable cost. Ideally, such a POC platform would be designed around a harmonized, decentralized manufacturing model based on a dedicated network of clinical sites, and wherever possible, by leveraging proprietary disruptive manufacturing infrastructures and technologies, thus enabling agile manufacturing [5]. Disruptive manufacturing technologies are designed to harmonize and optimize the decentralization manufacturing. It covers both the manufacturing environment requiring highest quality

standards, and the efficiency and scalability of the manufacturing process itself. Availability, affordability as well as accessibility are the corner stones of the realization of such cost-effective cell treatment:

- Availability: developing and optimizing cell processing for cell and gene therapy that are designed to be produced in closed, automated technology systems, reducing the need for high grade cleanroom environments.
- Affordability: Decentralized manufacturing in closed systems eliminates complicated logistics and reduces manufacturing failure risk and the high cost of manual processing. Standardization and harmonization of automated closed systems that are customized for each therapy and available as a total manufacturing solution that ensures consistent quality and supply.
- Accessibility: Mobile manufacturing environment solutions available for rapid on-site deployment without the need for expensive infrastructure. A global collaborative POCare Centers Network can serve local leading hospitals and medical centers applying cell and gene therapy; the required automation provides an inherited distribution channel for existing and future therapies.

Orgenesis has designed and developed a production framework according to applicable international quality standards. It has transformed the traditional fixed ("brick and mortar") production room into a mobile, harmonized unit: the Orgenesis Mobile Processing Unit and Lab (OMPUL) that can easily be deployed throughout a POCare Network [6]. OMPULs are designed to enable parallel processing of CGT products in a safe, reliable, and cost-effective manner at the point of care. CGT products manufactured in OMPULs may be used in validation studies, clinical trials, or, after approval, as marketed clinical therapies. The OMPUL design delivers an industrial scale solution. An OPMUL can be configured and deployed for use as the GMP manufacturing unit, quality control lab, or warehouse, or as a connector between different working OMPULs (Figure 2).

Fig 2: OMPUL



In conclusion, mesenchymal stromal cell therapy holds great promise in regenerative medicine and the treatment of various medical conditions. Its immunomodulatory properties, regenerative potential, and relatively favorable safety profile make it an attractive avenue for research and clinical application. Early biobanking of MSCs in animals who are prone to degenerative joint diseases will allow to have so-called "young" MSCs readily available for regenerative treatment later if required. Decentralized manufacturing and automation will enable a cost-effective provision of MSC products, thereby allowing cell-based therapies at a large scale at point of care.

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ROUND TABLE LEISHMANIOSIS – THE EVER-CHANGING STATUS: AN UPDATE ON DIAGNOSTICS

Friday 13 September | 08:30 - 10:30 | Amphitheater N. Skalkotas - Room A

- ***LEISHMANIA INFANTUM* CO-INFECTION: PATHOGENESIS AND CLINICOPATHOLOGICAL MANIFESTATION**
  Gaetano Oliva & Laia Solano-Gallego

- **CLINICAL ORIENTED DIAGNOSTIC APPROACH TO LEISHMANIOSIS**
  Laura Ordeix Esteve & Laia Solano-Gallego

- **WHAT METHODS SHOULD BE USED TO DIAGNOSIS LEISHMANIOSIS? Serological and molecular diagnostic methods: advantages and pitfalls**
  Luís Cardoso & Patrick Bourdeau

*Gaetano Oliva[1], Laia Solano-Gallego[2], Laura Ordeix Esteve[3], Luís Cardoso[4], Patrick Bourdeau[5], LeishVet**

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**The LeishVet association consists of a group of veterinary scientists from academic institutions in the Mediterranean Basin and North America with a primary clinical and scientific interest in canine and feline leishmaniosis. Its main goal is to improve the knowledge on different aspects of leishmaniosis in veterinary medicine and public health, including the development of consensus recommendations based on recent evidence-based literature and clinical experience that would represent the most current understanding of Leishmania infection in dogs, cats and other animals.*

Canine leishmaniosis due to the protozoan parasite *Leishmania infantum* is a global zoonosis potentially fatal to dogs, which represent the main reservoir of infection to humans and other animals. It is endemic in geographic regions of southern Europe, Africa, Asia and America, but also represents an important concern in non-endemic countries due to the movement of sick or infected dogs. The incubation period (i.e. from infection till the appearance of clinical signs) ranges from a few months to several years, but with the majority of infected dogs are apparently healthy. The clinical features of leishmaniosis vary widely as a consequence of the numerous pathogenic mechanisms of the disease process, the different organs affected and the broad range of immune responses by individual hosts (Baneth et al., 2008; Solano-Gallego et al., 2011).

Infection may involve a variety of lymphoplasmocellular and granulomatous inflammation, associated with the presence of *Leishmania* amastigotes within macrophages, and harmful immune-mediated responses, and susceptibility to the disease is influenced by a complex genetic basis (Baneth et al., 2008; Solano-Gallego et al., 2017). In lymphoid organs, areas of T cells become depleted, while areas of B cells expand. A very important pathogenic phenomenon of the humoral response is the formation of circulating immune complexes and among the lesions produced by their deposition uveitis stands out and, in particular, membranous, membranoproliferative, mesangial or focal-segmental glomerulonephritis. Glomerulonephritis and tubulointerstitial nephritis are the most common pathological findings, with the former frequently associated with the glomerular deposition of immune complexes and being mainly membranoproliferative and/or mesangioproliferative (Solano-Gallego et al., 2009).

Canine leishmaniosis is a multisystemic disease that may potentially involve any organ or tissue and is manifested by nonspecific clinical signs, making the list of differential diagnoses wide and extensive. The most common clinical manifestations found are cutaneous lesions, which may be seen along with other clinical signs, including localized or generalized lymphadenomegaly, weight loss, decreased appetite, lethargy, pale mucous membranes, splenomegaly, cachexia, polyuria and polydipsia, fever, vomiting and diarrhoea, but also ocular and other clinical manifestations (LeishVet, 2024a). Renal disease may be the sole clinical manifestation of canine leishmaniosis and it can progress from mild proteinuria to the nephrotic syndrome or to an end stage renal disease. Chronic renal disease is a severe result of disease progression and the main cause of mortality due to canine leishmaniosis (Solano-Gallego et al., 2011).

Clinicopathological abnormalities associated with canine leishmaniosis include mild to moderate normocytic normochromic non-regenerative anaemia, leukocytosis or leukopenia, thrombocytopathy, thrombocytopenia, impaired secondary haemostasis and fibrinolysis, hyperproteinemia, hyperglobulinemia, hypoalbuminemia, decreased albumin/globulin ratio, renal azotaemia, elevated liver enzyme activities and proteinuria (LeishVet, 2024a).

While subclinical feline infections are common in areas where canine leishmaniosis is endemic, clinical illness due to *L. infantum* in cats is less frequent than in dogs. The most common clinical signs and clinicopathological abnormalities compatible with feline leishmaniosis include lymph node enlargement and skin lesions such as ulcers or nodules (mainly on the head or distal limbs), ocular lesions (mainly uveitis), feline chronic gingivostomatitis syndrome, mucocutaneous ulcerative or nodular lesions, hypergammaglobulinemia and mild normocytic normochromic anaemia. Clinical illness is frequently associated with impaired immunocompetence, as in case of retroviral coinfections or immunosuppressive therapy (Pennisi et al., 2015; LeishVet, 2024b).

The diagnosis of canine and feline leishmaniosis is complex due to its variable and non-specific clinical spectrum and clinicopathological abnormalities (Miró et al., 2008; Pennisi et al., 2015; Solano-Gallego et al., 2017). A thorough and integrated approach needs to be adapted for each patient when assessing the suspicion of this disease. In addition, dogs and cats with leishmaniosis might be co-infected with other vector-borne diseases or suffering from other concomitant infectious or non-infectious diseases making the differential diagnoses more complicated and diverse (Peniisi et al., 2015; Solano-Gallego et al., 2011).

Pertinent clinical history, a thorough physical examination and several routine diagnostic tests such as complete blood count, biochemical profile, urinalysis and serum electrophoresis can help to raise the suspicion index for this disease. Other diagnostic tests such as coagulation profile, radiographs, abdominal ultrasound, cytological and histological evaluation of tissues or biological fluids would be performed on an individual basis. Several specific diagnostic

techniques have been developed to facilitate diagnosis. It is essential to understand the basis of each diagnostic test and its limitations and appropriate interpretation (Pennisi et al., 2015; Solano-Gallego et al., 2011; LeishVet, 2024 a,b).

Diagnosis is usually attempted out for two main reasons: (i) to confirm disease (i.e. to find out whether a dog or cat that shows clinical signs and /or clinicopathological abnormalities that are consistent with leishmaniosis has the disease); or (ii) to investigate the presence of infection for epidemiological studies, screening apparently healthy animals, including prior to vaccination, to prevent transmission from carriers by blood transfusion, to avoid the importation of infected animals to non-endemic countries or to monitor response to treatment. For these reasons, it is important to separate *Leishmania* infection from disease and to apply different diagnostic techniques accordingly (Miró et al., 2008; Pennisi et al., 2015; Solano-Gallego et al., 2017).

In dogs and cats with clinical signs and/or clinicopathological abnormalities consistent with leishmaniosis, the diagnostic methods include the detection of amastigotes in stained cytological smears of aspirates from cutaneous and ocular lesions, lymph nodes, bone marrow and spleen among other lesional tissues or biological fluids. *Leishmania* parasites may also be viewed in histopathological biopsy sections from the skin or other infected organs. Definite identification of parasites within tissue macrophages may be difficult by histology and an immunohistochemical staining method can be employed to detect or confirm the presence of *Leishmania* in the tissue (Solano-Gallego et al., 2009).

Microscopic observation of *Leishmania* amastigotes in cytological samples from tissues or biological fluids is regarded as conclusive. Lymph node and bone-marrow smear microscopy has been shown to be a sensitive and specific technique for the diagnosis of overt canine leishmaniosis, but its sensitivity is significantly lower (<30%) in subclinical canine infections. Histopathology of tissues with the use of immunohistochemistry is useful in increasing the sensitivity of detection when a low parasite load is present (Miró et al., 2008).

The diagnosis can also be based on the detection of specific serum antibodies by using preferably quantitative serological techniques, such as the immunofluorescence antibody test (IFAT) and enzyme-linked immunosorbent assay (ELISA). Immunochromatography-based assays are easy to use and provide rapid qualitative results on the spot, but their performance is still not optimal. High antibody levels are associated with high parasitic load and disease. Due to the relatively long incubation period, sick dogs are likely to be seropositive and a high level of antibodies is conclusive of a diagnosis of canine leishmaniosis. However, the presence of low antibody levels is not necessarily indicative of the disease and further work-up is necessary to confirm or exclude clinical leishmaniosis by other diagnostic methods (Solano-Gallego et al., 2011). Cross-reactions with other pathogens, especially other species of *Leishmania* and *Trypanosoma* in Central and South America, have been noted, mostly with those tests that use crude *Leishmania* antigens. To overcome this limitation, recombinant polypeptides containing specific epitopes, such as recombinant K39, have been adapted for the diagnosis of canine leishmaniosis (Miró et al., 2008).

Detection of parasite-specific DNA in tissues and fluids by polymerase chain reaction (PCR) allows sensitive and specific diagnosis. PCR on aspirates of lymph node and bone marrow has been shown to be more sensitive than microscopic detection of amastigotes in stained smears or parasite culture from the same tissues. Assays based on kinetoplast DNA appear to be the most sensitive for detection of *Leishmania* infection. However, the sensitivity of PCR assays is lower when performed on blood and urine. Sampling using non-invasive conjunctival swabs has proven to be very sensitive and specific for the detection of *L. infantum* in groups of seropositive

dogs with leishmaniosis. Quantitative real-time PCR is an advanced technique that can detect extremely low parasitic loads when compared with conventional PCR. Real-time PCR allows the quantification of *Leishmania* loads in tissues of infected dogs which is important for diagnosis as well as for follow-up during the treatment of canine leishmaniosis. It is important to highlight that information provided by PCR should not be separated from the data obtained from clinicopathological and serological evaluations (Solano-Gallego et al., 2011; LeishVet, 2024a,b).

Most diagnostic techniques for *Leishmania* infection which are available for dogs are also employed in cats. Diagnosis is made in the majority of cases by serologic, cytologic, histologic, culture or PCR methods (Pennisi et al., 2015). Antibody testing and blood PCR are advisable as indicated for dogs. Antibodies to *Leishmania* should always be evaluated by laboratories using serological methods validated in cats (Pennisi et al., 2015).
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ROUND TABLE: LEISHMANIOSIS – THE EVER-CHANGING STATUS: AN UPDATE ON TREATMENT

Friday 13 September | 11:00 - 13:00 | Amphitheater N. Skalkotas - Room A

- ***CANINE LEISHMANIOSIS, TREATMENT AND DRUG RESISTANCE***
  Gad Baneth & Gaetano Oliva

- ***HOW I CAN MONITOR A DOG WITH LEISHMANIA INFECTION?***
  Gaetano Oliva & Laia Solano-Gallego

- ***PREVENTIVE MEASURES AGAINST LEISHMANIA: MORE THAN A SUMMER QUESTION***
  Patrick Bourdeau & Gad Baneth.

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**The LeishVet association consists of a group of veterinary scientists from academic institutions in the Mediterranean Basin and North America with a primary clinical and scientific interest in canine and feline leishmaniosis. Its main goal is to improve the knowledge on different aspects of leishmaniosis in veterinary medicine and public health, including the development of consensus recommendations based on recent evidence-based literature and clinical experience that would represent the most current understanding of Leishmania infection in dogs, cats and other animals.*

In the Mediterranean basin and in other different countries of the world, mainly Brazil, leishmaniosis due to *Leishmania infantum* is one of the most prevalent vector-borne disease in dogs. A broad range of clinical manifestations have been described in canine leishmaniosis (CanL). CanL is a progressing disease characterized by a broad spectrum of signs, ranging from subclinical infection, frequently characterized by negative or low positive *Leishmania* serology and general healthy status, to severe, fatal disease condition . Subclinical infection is featured by the detection of parasite by the PCR method and/or the presence of a low antibody titers, in dogs with no clinical manifestations of the disease (Baxarias et al., 2023). In these dogs, a strong cellular immune response persists, with a balanced levels of tissue-specific immunity to prevent immune-mediated tissue damage and subsequent disease (Baxarias et al., 2023). The severity of late-stage disease is correlated with high antibody levels and increasing parasite load. Therefore, a clinical staging system in this infection is important to establish an accurate

prognosis and appropriate treatment. Infected dogs are considered the main urban reservoirs for *L. infantum*. Infectiousness to competent phlebotomine vectors has been associated with many factors, the main being the severity of the disease exhibited by infected dogs. Serological and specific PCR tests that detect *L. infantum* infection in dogs appear insufficient to provide information on the capacity of infected dogs to be infectious. The evaluation of dog's infectiousness remains still difficult due to the need to perform xenodiagnosis as the only valid method to assess it. Preventative and therapeutic strategies appear to be the only methods useful to limit the spread of parasite from infected dogs to other animal reservoirs and to susceptible human population. The treatment of infected dogs is allowed all around the Europe and many countries worldwide, however it appears not able to achieve a 100% sterile cure in dogs and it can induce drug resistance. For this reason, the World Health Organization (WHO) strongly suggests to avoid the use of drugs used for the treatment of humans for veterinary purposes. The first-line treatment for CanL is represented by the use of second line leishmanicidal drugs for humans (N-methylglucamine antimoniate [MA] and miltefosine [MIL] in combination with allopurinol [AL]. Despite its proven efficacy, MA has some drawbacks, including the costs, inability to prevent disease recurrence, the need for parenteral administration and the numerous reported side effects. MIL is a good alternative, it is administered orally and this is widely preferred by owners. This molecule has a low impact on renal function and can be used in dogs with severe proteinuria, one of the most frequent clinicopathological alteration reported in CanL. However, adverse reactions associated with MIL treatment have been reported too, mainly vomiting, diarrhea, abdominal pain and loss of appetite that tend to regress spontaneously within a few days after starting treatment, and recurrence of disease is expected when using MIL monotherapy within 4 to 6 months. Allopurinol is administered orally too, in combination of one of the two mentioned drugs. The time course of treatment, both for MA and MIL, is 4 weeks. After the first month, the length of allopurinol treatment depends on the severity of the disease, the clinical, serological and parasitological response to treatment and the individual tolerance to this drug. Due to its mechanism of action, allopurinol could cause massive xanthine crystalluria. In this case, the drug should be reduced in dosage or discontinued if there is no evidence for reduction of crystalluria with low purine diets, to decrease the risk of urolithiasis. Healthy infected dogs can be treated by using immune modulators such as domperidone. Dietary nucleotides with AHCC. These two treatments may be also combined with drugs for clinically sick dogs.

The emergence of drug-resistant strains of *L. infantum* infecting dogs and humans represents an increasing threat and requires a One Health framework for its control. Increased resistance renders current antileishmanial drugs less effective, requiring dose increase or prolonged treatment time, with the associated toxicity. Most evidence are related to canine *Leishmania* strains with drug resistance genotypes, relatively frequent in the *L,. infantum* populations currently present in the Iberian Peninsula/Mediterranean area. A few *Leishmania* vaccines have been marketed during the last 20 years, the main limitation of which is that they do not prevent the establishment of infection. *Leishmania* vaccines may reduce the infectiousness to sand flies, however vaccinated dogs should be considered always as a source of infection for humans and other animals. Protection from CanL strongly depends on the ability of the dog immune system to respond since control requires balanced levels of tissue-specific immunity to prevent immune-mediated tissue damage and subsequent disease. The current licensed vaccine [one

in Brazil - Leish-Tec® (Ceva Saúde Animal, Brazil), the second in Europe - LetiFend® (LETIPharma, Spain)] only have the ability to limit the progression of the infection to disease or to decrease the severity of the disease. This is due to the complexity of the immune response of naturally infected dogs against the parasite, which can result in immunological resistance or a susceptibility profile and different clinical forms of the disease. A new DNA vaccine based on the non-replicative antibiotic resistance marker-free plasmid vector pPAL which contains an encoding gene for the *L. infantum* activated protein kinase C receptor analogue (LACK) has been approved by the European Medicines Agency in 2023. This vaccine can only be administered intranasally, to healthy dogs which are 6 months of age or older.

Topical insecticides with proven efficacy against sand fly bite are considered the best tool to limit *L. infantum* infection. These compounds combine two positive effects against transmitting insects: a) the killing effect, the capacity to cause the death of sand flies after contact with protected dogs, b) the anti-feeding effect, the capacity to avoid the bite. Several topical formulations, such as collars, spot-on, or sprays, containing synthetic pyrethroids with proven anti-feeding (excito-repellent) and insecticidal effects against phlebotomine sand flies are currently used all around the world. After being applied to the dog's skin, their active ingredients spread over the entire surface of the body and the hair coat. Despite their large scale application, insecticide products are characterized by some limitations mainly due to instable compliance of the dog's owners, their cost and the regularity of application. Although discouraged by manufacturers, a combination of devices is commonly used by dog's owners, with the combination of collar and spot-on being the most frequently employed (Zini et al., 2020). Preventive measures against sand flies are typically adopted to protect healthy dogs from *L. infantum* infection, less so to avoid parasite spreading by CanL sick dogs, for which anti-leishmanial therapies may lead to decreased infectiousness to vectors, but have only temporary efficacy (Gradoni et al., 1987; Miró et al., 2011). Preventive and therapeutic measures against CanL should be considered an integrated program for the control of this zoonosis, both in dogs living or travelling into endemic areas. Future research should investigate new anti-*Leishmania* drugs and immunomodulators for specific use in the animals, effective vaccines for limiting the possibility of infection, low cost new insecticides and a less complicated method to assess the infectiousness of infected individuals. However, host and parasite factors that determine the clinical outcome of infection and if infected dogs will progress to clinical disease are still poorly understood.

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WHEN THE BRAIN JUST DOES NOT STOP ROCKING – NEW CONSENSUS STATEMENT ON STATUS EPILEPTICUS AND CLUSTER SEIZURES MANAGEMENT

Friday 13 September | 14:00 - 15:45 | Amphitheater N. Skalkotas - Room A

Holger A. Volk, PhD, DipECVN, PGCAP, FHEA, FRCVS

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Status Epilepticus (SE), a life-threatening neurological emergency, is characterized by persistent epileptic activity. Epileptic seizures lasting longer than 30 minutes can induce demonstrable histopathological brain damage in both humans and animals. SE is often defined in literature as a seizure lasting 30 minutes or longer. However, clinically, it is known that a seizure lasting five minutes typically requires appropriate medical intervention to be halted. The longer a seizure lasts, the more difficult it becomes to control.
Cluster seizures are defined as two or more seizures occurring within a 24-hour span, which can also lead to permanent brain alterations. In instances of SE or cluster seizures, immediate patient stabilization, decisive therapeutic action, and diagnostic measures conducted by a trained and cohesive team are vital.
The primary goal in managing SE or cluster seizures is to interrupt the seizure or series of seizures as quickly as possible while stabilizing the patient systemically. However, the evaluation of physiological and laboratory diagnostic parameters is crucial for further patient treatment. Nevertheless, patient stabilization should precede a thorough history taking.
Aetiologies: It's important to acknowledge the SE rule of three: 30 % due to poisoning, 30% structural epilepsy, and 30% idiopathic epilepsy.

ACVIM Consensus Proposal: Intravenous (IV) and intranasal (IN) administration of Benzodiazepines (BZDs) are currently considered the most effective and safest methods for both preclinical and clinical application.

First-Line Therapy at Home:
• IN-Midazolam (MDZ) in dogs or cats.
• Less highly recommended: Rectally administered Diazepam (DZP) in dogs or cats.
• Intramuscular (IM) administration of MDZ in dogs or cats; this option can only be used outside of the clinic when caregivers are medically trained. Legal frameworks in different countries must be considered prior of drug application.
• Other routes of BZD administration, such as buccal/sublingual, should only be considered if the aforementioned options are not feasible.

Therapy in a Clinic/Practice:
• IV-MDZ in dogs or cats.
• IN-MDZ in dogs or cats; IN-MDZ can be advantageous for achieving a swift anticonvulsant effect when IV access is not possible or until an IV-catheter is placed.
• IV-DZP in dogs or cats.

• IM-MDZ in dogs or cats.

While both MDZ and DZP are effective and safe options for SE treatment in dogs and cats, MDZ may be considered a more potent or safer BZD compared to DZP. A BZD bolus should be considered effective if the seizure ceases within <5 minutes after administration and no subsequent seizures occur within <10 minutes after cessation.

• Seizure activities controlled with BZDs, but resuming within 10-60 minutes, can be considered as recurrent SE.

• In the case of recurrent SE or if the SE does not stop at all after the first bolus, a second bolus of BZD should be administered at intervals of at least 2 minutes.

• If seizures persist after two BZD boluses, i) in the case of recurrent SE, another BZD bolus followed by an immediate BZD IV CRI should be administered, and ii) in the case of sustained SE, a final BZD bolus followed by second-line interventions should be conducted.

• In dogs, the options include MDZ IV CRI or DZP IV CRI.

• In cats, MDZ IV CRI is the preferred BZD CRI; DZP IV CRI should be avoided due to safety concerns.

Second-Line Treatment:

• Levetiracetam and Phenobarbital are typically utilized as second-line medications when the first-line treatment has failed to cease seizures. However, these medications can also be administered earlier, aiming to maintain sufficient seizure control in the short and long term (especially in cases diagnosed with epilepsy).

• Levetiracetam should be given IV in dogs and cats; if the IV route isn't an option, IM or R administration in dogs and cats might be considered.

• Therapy with IV Phenobarbital should also be considered at this stage in dogs and cats. Initial dosing schemas can be used on phenobarbital-naive animals with normal liver function if necessary. For animals undergoing long-term treatment with Phenobarbital, dosage increases should ideally be carried out after evaluating serum concentrations.

Third-Line Treatment:

• First step:

o Administer an IV-bolus of Ketamine, potentially followed by a continuous intravenous infusion (CRI).

o (Dex)medetomidin IV-bolus and CRI should be added in dogs (and cats) if SE persists after the initiation of Ketamine (or vice versa).

• Second step:

o Initiation of Propofol IV-bolus, potentially followed by a CRI, should be considered in dogs if SE persists after the administration of Ketamine and (Dex)medetomidin IV-CRIs.

o In cats, caution should be exercised with repeated bolus doses of Propofol, and particularly with CRI, due to safety concerns. Propofol should be administered under close monitoring of clinical and hematological parameters, and preferably only after other anesthetics have failed to halt the SE. When chosen, efforts should be made to limit the duration of Propofol IV-CRI to the minimum required to achieve ongoing seizure control in cats.

• Third step:

o Anesthetic barbiturates (Pentobarbital or Sodium thiopental) IV-bolus and CRI may be initiated in dogs and cats if SE persists following the administration of Propofol IV-CRI.

• Fourth step:

o Inhalational anesthesia should be initiated in dogs and cats if SE persists following therapy with the previous interventions.

When should no further antiepileptic drugs be added?

• No additional anesthetic drugs are necessary if no further seizure activities occur after the addition or dosage adjustment of the last intervention in the last 24-48 hours.

• All current anesthetic therapies should continue in doses that led to the cessation of seizures, for 24-48 hours until the seizures halt. Shorter periods, i.e., a minimum of 12 hours, can also be considered to reduce potential risks associated with extended hospital treatment and CRI of anesthetic medications.

• The EEG examination, in combination with the clinical confirmation of seizure cessation, is preferred over clinical confirmation alone, especially in the case of nonconvulsive status epilepticus (NCSE).

Tapering Therapy:

• Before starting to taper anaesthesia, it's recommended that animals are seizure-free for a period of at least 12-24 hours.

• Following the cessation of Status Epilepticus, a gradual reduction in anaesthetic drugs should ideally occur over a 24 to 48-hour period (minimum of 12 hours).

• Tapering multiple anaesthetics simultaneously is not recommended. • Inhalational anaesthetics can be discontinued first, followed by Propofol or Pentobarbital CRI, then Ketamine CRI, and finally Dexmedetomidin and BZD CRI — generally in reverse order of when they were initiated. However, variations in the order of tapering may be applied based on the veterinarian's judgment.

• Inhalational anaesthetics can be reduced and discontinued faster than intravenous anaesthetics.

• A CRI dose can be reduced by 25%-50% every 4-6 hours before it's discontinued. If there are no renewed seizures, the next CRI medication can be discontinued in the same manner.

• If relapses occur after the reduction and discontinuation of a particular anaesthetic agent, the CRI dosage should be raised to the previous dosage that sufficed to control the seizures (if seizures reoccurred during the dosage reduction) or the CRI should be reintroduced after a bolus injection (if seizures reoccurred after complete drug cessation).

• Non-anaesthetic antiepileptics (e.g., Levetiracetam or Phenobarbital) should be administered in constant doses and, if possible, in target concentrations at least until the animal's release from the hospital (for reactive seizures) or long-term (for an epilepsy diagnosis).

Further reading material:

- Podell M, Volk HA, Berendt M, Löscher W, Muñana K, Patterson EE, Platt SR. 2015 ACVIM Small Animal Consensus Statement on Seizure Management in Dogs. J Vet Intern Med. 2016 Mar-Apr;30(2):477-90.

- Charalambous M, Muñana K, Patteson EE, Platt SR, Volk HA. ACVIM Consensus statement on the management of status epilepticus and cluster seizures in dogs and cats. J Vet Intern Med 2024 Jan-Feb;38(1):19-40.

EPILEPSY MANAGEMENT (RE-)VAMPED

Friday 13 September | 14:00 - 15:45 | Amphitheater N. Skalkotas - Room A

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The most important step in the management of seizure disorders in small animals is to establish as accurate a diagnosis as possible prior to prescribing antiepileptic therapy.
Two articles which summarises how to best treat (consensus statement) can be found when you click on the link below:
http://bmcvetres.biomedcentral.com/articles/10.1186/s12917-015-0464-z
http://onlinelibrary.wiley.com/doi/10.1111/jvim.13841/abstract

An overview of data in the literature can be found here:
http://bmcvetres.biomedcentral.com/articles/10.1186/s12917-014-0257-9
https://bmcvetres.biomedcentral.com/articles/10.1186/s12917-016-0703-y

Antiepileptic drug therapy will have little efficacy against extracranial seizure disorders and it is imperative that an adequate work-up be performed to exclude metabolic causes.

Aim of Antiepileptic Drugs (AEDs)
What can I expect from an AED? When a new AED is established on the human market, it has to show at least a 50% or more reduction of seizure frequency. This is important to remember to give the perspective for the owner. AED are mainly anticonvulsant, but apart from a few AED they are not antiepileptogenic – they cannot alter the disease itself. We find it very useful to ask the owner to keep a seizure diary. This has two main advantages: 1st you can establish the seizure frequency over a certain time period and establish if the treatment is working; 2nd it helps the owner to de-emotionalize the seizure event.

When to start the treatment for Epilepsy? Epilepsy is defined as recurrent seizure activity (>2seizures). Even if pathology cannot be identified on an extra- or intracranial work-up there might be a variety of pathomechanisms involved for the animal to seizure. In general it is believed that epilepsy is a chronic disease process and the antiepileptic drug will change the seizure threshold but not the disease itself. Risk factors for epilepsy are important for the clinical decision making process: when and with which drug the treatment should be initiated. Unfortunately, risk factors are not well-established in veterinary medicine. In human medicine the identification of certain brain pathologies, interictal EEG changes and a history of severe postictal complications have been identified as relative risk factors. Several drug treatment guidelines have been established in human medicine which are not only based on reduction of seizure frequency, but also on reducing morbidity and mortality, seizure severity, to improve the quality of life and to reduce sociopathic impacts and to avoid adverse effects. An increase in AED dosage is mainly restricted by the adverse effects of the drug and therefore the development of new AEDs was focused on improving the tolerability with the hope to improve also its efficacy.

How does success look like:

http://bmcvetres.biomedcentral.com/articles/10.1186/s12917-015-0465-y

When to start the treatment for Epilepsy? 1) Status epilepticus; 2) Cluster seizures; 3) Severe post-ictal periods; 4) Identifiable structural lesion present or prior history of brain disease or injury; 5) Increasing seizure frequency and severity; 6) more than two or more isolated seizure in a six month period

Most of the AEDs alter the excitability of the brain, and reset the balance of excitation and inhibition so that seizures are abolished or at least reduced in frequency. There are several basic mechanisms thought to be involved in the action of AEDs:

1. Induction of a functional block of voltage-gated sodium channels
    - Phenytoin, carbamazepine, lamotrigine, valproate, topiramate
2. Direct or indirect enhancing of inhibitory GABAergic transmission
    - Imepitoin, benzodiazepines, barbiturates, tiagabine
3. Inhibition of excitatory glutamatergic neurotransmission
    - Topiramate, felbamate
4. Modulation of calcium ion channels
    - Ethosuximide, topiramate, gabapentin, pregabalin

The efficacy and safety profiles of AEDs are determined in large part by their pharmacokinetic properties. Drugs which are now generally used in veterinary medicine are focused on a good compliance of the owner based on the most favorable pharmacokinetic profile. The most desirable pharmacokinetic property of an AED is one that has nearly complete bioavailability, rapid blood brain barrier penetration, an elimination half-life long enough for daily or twice daily dosing, linear pharmacokinetics with a single compartment model, no enzyme induction which increases biometabolism, low protein binding and no pharmacokinetic interactions with other drugs.
Most epileptic dogs are treated pharmacologically successfully for life, with the standard seizure suppressing drugs (AEDs) PB and/or KBr. However, in about 20–30% of treated dogs, seizures are poorly responsive to treatment with a combination of PB and KBr. PB and KBr can only be increased to a certain level as this aggravates side-effects and toxicity (e.g. polyuria/polydipsia, polyphagia, ataxia, lethargy and hepatotoxicity). In human medicine there has been considerable progress in developing efficacious and better tolerated epilepsy treatment over recent decades. Conversely, in veterinary medicine there is still a lack of data concerning new pharmacological treatment options for epileptic patients, especially for pharmacoresistant patients.

2nd generation Antiepileptic drugs

Many of the newer AEDs that show some effect and are well tolerated in humans, are not efficacious in small animals due to inappropriate pharmacokinetics or life-threatening side-effects; these include vigabatrin, lamotrigine, tiagabine, oxcarbazepine. There are few alternative AEDs to use in canine pharmacoresistant patients. The human AEDs felbamate, gabapentin, levetiracetam and zonisamide have been successfully used as additional drugs in

dogs with pharmacoresistant epilepsy. Felbamate has been used successfully especially for partial seizures. Gabapentin, levetiracetam and zonisamide have been shown to provide good short-term seizure control, but their long-term efficacy is questionable. Especially, for Zonisamide and Levetiracetam a "Honeymoon period" was described in which dogs responded first significantly, but after 4-6 months they were refractory again. Drug-resistant epilepsy continues to be a major clinical problem in around one third of patients with epilepsy in human and veterinary medicine. Thus, new pharmacological treatment options with a high long-term efficacy and without risk of toxicity in dogs are urgently needed.

Importance of seizure type

Around 60% of human patients with intractable epilepsy suffer from partial seizures, mainly of the complex type. A similar study has not been performed in dogs to the author's knowledge. Interestingly, in a study using levetiracetam in PB and KBr resistant dogs with epilepsy 79% of the dogs' seizures were classified as complex-partial. It is generally believed that partial seizures can be more challenging to treat in both humans and dogs. Apart from the seizure type as a predictor for refractoriness a high seizure frequency has been suggested to be correlated with intractable epilepsy in human medicine and also in rodent models for epilepsy. In the aforementioned studies using 2nd generation AEDs the dogs had a high seizure frequency of around 3-4 seizures a month and most of them where described to have cluster seizures.

Further treatment options

Vagus nerve stimulation is an approved antiepileptic treatment for pharmacoresistant partial epilepsies in humans. Stimulation of the left cervical vagus nerve via a subcutaneously implanted device has been described in dogs. However, the overall result does not seem to be encouraging. Furthermore, it is very expensive. Ocular compression has also been described as a method of stimulating the vagus nerve to control seizures in dogs.

Diet and epilepsy

In the last decade, the field of neurogastroenterology and neurodietetic has emerged as fields of research. There is an increasing level of evidence that the intestinal gut with its microbiota (gut) may provide a crucial link between epilepsy, behavioural comorbidities and alterations in the neurotransmitter system (Verdoodt et al., 2022). Recent literature demonstrated that intestinal microbiota can modify host behaviour via the gut-brain axis and thus be involved in the development of mental disorders in people such as schizophrenia, autism and depression (Sampson and Mazmanian, 2015). The gut-brain axis is a bidirectional signalling system, communicating via the vagal nerve, via the blood (neurotransmitters, hormones, metabolites, immunological signals) and the immune system (microbe-associated molecular patterns, metabolites) (Sampson and Mazmanian, 2015).

The link between gluten intolerance and paroxysmal dyskinesia has been elegantly demonstrated by Lowrie and colleagues (Lowrie et al., 2015). Apart from Border Terriers, a variety of other dog breeds with paroxysmal dyskinesia can be tested positive for anti-transglutaminase 2 (TG2 IgA) and anti-gliadin (AGA IgG) antibodies and respond to a gluten free diet (Lowrie et al., 2015, Rogers et al., 2023). However, the link of gluten to other neurological or behavioural dysfunctions has not been established. In a recent study a link between dysbiosis,

with an increase in abundance of a Lactobacillus and phobic and aggressive behaviour has been shown (Mondo et al., 2020). Lactobacillus is a bacterium which can affect the production of the inhibitory neurotransmitter GABA. Changes in GABA concentration was, however, not assessed.

Peripheral neurotransmitter levels might be changed by gut microbiota, which might also be involved in the epileptogenesis and occurrence of drug-resistance (Dahlin and Parst-Nielsen, 2019). In one study in human patients with drug-resistant epilepsy an overall higher diversity of microbiota was seen, with significant increases in rare bacteria, such as Clostridium XVIII, Atopobium, Holdemania, Dorea, Saccharibacteria, Delftia, Coprobacillus, Paraprevotella, Ruminococcus, Gemmiger, Akkermansia, Neisseria, Coprococcus, Fusobacterium, Methanobrevibacter, Phascolarctobacterium and Roseburi (Peng et al., 2018). The increased abundance of Ruminococcus could have altered glutamate, glutamine and serotonin levels. Interestingly, the drug-responsive patients in this study had increased concentrations of bifidobacteria and lactobacilli, which also have been described to enhance the synthesis of the inhibitory neurotransmitter GABA. The authors assumed that these microbiota might have a protective effect in epilepsy.

Less than a handful studies have examined the intestinal flora of dogs with epilepsy. One study investigated also the abundance of Lactobacillus species in untreated dogs with idiopathic epilepsy, but could not find a difference compared to healthy dogs (Muñana et al., 2020). In contrast, García-Belenguer et al. (2021) identified significant alterations of the faecal microbiome in dogs with epilepsy. Drug-naïve dogs with epilepsy had a decrease in GABA (Pseudomonadales, Pseudomonadaceae, Pseudomonas and Pseudomonas graminis) and short-chain fatty acids (SCFAs)-producing bacteria (Peptococcaceae, Ruminococcaceae and Anaerotruncus) compared to healthy controls. Furthermore, bacteria (Prevotellaceae) which are supposed to have brain protective properties were also diminished in the dogs affected by epilepsy. Treatment with antiseizure medication (ASM, phenobarbital or imepitoin) did not affect the microbiome. In another study ASM treatment with phenobarbital only caused minor changes in the composition of the microbiome of dogs with idiopathic epilepsy, with increases in short chain fatty acid concentrations of butyrate and propionate (Watanangura et al., 2022). When PB responders were compared to non-responders, increase in butyrate levels was associated with drug-response. The influence of the microbiome on drug function has been also described for zonisamide, which is converted into its active metabolite by microbiota (mainly Clostridium sporogenes and Bifidobacterium bifidum) (Kitamura et al., 1997).

Diets can have an effect on seizure control and can potentially alter the canine microbiome (Pilla et al., 2020). In a recent study from our group, we showed that nearly two-thirds of owners of dogs with epilepsy change their pets' diet (Berk et al., 2018). Many owners changed to a medium chain triglyceride (MCT)-enriched diet or added MCT-oil as a supplement. Please refer to the effect of MCT on epilepsy in our recent review article (Han et al., 2021). MCT diets have a high ketogenic yield and have shown to affect the microbiome. MCT enriched diets can cause significant alterations in the microbiome and lipidome, with an increase in Bacteroidaceae, which is associated with positive non-aggressive behaviour in dogs (Pilla et al., 2018).

The landmark study of how microbiota could influence drug-response was from Olson et al. (2018). The authors demonstrated that seizure susceptibility could be transplanted by fecal transplant. In both antibiotic-treated and 'germ-free' mice, the anti-seizure effect of an ketogenic diet was missing. However, after fecal transplant of *Parabacteroides and Akkermansia muciniphila* the anti-seizure effect was seen. In a study in children with drug-resistant epilepsy ketogenic diet reduced the species richness and diversity of the intestinal microbiome (Zhang et al., 2018). After dietary intervention with a ketogenic diet, non-responders had a significant increase in *Clostridiales*, *Ruminococcaceae*, *Rikenellaceae*, *Lachnospiraceae*, and *Alistipes*. More precise treatment approaches are provided by administering specific probiotics. In human medicine, Peng et al. (2018) revealed bifidobacteria and lactobacilli functioning as protective factors in epilepsy. Patients with elevated levels of these microbiota solely experienced a small number of seizures per year in this study. Based on these findings, the authors suggested remodelling the intestinal microbiome, as a new treatment option in epilepsy. Gomez-Eguilaz et al. (2018) conducted a prospective study in patients with drug-resistant epilepsy investigating new complementary treatments. In the study a mixture of different probiotics was administered to patients with epilepsy for four months, with around a third showing a more than 50% reduction in seizure frequency and a significantly improved QoL (Gomez-Eguilaz et al., 2018). Another more drastic option is the treatment with antibiotics. After receiving antibiotics patients with drug-resistant epilepsy became temporary seizure free. It is suspected that after the anti-microbial therapy a subsequent regeneration of the intestinal microbiome occurs (Dahlin and Prast-Nielsen, 2019). Also, in veterinary medicine anecdotal reports exists that antibiotics temporaly improved seizure control.

There is an increasing level of evidence for a role of the gut-brain axis in epilepsy management. Far more research is needed to elucidate potential mechanisms of actions and its role for routine patients. As with any treatment in epilepsy, one will need to be realistic and not hope for a magic wand. It does have, however, the potential to be another tool in our armory against epilepsy.

Allergy

Few reports in humans suggesting that allergy is associated with epilepsy, migraine and hyperactivity in children. In these individuals, hypoallergenic diet can reduce the frequency of seizures. Recently eight dogs with refractory epilepsy were described who were treated with an exclusion diet. Seven of the dogs had chronic mild gastrointestinal disease. Seven out of eight dogs showed reduced seizure frequency. Further work needs to be done to determine the role of dietary allergy in epilepsy.

Table 1. Summary of the antiepileptic drugs available to treat epilepsy in cats.

Antiepileptic drug	**T 1/2 (hr)**	**Therapeutic range**	**Initial dose**	**Potential adverse effects**
Phenobarbital	34-43	10-30 mg/dl	2-3 mg/kg/day (q12-24 hr)	Sedation, hepato/ blood toxicity
Diazepam	15-20	500-700 ng/ml (nordiazepam)	5-10 mg q 8-12 hrs	Acute hepatic necrosis, sedation

Clonazepam	Unknown	500-700 ng/ml (nordiazepam)	0.5 mg q 12-24 hr	Acute hepatic necrosis, sedation
Gabapentin	Unknown	Unknown	5-10 mg/kg q 8-12 hr	Sedation, ataxia
Levetiracetam	~8hrs	10-50 mcg/ml (humans)	10-20 mg/kg q 8-12 hr	Sedation

Table 2. Summary of the antiepileptic drugs available to treat epilepsy in dogs.

Antiepileptic drug	**T 1/2 (hr)**	**Therapeutic range**	**Initial dose**	**Potential adverse effects**
Phenobarbital	24-40	15-30 mg/dl	2-3 mg/kg q12 hrs)	Sedation, hepato/ blood toxicity, PU/PD,ataxia idiosyncratic reactions
Imepitoin	~2hrs	N/A	10 mg/kg q 12hrs	Sedation, Hyperactivity, ataxia
KBr	15-20 d	0.7-2.3µg/ml	40 mg/kg/d	PU, PD, sedation, ataxia
Gabapentin	2-4 hrs	4-16 mg/l (humans)	10 mg/kg q 8hrs	Sedation, ataxia
Pregabalin	7 hrs	Unknown	2-4 mg/kg q 8hrs	Sedation, ataxia
Levetiracetam	3-4 hrs	10-50 µg/ml (humans)	10-20 mg/kg q 8 hrs	Sedation (rare)
Zonisamide	15-20 hrs	10-40 µg/ml (humans)	5-10 mg/kg q12hrs	Sedation, ataxia, GI signs
Felbamate	5-6 hrs	25-100 mg/l (humans)	20 mg/kg q8hrs	Blood dyscrasias, hepatopathy described in humans

Further reading material:

1. Podell M, Volk HA, Berendt M, Löscher W, Muñana K, Patterson EE, Platt SR. 2015 ACVIM Podell M, Volk HA, Berendt M, Löscher W, Muñana K, Patterson EE, Platt SR. 2015 ACVIM Small Animal Consensus Statement on Seizure Management in Dogs. J Vet Intern Med. 2016 Mar-Apr;30(2):477-90. doi: 10.1111/jvim.13841.
2. Bhatti SF, De Risio L, Muñana K, Penderis J, Stein VM, Tipold A, Berendt M, Farquhar RG, Fischer A, Long S, Löscher W, Mandigers PJ, Matiasek K, Pakozdy A, Patterson EE, Platt S, Podell M, Potschka H, Rusbridge C, Volk HA. International Veterinary Epilepsy Task Force consensus proposal: medical treatment of canine epilepsy in Europe. BMC Vet Res. 2015 Aug 28;11:176. doi: 10.1186/s12917-015-0464-z.
3. Berendt M, Farquhar RG, Mandigers PJ, Pakozdy A, Bhatti SF, De Risio L, Fischer A, Long S, Matiasek K, Muñana K, Patterson EE, Penderis J, Platt S, Podell M, Potschka H, Pumarola MB, Rusbridge C, Stein VM, Tipold A, Volk HA. International veterinary epilepsy task force consensus report on epilepsy definition, classification and terminology in companion animals. BMC Vet Res. 2015 Aug 28;11:182. doi: 10.1186/s12917-015-0461-2.
4. Potschka H, Fischer A, Löscher W, Patterson N, Bhatti S, Berendt M, De Risio L, Farquhar R, Long S, Mandigers P, Matiasek K, Muñana K, Pakozdy A, Penderis J, Platt S, Podell M, Rusbridge C, Stein V, Tipold A, Volk HA. International veterinary epilepsy task force consensus proposal: outcome of therapeutic interventions in canine and feline epilepsy. BMC Vet Res. 2015 Aug 28;11:177. doi: 10.1186/s12917-015-0465-y.
5. Charalambous M, Muñana K, Patterson EE, Platt SR, Volk HA. ACVIM Consensus Statement on the management of status epilepticus and cluster seizures in dogs and cats. J Vet Intern Med. 2024 Jan-Feb;38(1):19-40. doi: 10.1111/jvim.16928.
6. Verdoodt F, Watanangura A, Bhatti SFM, Schmidt T, Suchodolski JS, Van Ham L, Meller S, Volk HA, Hesta M. The role of nutrition in canine idiopathic epilepsy management: Fact or fiction? Vet J. 2022 Dec;290:105917. doi: 10.1016/j.tvjl.2022.105917.

Han FY, Conboy-Schmidt L, Rybachuk G, Volk HA, Zanghi B, Pan Y, Borges K. Dietary medium chain triglycerides for management of epilepsy: New data from human, dog, and rodent studies. Epilepsia. 2021 Aug;62(8):1790-1806. doi: 10.1111/epi.16972

EPILEPSY MIMICRY OR LOOK- A-LIKES AND HOW TO MANAGE THEM

Friday 13 September | 17:00 - 18:45 | Amphitheater N. Skalkotas - Room A

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A patient presenting with a history of paroxysmal episodes or "fits" can present an intriguing challenge for any experienced clinician. Firstly, the patient typically appears normal during the presentation. Secondly, identifying the specific type of episode relies heavily on a detailed description from an eyewitness. Thirdly, these paroxysmal episodes often seem unpredictable and uncontrollable for the owner, potentially leading to biased observations influenced by emotionally charged perceptions of reality. Nevertheless, before embarking on a diagnostic investigation, obtaining a comprehensive patient history is vital. Many owners now have the capability to record these events on video, which can assist in their characterization.

Paroxysmal events such as syncope, narcolepsy/cataplexy, pain, compulsive behavior disorders, vestibular attacks, certain movement disorders, neuromuscular weakness, and seizures share commonalities in their clinical presentation. The inter-episodic clinical examination may be normal for these presentations. Some animals may exhibit inter-episodic deficits, providing valuable guidance for clinical decision-making and aiding in the localization of the affected system. On occasion, animals may even manifest these "strange" episodes while at the clinic, such as prolonged seizure activity (status epilepticus [>10 minutes]), cluster seizures (≥2 seizures per day), or vestibular dysfunction.

Define the problem

Paroxysmal episodic disorders can manifest in various ways, affecting posture, muscle tone, causing uncontrolled movements, and leading to alterations in behavior. In addition to characterizing the episodes themselves, it is crucial to identify any triggers or clinical signs that the animal may exhibit before or shortly after an episode (as detailed in Table 1). Common episodic events that require differentiation include syncope, narcolepsy/cataplexy, behavior changes, vestibular attacks, movement disorders, neuromuscular weakness, and seizures.
When an animal presents with a history of episodic weakness, fatigability, or collapse, it is essential, albeit sometimes challenging, to define the problem accurately. Owners may describe these episodes as "collapsing," but it is imperative for the clinician to gather key information to precisely define the issue:

- What happens before or after the episode?
- What was observed during the episode?
- Does the animal lose consciousness during the episode? (Seen in syncope or seizures.)

This will enable the clinician to ascertain whether:

- The animal loses **consciousness** (indicating syncope or seizures).
- There is NO evidence of **convulsive** activity (more likely syncope than seizures).

- The animal is normal in between the episodes (**episodically weak)**, whether weakness is precipitated by exercise (**fatigability**) or the animal is consistently weak (**persistently weak)**.
- The animal shows a **spastic** or **flaccid** 'weakness' associated with or without incoordination (**ataxia**).

Other common presenting complaints that may be seen in the flaccidly weak patient include:

- Regurgitation
- Paresis
- Difficulty rising
- Exercise intolerance
- Episodic weakness
- Fatigability
- Altered voice
- Change in musculature
- Stiff stilted gait
- An inability to lift the head up normally or, especially in cats, a state of persistent
- cervical ventroflexion

Syncope

Episodes of syncope are typically characterized by sudden, brief, and transient losses of consciousness and postural tone. During these episodes, animals become flaccid but may experience a brief myoclonic jerk just before collapsing. This phenomenon is notably observed in cats with 3rd degree atrioventricular block, and it can sometimes be mistaken for brief focal seizures. However, most animals experiencing syncopal episodes do not display any pre- or post-episodic signs.

Syncopal episodes are often linked to exercise or movement and are less likely to occur at rest. Recovery from these episodes is usually almost instantaneous. Some individuals may experience multiple episodes in a day, occurring in close succession, and these episodes may not respond to anti-epileptic drugs. In fact, antiepileptic drugs can potentially impair cardiorespiratory function, exacerbating the frequency and severity of these syncopal episodes.

Narcolepsy

Narcolepsy is a rather rare disorder of the sleep-wake-cycle. Cataplectic attacks are common in narcolepsy, which can resemble syncopal collapse and seizures. Cataplectic attacks are usually triggered by food, excitement, and stress or pharmacologically (e.g. physostigmine). Following the 'trigger' the affected animal will become flaccid and collapse. Narcoleptic animals experience chronic fatigue, although they do not necessarily sleep more. They can be restless at night and sleepy during the day because of a disturbed and irregular sleep pattern. A history of others affected in the litter or in the breeding line is not uncommon.

Paroxysmal Behavior Changes

Episodic pain can trigger behavioral responses that resemble focal seizures, such as nerve root impingement or irritation resulting from lateral disc protrusion/extrusion. This can manifest as "freezing," myoclonic jerks, muscle spasms, and/or muscle fasciculations. Similarly, behavior disorders, including episodes of aggression or compulsive behavior changes (stereotypic behaviors like continuous rhythmic pacing, licking, and vocalizations), may appear similar to sensory seizures. Dogs and cats typically return to normal between these episodes. However, compulsive behavior changes are not associated with alterations in muscle tone or consciousness, and there is usually an identifiable behavioral trigger.

Vestibular Episodes

Transient vestibular episodes are a rare phenomenon characterized by the same cardinal signs as non-intermittent vestibular disease, including head tilt, nystagmus, and ataxia. While nystagmus and gait abnormalities can also be seen in seizures, it is uncommon for a seizure to cause a head tilt. Patients experiencing transient vestibular episodes typically do not exhibit altered consciousness during an episode and return to a fairly normal state before and after the episode. These episodes do not respond to standard antiepileptic drug treatment.

Paroxysmal Movement Disorders

Our understanding of and ability to identify paroxysmal movement disorders have improved in the last decade. Most of these movement disorders are triggered or exacerbated when the animal is excited or stressed. They are usually associated with movement, rarely occurring at rest or during sleep. These disorders are episodic and involve an increase in muscle tone (dystonia) but do not affect the level of consciousness. Some of these disorders were previously mistaken for seizures, but they do not respond adequately to standard antiepileptic drugs. Additionally, they closely resemble movement conditions described in humans and are now classified as movement disorders. Some of these disorders have even been genetically characterized.

As a general guideline, when presented with a purebred dog experiencing a paroxysmal episode that does not involve autonomic dysfunction, leaves the animal normal post-episode, does not resemble a generalized tonic-clonic seizure, maintains appropriate mentation during an episode, even if changes in muscle activity are bilateral, and does not respond well to antiepileptic drugs, consulting relevant internet databases for breed-specific movement disorders is advisable.

In brief, these paroxysmal movement disorders usually lack:

- An identifiable precipitating event like an aura (sensory seizure activity, such as behaviour change [attention seeking, sniffing, starring], lasting a couple of minutes just prior to the motor seizure activity).
- Autonomic signs (e.g. hypersalivation, urination, defaecation).
- Generalisation of increased motor activity (e.g. generalised tonic or tonic-clonic seizure).
- An impairment of consciousness. Usually dogs with impaired consciousness will not be able to look in the owner's eyes during the event and this is a good question to ask the owner. Animals will also often not listen to the owner due to the impairment of consciousness, although this is often falsely under reported due to the owner's perception of the event.

Seizures

The brain is a 'complex' structure, but has only 'simple' (limited) ways of expressing dysfunction. A seizure is a clinical sign caused by forebrain dysfunction – it is not a diagnosis (one specific disease). A plethora of structural and functional causes can result in seizures (see below when we talk about defining the lesion). Seizures can have many forms depending on which part of the brain is affected by seizure generation and propagation, e.g. a seizure could just affect a specific part of the sensory cortex and the animal might only have a change in behaviour (starring, freezing, sniffing, …) or only one part of the motor cortex is affected and the animal only demonstrates oro-facial automatisms. The location of the 'symptomatogenic' zone (area of the brain causing the observed clinical signs) usually overlays or is close to the epileptogenic zone (area of the brain causing the seizure) and therefore indicates the origin of the seizure. Seizure semiology, using clinical signs of cerebral dysfunctions caused by a seizure, not only helps to confirm that the event is a seizure, but also provides information about its origin. It is

relatively simple and is clinically and cost effective. Depending on the brain areas or parts being affected by the seizure motor, sensory (including behaviour changes) and vegetative changes and automatisms can be differentiated and help to characterise the seizure event.

Is it a seizure?

In brief:

- Increased muscle tone is far more likely in seizures. The most common recognised seizure is a generalised tonic-clonic seizure. Most commonly, the animal first goes stiff (tonic phase), loses proprioception and collapses into lateral recumbency, then the tonic-clonic phase (rhythmic alternating muscle contractions) starts followed often by running movements (automatisms). Atonic seizures are very uncommon and a 'floppy' collapse should guide the clinician to 'think' syncope or cataplexy.
- Rhythmic alternating muscle contractions are common in both focal and generalised seizures.
- Seizures often first involve the head and facial muscles (eye or facial muscle twitching).
- Stereotypical - most animals will have only one (or two) type(s) of seizure (seizure onset generalized, focal seizure onset with or without secondary generalisation). Seizures in an animal typically originate from the same epileptic focus and spread following the same brain pathways.
- The ictus (seizure itself) normally lasts 1-2 minutes.
- Most seizures exhibit several stages:
    - Pre-ictal behaviour changes (prodrome [hours to days] and/or aura [minutes]).
    - Ictus.
    - Post-ictal behaviour or neurological deficits (hours to days).

Apart from the seizure itself, it is the post-ictal changes that are recognised by the owner.

- Common post-ictal dysfunctions are:
    - Behaviour changes such as fear, aggression and disorientation.
    - Increased appetite.
    - Compulsive pacing.
    - Blindness, usually with normal pupillary light reflexes consistent with "central" blindness.
    - Menace response deficits.
    - Miosis contralateral to the lesion (if one lesion [secondary to disinhibition of the oculomotor nucleus]).
    - Gait abnormalities especially ataxia and "conscious" proprioceptive (paw position) deficits.
- Seizures often, but not always, occur at rest or while sleeping.
- Seizures usually impair the consciousness of the animal.
- Most of the seizure disorders will at least initially respond to antiepileptic treatment.

Further reading material:

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UPSIDE DOWN TURN AROUND – WHEN THE HEAD IS SPINNING: MANAGEMENT OF VESTIBULAR DISEASE

Friday 13 September | 17:00 - 18:45 | Amphitheater N. Skalkotas - Room A

Holger A. Volk, PhD, DipECVN, PGCAP, FHEA, FRCVS

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The vestibular system main function is to maintain an animal's equilibrium during movement and orientation against gravity. It is divided into two main sections, the peripheral and the central. The peripheral one is composed of cranial nerve VIII (CNVIII; vestibulocochlear nerve) and sensory receptors contained within the petrosal bone. The central one is that part of the vestibular system held within the cranial vault, i.e., the vestibular nuclei of CNVIII. The peripheral system detects linear acceleration and rotation movement of the head. It is responsible to maintain the position of the eyes, neck, trunk and limbs in reference to the position of the head.

The sensory receptors of the vestibular system are located in the inner ear. The sacculus and the utriculus are located in the vestibule and detect linear acceleration and head positioning against gravity. The semicircular ducts with their ampullae detect rotational acceleration.

Clinical signs

Clinical signs of dysfunction of the vestibular system are: loss of balance, head tilt, leaning, rolling, circling, nystagmus, strabismus, and depending on the type of vestibular disease, other cranial nerve deficits, Horner's Syndrome, cerebellar signs, mental depression and hemiparesis with postural reaction deficits. By defining the clinical signs present the clinician will be able to determine central vs. peripheral vestibular disease. Because the list of differentials depends on the location of the lesion, this determination is most important (see below).

Nystagmus

There is the "normal" physiological nystagmus that we can elicit performing the occulovestibular test or by spinning the animal (together with the clinician) around its on axis. Another type of "normal" nystagmus would be the pendulous nystagmus of particular cat breeds (Siamese, Birman and Himalayan), which is caused by a larger number of fibres crossing at the optic chiasm. The pendulous nystagmus is characterised by equal speed of eye movement to both sides. There is also a searching type nystagmus described in animals, which have been born blind.

Abnormal types of nystagmus would be the jerk nystagmus with a slow and a fast phase with varied directions; horizontal, rotatory or vertical. These may be conjugate or disconjugate, they may also be positional. Positional nystagmus will vary with the patient depending on its head position. The direction of the nystagmus is always defined by the fast phase, even if the slow phase is to the side of the lesion.

Strabismus

Certain cat breeds (Siamese) may have congenital divergent strabismus. A divergent strabismus may also be seen in severe cases of hydrocephalus. The strabismus seen with vestibular disease is ventrolateral (unilateral) and is not responsive to the occulovestibular test. It is seen in the eye ipsilateral to the lesion. This does not differentiate central from peripheral vestibular disease.

Leaning, Falling, Circling

The patient tends to lean or fall toward the affected side because the vestibular system facilitates the extensors of the ipsilateral side (see also above). The patient also tends to circle toward the affected side as with lesions of the forebrain. However, the circles of vestibular disease tend to be closer and tighter rather than the large roaming circles of forebrain disease. The patient with central vestibular disease is more likely to be non-ambulatory.

Head Tilt

The head tilt is on the side ipsilateral to the lesion, **unless**, the lesion is in the flocculonodular lobe of the cerebellum or the cerebellomedullary pontine angle; then the patient may have a **paradoxical** head tilt. In this case, the **head tilts to the contralateral side**. Because the lesion involves the cerebellar projections to the vestibular nuclei, and because the cerebellum is predominantly inhibitory in effect, the side of the lesion becomes overactive, giving excessive tone to the extensors of that side and causing the patient to lean and tilt away from the lesion. However, the side of the lesion can be determined by testing the proprioception, especially paw positioning which are reduced to absent on the side of the lesion.

Horner's syndrome

Horner's syndrome is characterised by the loss of sympathetic innervation to the eye. In dogs and cats fibres of the postganlionic sympathetic fibres travel through the middle ear before following the ophthalmic nerve of the trigeminal nerve. A damage at this site can cause a Horner's syndrome. The postganglionic sympathetic fibres innervate the smooth muscle of the periorbit and eyelids (also third eyelid in the cat). Furthermore, they innervate the dilator pupillaris and iris muscle. Therefore, the cardinal signs described by Dr. Horner were: 1. Enophthalmos; 2. Third eyelid protrusion; 3. Ptosis; 4. Miosis. As the sympathetic system also controls the smooth muscles in blood vessel, a failure of the system results in congested vessels. This can be best appreciated on the sclera and the ear.

Clinical sign	Central vestibular	Paradoxical vestibular	Peripheral vestibular
Paresis	Possible	Possible	No
Conscious proprioceptive deficits	**Same side as head tilt**	**Opposite site as head tilt**	No
Consciousness	Normal, obtunded, stupor, coma	Normal, obtunded, stupor, coma	Alert, disorientation possible
Cranial nerve deficits	Cranial nerves V-XII may be effected	Cranial nerves V-XII may be effected	Cranial nerve VII only
Horner's syndrome	Rare	Rare	Possible
Horizontal Nystagmus	Yes	Yes	Yes
Rotatory Nystagmus	Yes	Yes	Yes
Vertical Nystagmus	Yes	Yes	No
Nystagmus changes with head position	Yes	Yes	No

Symmetrical bilateral vestibular disease

Sometimes the patient may present with bilateral vestibular disease. One typically sees wide excursions of the head, symmetrical ataxia, no head tilt and the patient may not demonstrate a "normal" physiological nystagmus. Examples would be aminoglycoside toxicity, bilateral otitis

media/interna in cats, and congenital bilateral vestibular disease in young Doberman Pinchers.

Category	Acute nonprogressive	Acute progressive	Chronic progressive
Degenerative			Congenital vestibular syndrome
Metabolic		(Diabetes mellitus; indirect)	Hypothyroidism
Neoplastic		Metastatic	Soft tissue tumours Nerve sheath tumour
Inflammatory / infectious		Otitis media/interna (bacterial) Protozoal	Otitis media/interna (bacterial) Protozoal
Idiopathic	Idiopathic (vascular?)		
Traumatic	Fracture		
Toxic		Streptomycin Gentamycin	Streptomycin Gentamycin
Vascular	Infarction Septic emboli Hemmorrhage		

Diagnostics for peripheral vestibular syndrome
Differentials to consider:

The diagnostic work-up may vary greatly between central versus peripheral disease but all patients should have a complete blood count, biochemistries, thyroid screening and blood pressure evaluation. Even if it is only a geriatric with idiopathic vestibular syndrome, there may be an underlying renal deficiency and the nausea/vertigo may be enough to keep the patient from drinking adequately, precipitating renal failure.

Given a peripheral vestibular location, radiography of the skull with oblique views and open mouth can be considered, but the main investigation will be an otoscopic examination of the external ear canal and the tympanic membrane. If the potential for otitis media exists then myringotomy is simple and quick. It does necessitate some form of short acting sedation. Cultures and cytology may be obtained from within the bullae. Take note that the bullae of the canine are different from the cat. The feline has two compartments in the bulla. Myringotomy is done in the ventrocaudal aspect of the tympanic membrane. The resultant puncture in the membrane is quick to heal.

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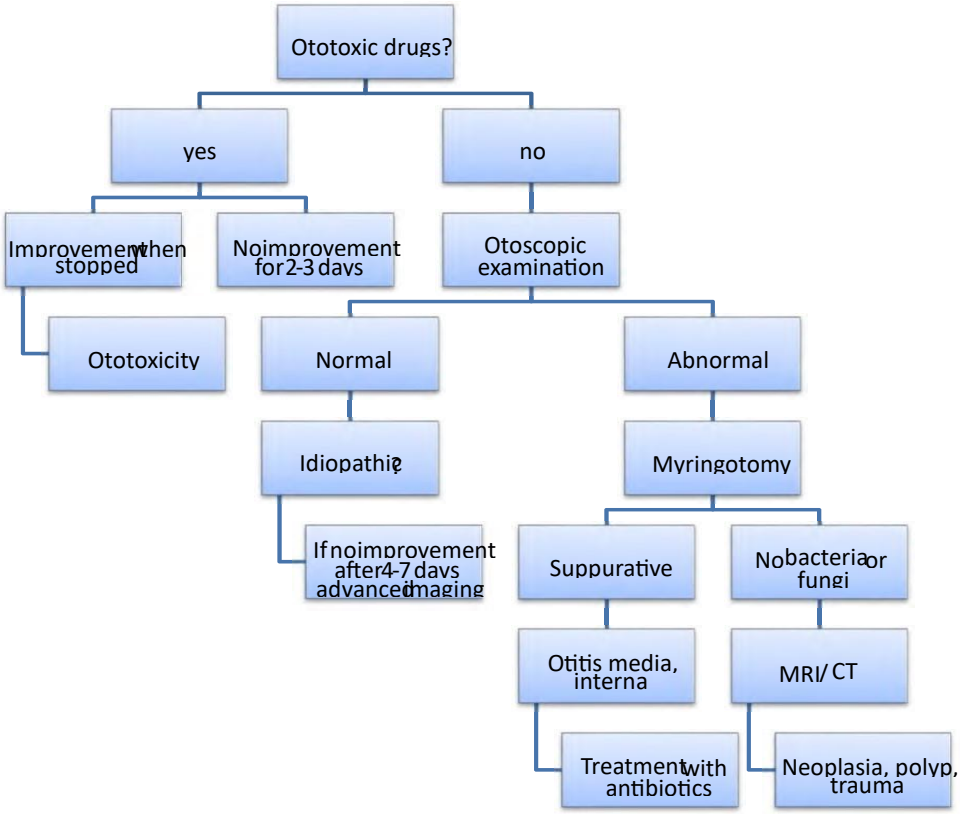
Algorithm for peripheral vestibular disorder work-up



Differentials to consider for central vestibular disorders:

Category	Acute nonprogressive	Acute progressive	Chronic progressive
Anomalous			(Hydrocephalus)

Degenerative			Neurodegenerative diseases Storage diseases
Metabolic		Hypoglycaemia	
Neoplastic		Metastatic	Primary: Choroid plexus papilloma, Glioma, Meningioma or secondary such as lymphoma
Nutritional		Thiamine def. (usually bilateral)	
Inflammatory / infectious		FIP Protozoal	FIP Protozoal
Toxic		Lead Hexachlorophene Metronidazole (usually bilateral)	Lead Hexachlorophene
Traumatic	Fracture/bleed		
Vascular	Infarction Septic emboli Haemorrhage		

Central vestibular disease will almost always require advanced imaging. This is the most important reason to localise as it will change the way how you work up the case. It is generally believed that it has to do with determining the prognosis. But the prognosis is determined by the diagnosed disease process and not by the location of the lesion. We have diagnosed many animals with soft tissue sarcomas invading the middle ear (poor prognosis) and vice versa have diagnosed dogs with cerebellar infarcts (good prognosis).

GENERAL APPROACH OF TOXICOLOGY CASES

Friday 13 September | 08:30 - 10:30 | MC 3 - Room B

Dr Joris H. Robben,
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The general approach of patients that have been poisoned encompasses therapies that are considered more or less irrespective of the (suspected) poison. These general measures try to reduce the absorption of the toxin by removing the toxin from the gastrointestinal tract (GI) or "absorbing" it to activated charcoal. The elapsed time after ingestion and transit time through the GI of the poison are the determinants for the effectiveness of these therapies. Transit time is primarily determined by the volume and state of matter (i.e. solid or liquid) of the poison, ingestion on an empty or filled stomach, and the pharmacological or toxicological effect of the poison on gastric emptying and intestinal motility.
During several decades the general approach to the poisoned animal has changed little. Treatment options have been primarily based on empirical experience. This approach has changed as a result of recent findings in toxicological studies, both in human and veterinary medicine. This has led to the suggestion of abandoning certain therapies completely or reducing their application dramatically. The five major treatment options are
1) induction of vomiting
2) gastric lavage
3) administration of activated charcoal
4) use of laxatives
5) gastrointestinal lavage.

Induction of vomiting
The use of apomorphine in dogs or xylazine/(dex)medetomidine in cats (Table 1) has been the main therapeutic intervention in small animals suspect of being poisoned, but still without symptoms as a result of the toxin. But it has been demonstrated that vomiting often does not accomplish complete removal of the poison from the stomach, with a wide variety of success between different toxins. This means that in poisonings in which absorption of even small amounts of the toxin could be hazardous or even lethal, induction of vomiting should not be the sole therapy. Furthermore, the effectiveness of induction of vomiting reduces dramatically during the time period after the intake of the toxin: with certain toxins, especially liquids, the effectiveness can be almost nothing after as short a period as 30 minutes. Often it should be considered futile in these situations and not applied. Current guidelines state that induction of vomiting should be considered in small animals without clinical signs within two hours of ingestion, and within four hours with poisons that may delay gastric emptying. However, one should realize with certain poisonings the "window of opportunity" may be much less.

Gastric lavage
What induction of vomiting is for the treatment of poisoning in small animals, has gastric lavage been for the treatment of poisoning in people. Its effectiveness has been questioned in humans, and this treatment modality is increasingly being abandoned in human medicine. In veterinary medicine gastric lavage has never been very popular, mainly because our patients have to be anesthetised. This not only means it can only be applied in patients without clinic symptoms, but it also is a more cumbersome treatment with an additional anaesthetic risk. As with vomiting, also the effectiveness of gastric lavage is much less than has been assumed, making this therapy even less interesting for veterinarians. Currently, gastric lavage is reserved at a very early stage

of the poisoning, and only for those toxins that could be potentially lethal once absorbed from the gastrointestinal tract.

Activated charcoal

Of all treatment options, the use of activated charcoal, i.e. the powder or paste formulation not the tablets, has held more or less its ground. Of course, not all toxins can be treated with activated charcoal as they are not "absorbed" by it, but if theoretically effective, the use of activated charcoal is still advised. However, its effectiveness is also time dependent. Activated charcoal can be administered once or twice, or over an one-day period if there is delayed absorption of the poison from the gastrointestinal tract or an enterohepatic cycle is anticipated. With proper application activated charcoal is still considered an effective treatment option in poisonings.

Laxatives

The idea behind the use of laxatives has been to accelerate the passage of the activated charcoal through the gastrointestinal tract. This should limit the potential release of the poison from the activated charcoal and delayed absorption from the gastrointestinal tract. It should also limit the risk for constipation that activated charcoal could cause. Although a very attractive concept, currently because of lack of scientific proof, the use of laxatives has been almost abandoned with the onetime use of activated charcoal. The chance of constipation or a delay in the transit time through the gastrointestinal tract is with the short use of activated charcoal very limited. However, it still may be considered initially if activated charcoal is repeatedly administered.

Intestinal lavage

This treatment option should only be considered if the poison is potentially lethal after absorption and has a delayed, controlled release, e.g. calcium channel blockers, cocaine balls. Also toxins that are not absorbed by activated charcoal, e.g. lithium, iron preparations, could be dealt with in this way.

The suggested application of treatment options in small animal poisonings has been reduced in recent years. Although this may suggest that "life becomes easier", the treatment of poisonings also can become a frustrating experience in the absence of simple and effective treatment modalities. But, as we are moving towards a more evidence-based approach, it should be reassuring that what you do as a veterinarian actually does have an effect on morbidity and patient outcome. Furthermore, it is good to realize, also in relation to the owner, that our treatments may have an effect, but potentially not a 100% effect. A 50 to 70% reduction in toxin absorption from the gastrointestinal tract may not be very effective, but it could be the difference between a patient that develops serious toxicological symptoms and a patient that shows no clinical symptoms at all.

References

1. Kan AA, Dijkman MA, de Vries I, Robben JH. Orale vergiftigingen bij hond en kat - Absorptie-verminderende maatregelen na orale vergiftigingen bij hond en kat. Tijdschr Diergeneesk 2016;141(3):30-35. (aanvullend commentaar Tijdschr Diergeneesk 2016;141(6):6)

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NEUROTOXICITY : CASE APPROACH

Friday 13 September | 08:30 - 10:30 | MC 3 - Room B

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Introduction
When an practitioner is confronted with a patient with acute symptoms from the central nervous system, neurotoxins as a cause is high on the list. The list of neurotoxins is long and contains toxins like permethrin (cats), alfa-chloralose, metaldehyde, avermectins, tetanus, organophosphates/ carbamates, strychnine, amatoxin, and several medications (metronidazole, baclofen, etc.). Furthermore, neurological symptoms can develop as a complication of xenobiotics, like hypoglycaemia as a result of a xylitol poisoning.
Rarely if at all antidotes exist and a general decontamination or a symptomatic approach is necessary. General gastro-intestinal decontamination measures are limited to those patients with a known or a high suspicion intake of a neurotoxin prior to the development of central neurologic symptoms. Once neurological symptoms have developed a general symptomatic approach is necessary.
Neurotoxicity can lead to a range of neurological signs, such as ataxia, postural deficits, muscle fasciculations, paresis, paralysis, seizures, and gait disturbances. But especially muscle spasms and seizures warrant symptomatic treatment.

Sedation and anticonvulsants
To control muscle spasms and convulsions sedatives, muscle relaxants and anticonvusant drugs are available. The most widely used are

- benzodiazepines
  - diazepam: 0.5-1 mg/kg IV, rectal
  - midazolam: 0.1-0.5 mg/kg(/h) IV, CRI
- propofol: 1-6 mg/kg IV; 0.05-0.5 mg/kg/min CRI
- levetiracetam
  - loading dose: 60 mg/kg IV
  - maintenance: 20 mg/kg IV/PO
- phenobarbital
  - loading doses: 3 mg/kg every 30-120 min 4-8 times
- alphaxalone: 2-5 mg/kg IM, IV
- opiates (gives additional analgesia)
  - butorphanol
    - 0.2–0.4 mg/kg SC IM IV
    - 0.1-0.4 mg/kg/h CRI (Loading dose: 0.1-0.4 mg/kg)
  - fentanyl: 2-5 microg/kg/h CRI
  - sufentanil: 0.2-0.5 microg/kg/h CRI
- dexmedetomidine: 0.5-1 µgr/kg/h
- methocarbamol (central muscle relaxant)
  - 55-220 mg/kg IV (<330 mg/kg/day)
  - on effect, start with half the dose

To reach an optimal effect with as little as possible adverse effects a multimodal approach is often warranted.

Intravenous lipid emulsion therapy

The use of intravenous lipid emulsions (ILE) in human clinical toxicology has become a common practice as life-saving treatment for cardiotoxicity after local anaesthetics overdose. The mechanism behind this "antidotal" effect has not yet been fully elucidated. Case reports indicate ILE may be useful in the resuscitation from toxicity induced by a variety of other lipophilic cardiotoxic drugs like various tricyclic antidepressants (TCA), lipofilic β blockers and calcium channel blockers. Several veterinary case reports and case series have demonstrated that ILE are primarily used in the management of long-lasting neurotoxicity like permethrin toxicosis in cats and ivermectin toxicosis in dogs. Treatment with ILE can result in a faster recovery leading to shorter admission times in the veterinary practice.

ILE therapy can be considered in cases of severe neurotoxicity caused by strong lipophilic substances with a long elimination half-life and no other treatments have been effective.

- Consider temporarily discontinuing other infusions to minimize volume overload.
- Administer an intravenous (IV) bolus injection (peripheral or central venous) of 1.5 mL/kg ILE 20% over 1-2 minutes.
- Follow this with a continuous infusion of 0.25 mL/kg/min (15 mL/kg/hour) for 30 to 60 minutes
- (Alternative: 0.07 mL/kg/min (4 mL/k//h) for 4 hrs).
- Monitor the animal closely for possible pyrogenic and allergic reactions, especially during the first 20 minutes.
- If side effects occur, discontinue intravenous fat emulsion administration immediately.
- Evaluate the patient 4-6 hours after stopping the fat emulsion infusion.
- If there is insufficient or no clinical improvement, repeat the above administration 2-3 times once the patient's blood/serum is no longer visibly (macroscopically) lipemic. If still no or inadequate effect, discontinue use.
- If there is significant clinical improvement, keep the patient hospitalized for at least 12 more hours before discharge.

Supportive therapy

As sedation often causes the patient to be immobile supportive measures should be taken as necessary. Nursing care in these situations is important to make the patient as comfortable as possible and limit the risk of complications. Measures that could be considered: regularly moving the patient in another position, especially when in lateral recumbancy, physiotherapy, closed urine collection system, enteral tube/parenteral feeding, control of body temperature, oxygen therapy, fluid therapy, gastroprotectants, etc.

In extreme cases with severe paralysis and respiratory failure or the need for general anaesthesia to control symptoms positive pressure ventilation required.

Conclusion

Neurotoxicity in dogs and cats is a complex and multifaceted issue that requires a thorough understanding of the underlying mechanisms, potential causes, and appropriate management strategies.

Reference

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THE USE OF SYMPATHOMIMETICS IN DOGS AND CATS: HOW TO CHOOSE

Friday 13 September | 09:50 - 10:30 | MC 3 - Room B

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Hypotension is a significant cardiovascular complication during general anesthesia in dogs and cats. Many anesthetic drugs compromise cardiac function, affect vascular tone, and alter vascular volume. Additionally, numerous animals hospitalized in intensive care units experience severe hypotension due to underlying diseases impacting cardiovascular function. Sympathomimetics (SPM), are frequently administered in veterinary anesthesia and intensive care to support cardiovascular function by imitating the function of the sympathetic nervous system. SPM include natural catecholamines (epinephrine, norepinephrine, dopamine), synthetic catecholamines (isoproterenol, dobutamine), and synthetic non-catecholamines (ephedrine, phenylephrine). These agents are vital for maintaining hemodynamic stability and ensuring adequate tissue perfusion in critically ill or anesthetized patients. The pharmacological properties of these drugs, including their pharmacokinetics and pharmacodynamics, are crucial for their effective clinical application. Key drugs such as dobutamine, a selective beta-1 agonist, and dopamine, which has dose-dependent effects, are instrumental in enhancing myocardial contractility and cardiac output. Vasopressors like norepinephrine, primarily an alpha-adrenergic agonist, are essential for managing hypotension, particularly in septic shock, due to their potent vasoconstrictive properties. Epinephrine, a non-selective agonist, is frequently used in emergencies such as anaphylaxis and cardiac arrest for its broad adrenergic effects. These drugs are mainly administered via intravenous (IV) infusion for precise titration, though intraosseous route may be an alternative when IV access is difficult. Despite their therapeutic benefits, SPM may cause adverse effects such as tachycardia, arrhythmias, hypertension, and tissue ischemia, requiring careful monitoring. A thorough understanding of the pharmacological properties, clinical applications, and potential side effects of sympathomimetics is essential for optimizing outcomes in critically ill or anesthetized animals.

TETANUS

Friday 13 September | 11:00 - 13:00 | MC 3 - Room B

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Introduction
Tetanus is caused by toxins released by Clostridium tetani, a ubiquitous, motile, gram-positive, non-encapsulated, anaerobic, and spore-forming bacillus. The disease has an incubation period of 3 days to 3 weeks, typically following a deep penetrating wound. Clinical signs often worsen within days after initial presentation. A localized form of tetanus can escalate to a generalized form, with mild symptoms potentially evolving into a life-threatening condition.
A treatment plan should be tailored to the severity of the disease, requiring adjustments based on its progression. A multimodal approach is often necessary but challenging due to the need to balance benefits and risks. Therefore, a stepwise treatment plan is suggested, considering different options at predefined stages of the disease. Each stage is defined by the severity of clinical symptoms, especially muscle spasms and autonomic dysregulation, in combination with the response to treatment.

Basal Treatment Level
For localized tetanus or mild generalized symptoms where the patient can still walk and eat, initial interventions include debridement if a wound has not healed to eliminate the source of toxin production. Antimicrobial therapy is essential if signs of C. tetani infection persist. Metronidazole for 7 to 14 days is preferred, but penicillin G, tetracycline, and clindamycin are alternatives. The effectiveness of human tetanus immunoglobulin (TIG) and anti-tetanus serum (ATS) to neutralize toxin activity is limited as neither can cross the blood-brain barrier sufficiently. A one-time dose of 500-1000 IU may be administered early in the disease process, with prior intradermal testing recommended to prevent hypersensitivity reactions. Muscle spasms can be reduced in a quiet, darkened room by minimizing tactile stimuli. Anti-emetics and antacids may reduce the risk and severity of aspiration pneumonia due to regurgitation.

Level 1
At this level, the patient has generalized tetanus with increased muscular tone but little autonomic derangement. The patient can still swallow, and respiration is adequate. Proper hygiene and handling of catheters and other invasive devices are crucial. Repositioning the patient regularly (2-4 hours) helps prevent atelectasis and decubital ulcers, keeping the patient comfortable. A urinary catheter with a closed system is necessary. Limiting auditory stimulation with cotton or gauze plugs in the external ear canal and reducing visual stimulation by covering the eyes can help. Physiotherapy may benefit patients recumbent for extended periods to prevent joint lock and muscle spasm. Maintaining body temperature between 37 to 38°C (98.5-100.5°F) is important. Oral care protocols used during mechanical ventilation are necessary for sedated patients. Hypermetabolic states may arise due to hyperthermia, increased muscle activity, and sympathetic discharge. Enteral feeding may be limited by trismus, a compromised swallowing reflex, megaoesophagus, and oesophageal hiatal hernia, increasing the risk of

regurgitation, vomiting, and aspiration pneumonia. However, in a stable clinical situation, enteral feeding can be considered with the patient's head raised at a 30-degree angle.
Although the patient may not be hypoxemic, early oxygen therapy is warranted due to the risk of slow and unnoticed deterioration. The goal is to control muscle spasms and convulsions without inducing profound respiratory depression that would require mechanical ventilation. Continuous intravenous infusion (CRI) of drugs provides better control and a more stable situation. A multimodal approach is used to achieve appropriate muscle relaxation and adequate sedation while minimizing the adverse effects of individual medications. In the early stages, midazolam and methocarbamol are often recommended to control muscle tone, combined with acepromazine to reduce responsiveness to external stimuli. Magnesium at supra-physiologic plasma concentrations effectively supports muscle rigidity control. Arousal and muscle spasms during procedures may be prevented by administering a short-acting sedative/muscle relaxant such as propofol beforehand. Intravenous fluid therapy is needed for patients unable to drink sufficiently, are hyperthermic, or are tachypnoeic. Parenteral feeding can be initiated if enteral feeding seems too risky. Additional pain medication is unnecessary when muscle spasms are adequately controlled. However, in cases of severe reflex spasms and convulsions due to sensory stimuli, pain management becomes necessary. Low doses of opioids (combined with low-dose CRI ketamine) can control pain, preventing arousal and further muscle spasms. The use of nonsteroidal anti-inflammatory drugs (NSAIDs) should be carefully considered, with close monitoring for signs of gastrointestinal ulceration, bleeding, and renal compromise. Pre-emptive treatment for GI ulceration and fluid therapy should be considered. Opioids such as fentanyl can be used as CRI in low doses with little effect on respiration. However, combined with sedative doses of other anesthetics, even low doses can cause respiratory depression due to synergism. Eye lubrication is strongly advised.

Level 2
Level 2 is reached if level 1 interventions no longer result in a stable clinical situation. Treatment interventions from level 1 can be combined with, or replaced by, level 2 interventions. At this stage, the risk of aspiration and respiratory failure increases due to respiratory muscle rigidity, reflex spasms of the larynx, increased airway secretions, and medication effects. Monitoring end-tidal (ET) CO_2 and blood gases becomes mandatory, requiring endo/trans-tracheal intubation and extended oral and bronchial care. To achieve deeper sedation and improve muscle relaxation, dosages of level 1 drugs can be increased, or propofol and barbiturates may be considered. Higher doses of opioids and/or combination with ketamine can also be considered. However, these interventions increase the risk of respiratory depression. Autonomic dysfunction may become more prominent as tetanospasmin interferes with the autonomic nervous system, causing brady-/tachyarrhythmia, hypo-/hypertension, and increased salivation and airway secretions. Symptomatic treatment could involve vasopressors and parasympatolytics.

Level 3
Level 3 is reached if level 2 interventions no longer result in a stable clinical situation. Instability often results from inadequately controlled muscle rigidity, leading to inadequate tidal volumes due to respiratory muscle spasms, respiratory depression (indicated by increased $ETCO_2$ or PCO_2), and increased autonomic dysregulation. Treatment interventions from levels 1 and 2 can be combined with, or replaced by, level 3 options. Mechanical ventilation is initiated to control and support respiration, as this can no longer be guaranteed. Level 3 medications also compromise respiration. Positive pressure ventilation should be considered early in the disease process rather than as a last resort, following human medicine practices when clinical symptoms warrant a more aggressive approach. An extensive protocol of oral, tracheal, and tube care complements mechanical ventilation.

A combination of fentanyl, midazolam, propofol, and barbiturates is used to maintain adequate general anaesthesia. Keeping the patient under general anaesthesia for several days may be

required. Although periodically decreasing the depth of sedation or anaesthesia is necessary to monitor recovery from tetanus, frequent titration or prolonged periods of inadequate muscle relaxation and/or sedation/anaesthesia increase the risk of complications such as aspiration pneumonia, hyperthermia, and depletion of catecholamine stores/autonomic dysregulation. Using dexmedetomidine as CRI in the nano- to microdose range (0.25-2 µg/kg/hour) may prevent these scenarios. Complete muscle relaxation may be considered if muscle rigidity cannot be adequately controlled, interferes with mechanical ventilation, or requires unacceptable deep levels of anaesthesia. Monitoring muscle relaxation with appropriate equipment is mandatory, and patients should be maintained at an adequate level of anaesthesia to prevent awareness. However, clinical assessment of anaesthesia depth is hampered when the patient is paralyzed.

Conclusion

While tetanus and its sequelae impact many organ systems, treatment demands a multimodal approach where the outcome is determined by combining therapies. This makes tetanus a challenging and complicated disease to treat.

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PERITONEAL DIALYSIS IN RENAL PATIENTS - NEW ASPECTS, CLINICAL ASPECTS AND PRACTICAL ADVICE

Friday 13 September | 11:00 - 13:00 | MC 3 - Room B

Prof. Habil. Dr. Alexandru Bogdan VIȚĂLARU

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DIALYSIS, dialize, s. f. From a medical standpoint, dialysis is the process of separating a substance with colloidal dispersion from particles with molecular dispersion, based on the property of some membranes to retain only colloidal particles. [Pr.: di-a-] – Din fr. dialyse.

KIDNEYS:
- filtration of residues, drugs and toxins in the blood;
- concentrate or dilute urine to prevent dehydration or over-hydration;
- adjusts blood pressure;
- production of certain hormones.

PERITONEAL DIALYSIS PRINCIPLE

Transfer of a solution through a semi-permeable membrane based on the principle of diffusion, where the membranes are represented by the parietal and visceral peritoneum.

Solutions with the highest concentration cross the membrane pores and they are eliminated from the body.

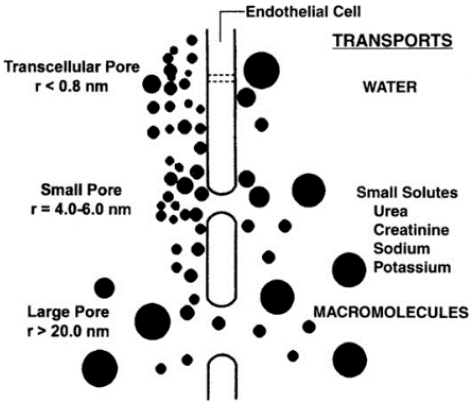
Peritoneal dialysis is an excellent substitute for hemodialysis in cases where, for various reasons, patients cannot stand hemodialysis.

Peritoneal dialysis therapy plays an important role in kidney failure in dogs and cats, especially in the elderly and weighing up to 10 kg that cannot be placed on hemodialysis due to insufficient body mass.

The indications of peritoneal dialysis are acute kidney failure and chronic kidney failure, including fluid overload situations (using hypertonic dialysate), pulmonary edema and ethylene glycol or barbiturates poisoning.

The ideal peritoneal catheter for peritoneal dialysis allows the proper administration and evacuation of the dialysate with minimum subcutaneous losses, minimizes infections in both the peritoneal cavity and the skin tissue.

Acute dialysis catheters are inserted under local anesthesia, percutaneously through the stiletto – HEPARINISATION.



Chronic peritoneal dialysis catheteres have specific models, both intraperitoneal and extraperitoneal, to reduce side effects and minimize clotting. The catheters are made of silicone, rubber, or polyurethane. The catheter portion that enters the abdomen often has 1 or 2 Dacron cuffs - local inflammatory response - fibrous granulation tissue - that prevents migration bacteria and causes fixation.

It is mandatory for the catheter placement to be made under aseptical conditions, in an operating room, on the white line or paramedian/lateral of the umbilical scar. The catheter needs to be caudally oriented and positioned in the lower part of the pelvis. Before the final fixing, the permeability of the catheter is checked by introducing a small amount of dialysate.

PERITONEAL DIALYSIS FLUID

The concentration gradient between the blood and the dialysate determines an effective treatment of accumulated body toxins.

Commercial solutions contain glucose, lactate, potassium, calcium and sodium in different concentrations.

Bicarbonate and lactate or a mixture of the two are used to create a solution with a neutral pH.

Glucose is the most common osmotic agent that draws fluid through the peritoneal membrane.

Newest peritoneal dialysis solutions contain an osmotic icodextrin agent (glucose polymer) supporting ultrafiltration.

Moreover, when there is hypoproteinemia, we can use amino acids solutions that provide body nutrition.

The volume of the introduced dialysate varies depending on the concentration, composition, and individual patient needs between 40-60ml/kg/exchange.

In practice, we use a more convenient formula, essentially the amount introduced is 1 l/1square meter on each shift.

When initiating peritoneal dialysis for AKI, the goal is not to normalize UREMIA immediately!

The initial objectives are: normalization of hemodynamic, acid-base and electrolyte patient status and the reduction of BUN at more than 100 mg/dL and creatinine 4.0-6.0 mg/dl in 24-48 hours.

COMPLICATIONS

- catheter obstruction- omentectomy before implanting the catheter and the introduction of heparin at a dose of 500 IU/liter in the solution with the role to reduce the incidence of peritoneal adhesions or the use of catheters with a heparin film;
- associated peritonitis – liquid examination or white cell count;
- difficult catheter placement;
- accidental puncture of the urinary bladder;
- laceration of large vessels.

THE 2024 ISFM GUIDELINES ON THE LONG-TERM USE OF NSAIDS IN CATS: WHAT'S THE TAKE-HOME MESSAGE?

Friday 13 September | 14:00 - 15:45 | MC 3 - Room B

Paulo Steagall

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Non-steroidal anti-inflammatory drugs (NSAIDs) are used for several long-term painful conditions and they have now robust evidence for their safety and efficacy in cats. The 2024 ISFM Guidelines[1] on the long-term use of NSAIDs in cats have been published after its first edition in 2010.[2] The goal is to support veterinarians in decision-making around prescribing NSAIDs in situations of chronic pain while minimizing adverse effects and optimizing pain management. This lecture will provide an overview of their highlights including their mechanism of action, indications for use, screening prior to prescription, use in the presence of comorbidities, monitoring of efficacy, and avoidance and management of adverse effects. The use of long-term NSAIDs in cats with chronic kidney disease will be presented based on the latest evidence-based information but also the concomitant use of these drugs with other therapies.

[1] Taylor S, Gruen M, KuKanich K, Lascelles BDX, Monteiro BP, Sampietro LR, Robertson SA, Steagall PV. 2024 ISFM and AAFP consensus guidelines on the long-term use of NSAIDs in cats. J Feline Med Surg. 2024 26(4):1098612X241241951.

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THE 2024 HIGHLIGHTS ON PAIN MANAGEMENT

Friday 13 September | 14:00 - 15:45 | MC 3 - Room B

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This lecture will give an overview of current practical techniques and drug protocols for small animal pain management that are readily applicable to clinical practice. This will involve a dynamic and interactive approach including some video-based teaching with several resources presented to the audience. The audience will have access to the ultimate information and "news" regarding pain management for canine and feline patients. This may involve the use of intraperitoneal and incisional anesthesia, intratesticular block, gabapentinoids, opioid-free anesthetic protocols, monoclonal antibodies and novel methods for pain assessment in feline osteoarthritis.

REAL-LIFE ANALGESIC PROTOCOLS IN SMALL ANIMAL PRACTICE

Friday 13 September | 17:00 - 18:45 | MC 3 - Room B

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In this lecture, participants will be invited to interact with the speaker and discuss the analgesic management for a variety of patients and situations. There will be a "bit of everything" related to canine and feline analgesia. The discussion will go from pain management in healthy patients undergoing routine procedure such as ovariohysterectomy and dentistry but also those in critical condition with urethral obstruction and lower urinary tract disease, and abdominal laparotomy and cesarean section. The lecture will explore novel concepts and techniques in canine and feline pain management with a practical and interactive approach including protocols with dosage regimens. Treatment of perioperative pain relief and considerations on the use of analgesics in cats with chronic pain will be discussed. Controversial topics will be broken down using current literature and evidence. We will explore the multifactorial cause of osteoarthritis, chronic pain assessment and treatment including therapy with NSAIDs. This lecture will encourage attendees to engage with the speaker, discussing analgesic protocols for a range of patients and scenarios.

FROM THE BEGINNING TO THE END: ANAESTHETIC MANAGEMENT OF BRACHYCEPHALIC DOGS

Friday 13 September | 17:00 - 18:45 | MC 3 - Room B

Kiriaki Pavlidou

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Brachycephalic dogs (e.g. Bulldogs, Pugs, Shih Tzus) are extremely popular as pets, and the need for procedures that require anaesthesia is common. This general review of anaesthetic management of brachycephalic dogs focuses on dogs with components of brachycephalic obstructive airway syndrome (BOAS) but does not address specific procedures for airway surgery. The overall health of the animal must be considered before choosing anaesthetic protocols as brachycephalic dogs demand a specific anaesthetic management.

The flattened features of the brachycephalic skull compress upper airway structures, which can cause a variety of medical problems and be particularly concerning for anaesthetic safety. The most common disorders which are usually seen in these animals are the stenotic nares, elongated soft palate, everted laryngeal saccules and tracheal hypoplasia. In some animals, further abnormalities of the airway due to cartilage defects may be seen such as collapsing trachea and laryngeal collapse. In a very few instances, grossly enlarged tonsils may contribute to the airway obstruction. The main effect of narrowed airway structures in these animals is increased work of breathing. Any increase in respiratory effort, such as that caused by stress, excitement, pain, or hyperthermia, causes increasingly negative airway pressure and further airway narrowing with subsequent hypoventilation, hypoxemia, hypercarnia, and, potentially, airway collapse. Thus, a major goal of anaesthetic management in these patients is avoidance of stressfull conditions.

Brachycephalic dogs are twice as likely to have anaesthesia complications as nonbrachycephalic dogs, with most complications, primarily dyspnoea, regurgitation, and aspiration pneumonia, occurring in the postoperative period. Prevention of aspiration pneumonia is also a main goal of anaesthetic management, and the author recommends antiemetics for all brachycephalic patients undergoing anaesthesia.

They have also higher vagal tone than dogs of other breeds, and those with BOAS can have an exaggerated vagal response with rapid and potentially profound bradycardia when the upper airway is manipulated, as during surgery, intubation, or extubation.

Esophageal and gastrointestinal (GI) tract lesions, including esophagitis, gastroesophageal reflux, gastritis, and hiatal hernia, are prevalent in brachycephalic dogs with upper respiratory dysfunction. A history of signs of GI abnormalities is highly linked to risk of aspiration pneumonia. Stabilization or treatment of GI disease prior to anaesthesia is recommended. However, correction of upper airway dysfunction is often the key to resolution of GI signs.

Prolonged fasting may not be appropriate for brachycephalic dogs. A fast time of less than 6 hours is recommended in the American Animal Hospital Association guidelines, and a small meal 3 hours prior to anaesthesia may be beneficial to decrease reflux. However, ideal fasting times are still unknown and "standard" fasting times may still be appropriate. Antacids and gastroprotectants, along with prokinetics, are often recommended for brachycephalics but can be overused. The American College of Veterinary Internal Medicine has published an in-depth review and consensus statement on the use of these drugs.

Safe anaesthesia for patients with upper airway dysfunction depends more on patient

management than on drug choice. Both intubation and extubation can be difficult for the anaesthetist and dangerous for the patient. Almost all anaesthetic and sedative drugs are acceptable for use in brachycephalic patients, but the most appropriate drugs are those that are fast acting for rapid intubation, have a short duration of action, and/or are reversible for quick return to consciousness and normal breathing.

During to the recovery period, the animal should be kept calm in a quiet environment free of pain. The patient should be kept warm for optimal recovery. Hypothermia will prolong recovery time and return to normal breathing. Shivering increases oxygen consumption, which may not be met by oxygen delivery if the patient cannot breathe, and oxygen debt

(inadequate tissue oxygenation) may occur. Use the pulse oximeter to monitor adequacy of oxygenation, especially after extubation. If the tongue is not accessible, alternative sites of pulse oximeter probe placement can be used. Brachycephalic patients often still tolerate the endotracheal tube when completely conscious and it can be carefully extubated at this point.

Concerning the particularities that these breeds have, the anaesthetist should be very careful during the pre- and post-anaesthetic period. The guidelines that are given to the owners should be specific foe each case.

DIAGNOSIS AND MANAGEMENT OF COMMON SHOULDER SOFT TISSUE PATHOLOGIES IN DOGS

Friday 13 September | 08:30 – 10:30 | MC 2 – Room C

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Hip dysplasia (HD) in dogs is a heritable developmental disorder characterized by an abnormal formation of the coxofemoral joint. The pathogenesis of hip dysplasia is multifactorial, mainly involving genetic predisposition and various environmental influences. The disease manifests in genetically predisposed animals exposed to environmental (nongenetic) factors that promote the expression of the genetic weakness.

The earliest sign of canine hip dysplasia has been defined as hip joint laxity. Over time, abnormal joint biomechanics contribute to secondary degenerative joint disease, including cartilage degeneration, synovial inflammation, bone remodeling, and osteophyte formation. Every dog is born with normal hips. If congruity between the femoral head and the acetabulum is maintained, the coxofemoral joint will continue to develop normally. The earliest signs of hip dysplasia are seen at about four weeks of age. The ligament of the femoral head, acting as the primary stabilizer of the joint at that time, increases in volume and suffers small partial tears and hemorrhage, leading to joint inflammation and increased synovial fluid volume—this finding, together with lengthening of the ligament of the femoral lead to joint subluxation. The earliest radiographic signs of hip dysplasia are seen at seven weeks of age, including joint incongruity and an abnormal conformation of the dorsal acetabular rim. Ongoing subluxation, stretching of the joint capsule, and further lengthening of the ligament of the femoral head at the age of 8-12 weeks lead to a worsening of the radiographic signs and cartilage degeneration. The most susceptible areas for cartilage damage due to uneven distribution of weight-bearing forces are the femoral head and the dorsal acetabular rim. The time window to prevent the development of degenerative joint disease that eventually leads to osteoarthritis is very narrow (16-20 weeks of age).

Research on canine hip dysplasia genetics continues, but progress has been sluggish compared to expectations. For this reason, veterinarians need to focus on the dog's phenotype to identify dogs with lax hips who may already suffer or are susceptible to developing joint degenerative changes. Joint laxity (clinical and radiographic) appearing before degenerative and structural changes is the key to the efforts to prevent the progression of the disease.

Early diagnosis, ideally between 12 and 20 weeks of age, is based on the dog's signalment, physical and orthopedic examination, and, most importantly, radiographic findings/measurements. It is essential to understand that one must not wait for clinical signs to screen a young dog for hip dysplasia. The owner of dog breeds at risk of developing hip dysplasia should be informed about the early screening at the time of the first vaccination. The reason is that early acute clinical findings, such as lameness, exercise intolerance, and pain of the hindlimbs, are thought to result from extreme joint laxity. Joint laxity leads to capsular strain and inflammation as dogs age, resulting in periarticular fibrosis. This stage of the condition commonly leads to decreased or absent clinical symptoms.

The most common clinical signs include muscle atrophy of the hind limbs, hip or spinal sway movement, bunny hopping, lameness, and pain on palpation (especially during joint extension and abduction). The Ortolani test may be performed in the awake animal, but it is usually very painful. The animal is then evaluated in deep sedation. In young dogs, a positive Ortolani sign is the most reliable clinical feature of hip dysplasia. It should be negative in all dogs 12-16 weeks. The angles of subluxation (AS) and reposition (AR) of the joint can be measured with a designated goniometer. After clinically evaluating joint laxity, objective radiographic measurements are performed.

The most widely performed radiographic views include the standard ventrodorsal (VD) extended view, the frog VD view, the distraction view, and the dorsal acetabular rim (DAR) view. The VD extended view is evaluated for signs of joint incongruity (femoral head coverage/Norbert angle), abnormality of the morphology of the acetabulum, and early signs of degenerative joint disease (subchondral bone sclerosis, morgan line, acetabular cupping, femoral head flattening and osteophytes). In the frog VD view, the acetabular depth/filling and coverage of the femoral head are evaluated. Unfortunately, the VD extended view lacks sensitivity to diagnose laxity as it masks joint incongruity due to the wind-up phenomenon. Distraction-based radiographic techniques have been developed to improve the identification of hip joint laxity. For example, the distraction view of the PennHip evaluates non-weight-bearing laxity and provides a predictive index for the development of osteoarthritis. The index can be measured with two different distraction devices (PennHip distractor - DI and Vezzoni modified Badertscher distension device-LI). Both methods were shown to be equally reproducible. In general, a distraction index (DI) or laxity index (LI) below 0.3 is linked to physiological laxity and a favorable outcome regarding the risk of osteoarthritis development. An index ranging from 0.3 to 0.7 indicates an abnormal laxity, whereas an index exceeding 0.7 correlates with excessive laxity and is associated with an unfavorable prognosis. It is essential to know that breed variations exist, and numerous publications concerning the DI can be found in the literature. Finally, the DAR view measures the DAR slope and can evaluate whether the DAR is preserved or shows pathological changes.

Treatment options depend on the severity of clinical signs, degree of joint laxity, and radiographic findings. Shortly, conservative treatment includes NSAIDs, weight management, physiotherapy, polysulfated glycosaminoglycans, and Omega-3 fatty acids-rich diet. Surgical preventive methods include juvenile pubic symphysiodesis (JPS) and double pelvic osteotomy (DPO). Surgical therapy procedures can be preventive, restorative, or palliative. Juvenile Pubic Symphysiodesis (JPS) and double pelvic osteotomy are preventive methods. Dogs with severe clinical signs, femoral head and acetabulum erosion, acetabular filling, radiographic signs of osteoarthritis, and a difference between AR and AS of more than 15° are no candidates for preventive procedures. Total hip replacement (THR) is the restorative method of choice, while femoral head and neck excision (FHNE) is a palliative procedure. More recently, custom-made implants to improve femoral head coverage have been used. Joint laxity and pain scores improved in most cases. On the other hand, force plate analysis showed no improvement, and osteoarthritis scores increased. Treatment recommendations should always be individualized for each dog, and owners' expectations and financial aspects should also be considered.

- Age: 4-5 months

- Mild joint laxity, no clinical symptoms→ Conservative treatment
- Mild-moderate joint laxity, no clinical symptoms→ conservative treatment or JPS
- Moderate joint laxity, with/without clinical symptoms→ JPS
- Moderate- severe joint laxity, with symptoms→ conservative, DPO or THR later
- Severe joint laxity, with clinical symptoms→ conservative, THR or FHNE later in life, depending on symptoms

- Age: > 5-6 months

- Mild joint laxity, no clinical symptoms→ Conservative treatment
- Mild-Moderate joint laxity, no clinical symptoms→ conservative treatment or DPO
- Moderate joint laxity, with/without clinical symptoms→ conservative treatment or DPO
- Moderate- severe joint laxity, with symptoms, no osteoarthritis→ conservative, DPO or THR later in life
- Severe joint laxity, with clinical symptoms and signs of osteoarthriris→ conservative, THR or FHNE later in life, depending on the severity of symptoms

Early diagnosis of hip dysplasia in dogs is crucial for implementing effective management strategies and minimizing disease progression. Identifying the condition early in life allows for interventions to restore joint congruity, slow or prevent osteoarthritis development, and improve the dog's quality of life. Moreover, early screening of hip dysplasia can guide breeders and provide valuable information in choosing which dog should be selected as a breeding dog.

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MOST COMMON REASONS FOR FRONT LIMB LAMENESS

Friday 13 September | 08:30 – 10:30 | MC 2 – Room C

Svetoslav Hristov
DVM, AVSB CertSAS

Diagnosis and management of front limb lameness is often a time-consuming, require lot of knowledge on normal anatomy and possible list of diagnoses and access to a different imaging modalities. A different factors play an important role and challenge the diagnostics and treatment of front limb lameness in dogs. Such a factors are complex anatomy of the joints in the front limb, a normal weight distribution over the front limbs, dog's activity level, age, concurrent pathologies of the hind limbs or the spine. A different diagnostic algorithms are available but often they are really labor-intensive and related to a multiple imaging modalities. A breed oriented approach is also often implement in diagnosis front limb lameness having the signalment and the breed as important consideration in possible front limb pathology. For example a form of elbow dysplasia (coronoid disease or medial compartment syndrome) is statistically the most common reason for front limb lameness in young Golden Retriever. Another common clinical scenario is a young Cane Corso dog with subtle lameness and shoulder pain in flexion/extension. A presumptive diagnosis of humeral head OCD is often easily confirmed on a medial-lateral radiographic view of the shoulder area.

However, many of the cases may require more advanced imaging modalities – CT, ultrasound, arthroscopy or MRI. For example young adult male Staffordshire terrier with grade 2 lameness is presented due to right front limb lameness after significant physical activities (intensive playing with a ball or long walks). The orthopaedic examination didn't showed any significant findings and the dog went through radiographic examine of the limb, CT scan of the front limb and the cervical spine and ultrasonography of the shoulder muscles and tendons. The only finding was a slight hypertrophy of the biceps tendon with supraspinatus impingement on a ultrasonographic examination of the shoulder area. Adapted activity program was recommended to the owner.

Mature poodle was reluctant to play with a ball and the owner noticed intermittent lameness with the front right limb. The clinical examination didn't showed anything and slight osteoarthritic changes were noticed in the right elbow joint (mild subchondral sclerosis on the ulnar notch). The CT study revealed radiolucent line across the humeral condyle which is consisted finding for HIF (humeral intercondylar fissure). The dog was treated with percutaneously applied cannulated screw.

Seven year old female boxer is presented due to a chronic progressive lameness with the front left limb. The orthopaedic examination showed a marked atrophy of the shoulder musculature and palpable firm mass at the medial aspect of the distal ante brachium. A radiographic findings of stenosing tenosynovitis of the abductor pollicis longus muscle were identified and the dog was scheduled for steroid infiltration around the tendon as a first treatment option. As the lameness progressed in the next few weeks, the dog was scheduled for a CT study. A contrast enhanced lesion was found at the caudal medial aspect of the shoulder joint and the followed histopathology revealed synovial cell carcinoma. Age-dependant degenerative changes are often findings in mature dogs. They are also commonly mislead as a clinically significant finding,

responsible for the lameness. On contrast, a neurological lameness or lameness due to a neoplastic mass is often found as the primary cause of the lameness.

Despite of importance of diagnostic imaging, a properly performed orthopaedic examination is the key element in front lameness cases. In subtle lameness cases it is challenge sometimes to identify which leg is affected. Stand evaluation and watching the dog in walk, trot or gallop, going down on stairs or circling are important observing points during gait evaluation. The so called head nod is best to be evaluated during walk or trot and ideally documented in slow motion mode. The rest of the orthopaedic examination is "hands on" and it is consisted of detailed palpation starting from distal to proximal along the limb, putting each joint in complete range of motion and measuring the range of motion, testing for abnormal joint motion (collateral stress testing), deep palpation on a specific anatomical areas, measuring the muscle mass and comparing to the other front limb.
Many grading systems for subjectively score the lameness in dogs are available, but in fact non of them are validated in dogs. The most popular one is the American Association of Equine Practitioners system (Ross, 2011) where the lameness is scored in five lameness grades:

Score Lameness degree Lameness description
0 None No identifiable lameness.
Weight-bearing at all times
1 Slight Inconsistent lameness that is difficult to observe and it is difficult to determine the affected limb.
Weight-bearing at all times
2 Mild Clearly detectable lameness associated with minor head movement.
Weight-bearing at all times
3 Moderate Clearly detectable lameness associated with obvious head movement.
Weight-bearing at all times
4 Severe Clearly detectable lameness associated with obvious head movement.
Occasionally non-weight wearing/toe touching
5 Non-weight bearing Always non-weight bearing/toe touching

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CURRENT TRENDS IN SURGICAL MANAGEMENT OF FELINE STIFLE INJURIES

Friday 13 September | 11:00 - 13:00 | MC 2 - Room C

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Cranial cruciate ligament rupture

The etiology of cranial cruciate ligament (CCL) rupture in cats is unknown. Most published reports describe traumatic ruptures in younger cats. A recent study revealed that cats suffering from CCL rupture without a history of trauma were significantly older. The degeneration is not likely an aetiological factor itself, like in dogs. Additionally, the study highlighted that fibrocartilage in the cranial cruciate ligament should be viewed as a physiological reaction to normal forces in the ligament and should not be classified as a degenerative change.

Diagnosis of feline CCL rupture is usually easily confirmed on physical examination. The drawer test is positive for most affected cats. Radiographic signs include joint effusion, degenerative joint disease (osteophytes, enthesiophytes, subchondral bone sclerosis of the distal femur and tibia), and, in some cats, distal displacement of the popliteal sesamoid bone)

Management of CCL rupture in cats remains controversial. A few studies look at no treatment or single techniques, but none compare conservative therapy to one or multiple techniques. Treatment (at least surgical) aims to resolve lameness and signs of pain caused by craniocaudal instability and improve the affected limb's function and mobility. The only existing study concerning conservative management favored conservative therapy could show satisfactory clinical results, although instability was still present in 80% of the cats. Published results of surgical therapy are at least as good as those achieved with conservative treatment, and it seems that surgery provides a quicker and more reliable return to function and a more consistent recovery. Concurrent meniscal injury has been reported to be up to 67%. Given this high rate of meniscal pathology and the constant progression of degenerative joint disease, exploratory surgery for meniscal assessment and joint stabilization should be considered in feline patients. Surgical stabilization with an extracapsular technique is the most commonly performed procedure in cats. The non-absorbable suture material is traditionally passed around the fabella and through a bone tunnel in the proximal tibia, preferably at the isometric or quasi-isometric points. Among specialists, bone anchors are preferred to the circumferential suture around the fabella, as they provide more secure and stable bone-to-bone fixation. To date, there is only one published in vitro study evaluating the use of bone anchors. In dogs, it has been shown that tibial plateau leveling osteotomy (TPLO) is superior to extracapsular techniques. TPLO and TTA have been successfully applied to cats. Feline CCL treatment is based on subjective surgeon experience and preference. Prospective, randomized clinical trials, including long-term follow-up, are needed to provide unbiased scientific evidence for the best therapeutic protocol.

Patellar luxation

Patellar luxation in cats can be of congenital or traumatic origin. Medial luxations are more often than lateral ones, and the disease is usually bilateral.

Cats with patellar luxation often show a crouched gait and inability to jump. Some cats develop intermittent high-grade lameness or sudden vocalization and a non-weight-bearing lameness of the affected hindlimb. It is essential to know that the feline patella is relatively loose compared to dogs and can be manually luxated (over the femoral sulcus) in many normal cats. In those cases, it is considered an incidental finding, and surgical therapy is not indicated. Patella luxation has been associated with hip dysplasia. Radiographic examination of the hips should always be performed in cats with patellar luxation.

Surgical therapy (unilateral or bilateral single stage in severy cases) should be considered in cats with symptoms associated with patellar luxation and immature cats with grade 3 or 4 patella luxation. The most widely used methods include tibial tuberosity transposition (TTT), femoral trochleoplasty, and soft tissue imbrication/release. Other stabilization procedures include antirotational suture and corrective osteotomies. TTT is rarely needed in cats compared to dogs and is contraindicated in immature animals. The decision on whether to perform a TTT is usually made on intraoperative assessment of the alignment of the quadriceps mechanism. Femoral trochleoplasty (block or wedge) is considered a mainstay for the surgical management of patellar luxation in cats. Block recession is my preferred method. Recently, semi-cylindrical recession trochleoplasty has been published. Soft tissue procedures include medial fascial release and lateral imbrication (for medial patellar luxation). Those structures are secondary stabilizers of the joint and tend to loosen with time. For these reasons, their correction does not usually provide long-term stability for the patella. The only exceptions to this rule are cases of acute traumatic luxation. Partial patellectomy is a newly published procedure. More evidence concerning its success, complications, and long-term outcome is needed. It should be considered only in refractory cases combined with the abovementioned techniques.

Patella fractures

The patella is the most prominent sesamoid bone in the body, crucial for protecting the quadriceps tendon during weight-bearing activities like jumping. It plays a vital role in the extensor mechanism of the stifle joint. Fractures are classified into various types, such as simple, transverse, comminuted, longitudinal, and marginal. They can arise from traumatic incidents (e.g., road traffic accidents) or pathological conditions like Patellar Fracture and Dental Anomaly Syndrome (PADS), previously known as Knees and Teeth Syndrome (KaTS). This syndrome involves atraumatic fractures, often accompanied by dental anomalies like persistent deciduous teeth. It is more common in young cats and can result in bilateral patellar fractures, often at different times. If there is no evidence of a traumatic etiology for a patellar fracture, the cat should be checked for persistent deciduous or unerupted adult teeth and signs of concurrent fractures.
Cats with patellar fractures may present with lameness, swelling, and pain around the stifle joint. Diagnosis often involves physical and orthopedic examinations to rule out other injuries and identify fracture characteristics. Radiographs are a critical diagnostic tool, with specific views helping to visualize different types of fractures. Treatment may be conservative or surgical, depending on the type and severity of the fracture. Conservative treatment may suffice for minimally displaced fractures, while surgical intervention is necessary for more severe cases. The decision is influenced by factors such as the cat's age, the type of fracture, and the presence of other injuries. In cases with suspected PADS or complex fractures, advanced imaging like CT or MRI may be employed.

Conservative treatment has been successful in cases with stable, non-displaced fractures, with cats often regaining good function. There is no definitive study comparing conservative management with surgical intervention in cats. Surgical therapy depends on the specific nature

and stability of the fracture, the presence of other injuries, and whether the fracture is traumatic or pathological in nature. Surgical methods include:

Pin and Tension Band Wire: This technique is typically used for transverse fractures, where the extensor mechanism is disrupted. However, it has shown poor outcomes in cases of suspected Patellar Avascular Disease Syndrome (PADS) due to brittle bones and implant failures. In such cases, circumferential sutures or wiring may be more effective.

Circumferential and Figure-of-Eight Wiring: For cases where pin and tension band wire methods are not viable, particularly in PADS cases, circumferential wiring or suturing without a pin has been suggested as a better alternative. This method aims to re-establish the quadriceps mechanism rather than achieving bony union.

Patellectomy: Total removal of the patella is not recommended due to the loss of quadriceps function and subsequent degenerative changes. Partial patellectomy may be considered if the fragments are too small for other surgical options.

Tibiopatellar Suture: This technique involves placing a suture around the patella and the tibial tuberosity to protect the patellar fracture reduction. It helps manage the tension forces the quadriceps muscle exerts during knee flexion.

The healing of patellar fractures can be slow, often requiring extended periods, sometimes up to 12 weeks or more, for radiographic confirmation of healing. This slow process is typical even in young cats, and some fractures may not show complete radiographic union but still result in satisfactory clinical outcomes. Most cats return to good function. This also includes cases with persistent non-union, where the primary goal is to re-establish the functionality of the quadriceps mechanism rather than achieving complete bony union.

Traumatic stifle joint disruption/Multiligamentous stifle injury

Stifle joint disruption is a severe injury that results in luxation or subluxation of the stifle joint and severe instability. Affected cats typically present with non-weight-bearing lameness, localized pain and swelling, and noticeable instability or luxation of the stifle joint. Young male cats are frequently affected, although a retrospective study revealed an almost equal sex distribution.

The injury is caused by the rupture of several ligamentous joint stabilizers, including the collateral ligaments, cruciate ligaments, and joint capsule. The most common combination of injuries is rupture of the cranial and caudal cruciate ligaments with rupture of the medial collateral ligament. Additional injuries, such as thoracic, abdominal, or urinary tract trauma, may accompany the joint disruption.

The surgical goal is to achieve anatomical joint reduction and stability. This involves primary repair of damaged structures and temporary joint immobilization, often using an external skeletal fixator or transarticular pin for two to three weeks. Both medial and lateral surgical approaches may be necessary to address all damaged structures, including meniscal injuries, cruciate ligament damage, and collateral ligament ruptures. Various techniques are employed to repair specific structures in feline stifle joint disruption cases. The cranial cruciate ligament is typically addressed using lateral extracapsular sutures. For the caudal cruciate ligament, stabilization is often achieved through a fibulopatellar suture, which prevents caudal displacement of the tibia. The medial collateral ligament, which may be severely damaged or ruptured, can be repaired either through direct suturing or the placement of prosthetic ligaments, depending on the extent of the injury. Several materials and fixation methods are available.

Temporary stabilization is a critical component in surgical management. This stabilization is typically achieved through techniques such as using an external skeletal fixator or a transarticular pin. The use of transarticular pins was associated with a higher rate of complications and poorer outcomes. Careful consideration is needed regarding the duration and type of immobilization used to balance the benefits of immediate stability with the potential for complications. While surgical treatment is generally linked with a high rate of short-term complications, many cats achieve good to excellent long-term outcomes.

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PATIENT SPECIFIC APPROACH IN CRANIAL CRUCIATE LIGAMENT RUPTURE IN DOGS

Friday 13 September | 11:00 - 13:00 | MC 2 - Room C

Svetoslav Hristov
DVM, AVSB CertSAS

Cranial cruciate ligament injury has been stated as the most common hind limb lameness in dogs which makes its management as the most important among all elective orthopaedic surgical procedures. Despite of current trends in the surgical procedures treating this condition, there is still controversy about the best treatment method. In fact, small animal veterinarians see a huge variety of sizes and breed of dogs with cranial cruciate deficient stifles, which also means different stifle anatomy, need of specific implants and dedicated surgical equipment.
Often asked questions are if the case should be treated surgically or managed conservatively, if the so called extra capsular surgical techniques bring the same clinical outcome as the geometry modified osteotomy procedures, which is the best osteotomy procedure, what should be the surgical approach in very young dogs with traumatic cranial cruciate ligament rupture/avulsion, which is the best treatment method in dogs with altered anatomy of the proximal tibia and excessive tibial plateau angle?

A common clinical scenarios we see are as follow:

Young giant breed dog with partial rupture cranial cruciate ligament injury. Often breeds presented are Cane Corso, Giant Asian Shepherd dogs (Caucasian, Middle Asian, Turkish Shepherd) and others. They are often presented with subtle lameness and under the presumptive diagnosis of hereditary hip problems.

Surgical procedure	Advantages	Disadvantages and potential challenges
Lateral suture	NO	
TTA	Yes, if the stifle anatomy allows applying a cage size achieving stifle stability in the stance phase of the gate	Available cage sizes Moving the patella away from the femoral trochlea Big quadriceps extension forces and potential construct failure
TPLO	Yes	Higher complication rate in giant breeds (infection, construct failure), need of double plating, need of extra equipment
CBLO/CCW	Yes	Big quadriceps extension forces and potential construct failure. Patella brought in lower position (patella Baja)

2. Active middle size large breed dogs. This group often represent Labrador-type of dogs, German shepherds despite not often having cranial cruciate disease, Rottweilers , Staffordshire terriers and others. We do not consider extracapsular techniques as reliable for this group as well. But properly performed TTA seems to be a good option here as most of the cases are presented without concurrent tibial deformities, tibial plateau angle appreciated as normal for the breed and appropriate proximal tibia anatomy (well developed and relatively highly positioned tibial crest). TTA could be also extremely helpful in cases of patella alta which might affect the physiological position of the patella in the femoral trochlea. Also the reduced contact between the patella and the femoral trochlea could reduces the pain and the progression of the osteoarthritis in the patella-femoral joint. The major disadvantage of TTA remains the subjective and surgeon dependant preoperative planning which probably might not brings the same outcome after the surgery among different surgeons.

3. Adult to mature toy breed dogs with or without concurrent medial patella luxation. This group of dogs represent dogs with anatomical challenges (relatively steeper tibial plateau angle) and probably related to this a significantly unstable cranial cruciate deficient stifle. The miniature size of the tibia and the limited bone stock could be the reason why extra capsular suture techniques are still the main choice of surgical treatment in this group. Additional intervention for the medial patella luxation is another potential advantage to the lateral suture techniques. Conservative management is also often approach, especially in mature individuals with health co-morbidities.

Surgical procedure	**Advantages**	**Disadvantages and potential challenges**
Lateral suture	Similar long term outcome.	Slow recovery. Early suture failure
TTA	Yes	Available cage sizes Technically challenging due to limited bone stock. In concurrent patella luxation consider the reduced patella to trochlea contact
TPLO	Yes. Very quick recovery	Higher complication rate in giant breeds (infection, construct failure), need of double plating, need of extra equipment
CBLO/CCW	Yes. More bone stock in comparison to the other GMO procedures	Big quadriceps extension forces and potential construct failure. Patella brought in lower position (patella Baja) which might complicates MPL

In combined CrCLR and medial patella luxation a modified TPLO can be considered as a surgical treatment when some amount of external tibial torsion brings the tibial tuberosity more medially and predisposes the patella to dislocates. The modification of the technique changes the osteotomy apposition in such a way so the distal fragment with the tibial tuberosity attached

is translated slightly laterally. This mimics lateralisation of the tibial tuberosity which may align better the patella tracking on the femoral trochlea.

4. Young dogs with traumatic rupture/avulsion of the CrCL. If the dog is still growing and with significant growth potential of the tibial plateau growth plate, then a proximal tibial epiphysiodesis might achieves reduction of the tibial plateau angle. The biggest advantage of the procedure is the relatively simple positioning of the screw and achievement of tibial plateau levelling without performing of actual tibial osteotomy. The disadvantage is proper case selection, the time need for achieving the correction and the potential need of screw removal as a preventive measure for overcorrection.

5. Adult dogs with acute traumatic cranial cruciate ligament rupture or combined multi-ligamentous injury. A major difference of these cases in comparison to the ones of cranial cruciate disease is the amount of stifle instability. These dogs are usually presented with complete luxation and often require intra- or extracapsular ligaments prosthesis or ligaments reconstruction.

6. Dogs with altered anatomy of the proximal tibia - excessive tibial plateau angle or complex tibial deformities. Such a cases present a therapeutic challenges to the veterinary practitioners due to their complexity and the need of extra knowledge, skills and equipment for their solving. They often require advanced imaging for proper understanding of the deformity, assessment of the amount of the deformity and precise planning of the surgery. The access to a CT imaging, 3D printing technologies and the opportunity to rehearse the surgery gives enormous advantage in treating such a cases.

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COMMON MISTAKES IN FRACTURE TREATMENT IN SMALL ANIMALS

Friday 13 September | 11:00 - 13:00 | MC 2 - Room C

Svetoslav Hristov,
DVM, AVSB CertSAS

"Life is too short for postoperative complications"
Ross Palmer

Fracture repair complications often have a significant emotional and financial impact to both the owner and the veterinary practitioner. And if some of them could be really unexpected and unusual, in fact most of them are quite predictable.

There are three common types of surgical errors which leads to a fracture complications. Unfortunately all of them are surgeon's mistakes:
Improper choice of fracture fixation method
Improper choice of implant
2. Technical errors in the execution of the fracture fixation
3. Lack of owner communication in the postoperative period

Knowledge in fracture forces, preservation of bone biology and soft tissues, proper use of the variety of fixation methods are the key factors in the 158eutralize fracture treatment. All these are 158eutralize as the four major AO principles:

1. AO Principles of Fracture Repair
Anatomical reduction of bone fragments
Fracture fixation, adequate to the fracture forces
Preservation of blood supply to soft tissue and bone
Early and safe mobilization of the injured leg and the patient

A common reason for a fracture complications is poor fracture 158eutralize followed by a bad preoperative decision making process. Typical example would be a small breed puppy presented with a non weight bearing with the front limb after being dropped from its owner's hands. A single medial to lateral radiographic view has been performed, no pathology detected by the clinician and send home for a conservative treatment and rest. In this case, a displaced fracture involving the lateral part of the humeral condyle is easily missed on that medial to lateral view. Such an intra articular fracture requires an immediate treatment consisting of open surgical approach, direct fragment reduction, perfect reposition and rigid fixation. Unfortunately, the bad decision making in this case is due to improper fracture assessment because of bad radiographic assessment of the limb. Another example could be a similar patient in which a short oblique fracture in the distal radius and ulna has been discovered radiographically. A decision making was made to treat conservatively the fracture using a splint following the external computation principles. The fracture configuration in this case and the ongoing fracture forces are not resisted by the applied external coaptation method which can not provide adequate

stability for fracture healing. The oblique fracture line and the shear forces makes the external coaptation method as a poor fracture 159eutralize159on method and with predictable poor bone healing outcome.

"Failure to plan is planning to fail" – **Winston Churchill**

A fundamental question in the fracture decision making is *"am I able to reconstruct the fracture line and does this will has a mechanical benefit for the fracture stabilization"?* Unfortunately the surgeon is often led by the desire to reconstruct all of the fracture fragments which often is not only out of mechanical benefit, but also compromises the biology. As a consequence a bone healing complications will result as delayed bone union or nonunion, bone infection and premature implants loosening.
Knowing of the variety of fixation methods and implants, their proper use, the recommendations for their use based on body weight in different bones is another important requirement in fracture treatment in small animals. Inadequate implant sizes often fail in two different ways – by plastic deformation and fatigue failure and implant breakage. A surgeon's experience using a different fixation methods would be an important task in the fracture repair decision making process and in the adequate fracture forces resistance in the postoperative period.
Another common reason for a fracture complications are technical surgical errors. For example, a retrograde pin insertion in the femur is related to a high incidence of iatrogenic sciatic nerve injury. Objective and systematic approach should be used in the assessment of the postoperative radiographs using the four A's. If based on the postoperative radiographs a revision surgery is required, thus much better approach would be an immediate action instead of "wait to see" approach and the risk of major postoperative complication. In such a case, the self criticism would be a part of the so called "evolution of the surgeon" in its ability to detect a potential major postoperative complications.

Common surgical errors in fracture treatment:

Cerclage wires: most commonly misused implants. There are a strict requirements under which the cerclage wires are effective – entire circumference of the bone is reconstructed and fracture line length at least twice the bone diameter. Single wire acts as a fulcrum and should never be used.
Intramedullary (IM) pins: IM implant is the best implant to 159eutralize the bending forces, but has a little resistance to axial load and do not resist to rotational forces. Thus, IM pin should always been combined with other type of fixation such that the overall implant construct counteracts all the fracture forces.
Plates and screws: Common technical errors in plate application are failure to secure sufficient number of cortices / use of too short plate, leaving an empty screw hole / creating a stress riser point over the fracture line when the fracture can not be reconstructed and compressed, leaving a gap at the trans cortex in a non reconstructable fracture and overestimating the resistance of the plate to cyclic bending.
The most common complication resulting from locking plates is due to insufficient number of screws being used on each side of the fracture. As the screws are angle stable, weight-bearing will result in large loads at the plate/screw interface and results in screw breakage or bone slicing. A common technical errors in an angle stable implants are intraarticular placement of screw, bridging a growth plate, insufficient screw purchase in the bone
External Skeletal Fixation (ESF) : The infinite point in ESF is the pin/bone interface. The transfixation pins ideally should be a positive threaded ones, engaging two cortices, be around 25-30% of the bone diameter, placed in "safe corridors" and avoiding large muscle masses. Thus, the use of ESF in a femoral fractures is best to be avoided due to the high incidence of "pin related morbidity" and quadriceps muscle contracture.

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DIAGNOSTIC IMAGING ON VETERINARY ONCOLOGY

Friday 13 September | 14:00 - 15:45 | MC 2 - Room C

Massimo Vignoli

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The imaging modalities used in oncology are numerous, and each contributes to the final diagnosis. In veterinary medicine the most used are radiology and ultrasound, due to the wide availability and low cost. Radiology guarantees considerable information in the study of the skeleton, in particular the appendicular skeleton, in addition to the thorax, with some limitations for small lesions or adjacent to other structures. The limitation of radiology is linked to the fact that three-dimensional organs are represented on a plane in the image, so there are overlaps of organs. Fluoroscopy is a limited used technique, both for costs and for the exposure of operators to X-rays. It can be useful for obtaining guided biopsies. Then there are stratigraphic techniques that avoid the aforementioned overlaps and are more accurate. Ultrasound (US) allows to obtain important information in soft tissues, in particular with regard to the abdominal organs or superficial intra-thoracic lesions. It also represents a guide for performing targeted biopsy sampling. It is limited by the bone structures and gas. Computed tomography (CT) and magnetic resonance imaging (MRI) have higher costs, are less available, but give significantly more accurate information. The CT in particular also allows to obtain the study of the whole body ("total body"), so to give information both on the primary tumor and on the possible presence of metastases, thus carrying out a complete staging. It also allows for guided biopsies. Scintigraphy, little used in veterinary medicine, has a good sensitivity in the search for metastases, but has a low spatial resolution, therefore a radiographic or CT study is needed after the scintigraphic localization. Other techniques such as PET or SPECT are still relegated to some research centers today, while clinical application is not possible due to the high costs. Of all these imaging modalities, CT is considered the method of choice in veterinary oncology (Collivignarelli et al, 2020), and is considered the most used modality by surgeons to verify tumor operability (Long et al., 2005).
The rapid technological evolution now makes it possible to obtain full-body studies in a few seconds with multidetector machines, with a single administration of contrast medium and high resolution, using slice thicknesses ranging from 0.6 to 2.5 mm.
Subjects undergoing a CT scan are anaesthetized by trying to use protocols with rapid-elimination anaesthetics. To avoid movement artefacts (eg respirators), apnea is determined through hyperventilation or an anaesthetic bolus (Schwarz, 2011). To minimize the collapse of the lungs under anaesthesia and therefore the possibility of not seeing small peripheral lesions, the study is performed in sternal recumbency. Finally, performing a pre and post-contrast study, after i.v is always necessary. administration of non-ionic iodinated contrast medium at 600 mg/kg of iodine.
The contrast study may or may not indicate the malignancy or not of the lesion (Henninger, 2003; Fife et al., 2004). Concerning the primary tumour, information is obtained on the size of the tumour, its exact location and extent (local invasiveness). In a study that considers non-cardiac intrathoracic diseases in dogs and cats, it is reported that CT compared to radiology gives more information on localization and extent, on involvement of the mediastinum and in general by additional information in 100% of cats and in 75% of dogs studied, resulting in a change in diagnosis in 60% of cats and 46% of dogs (Prather et al., 2005). Another important function of CT

in oncology is the search for metastases. One study reported that of the nodules visualized on CT, only 9% were visualized radiologically. Furthermore, the lower limit of the nodules seen in CT is 1 mm compared to 7-9 mm in radiology. The study concludes that CT should always be considered in cancer patients with tumours with a high frequency of metastasis (Nemanic et al., 2006). In another study comparing radiology with three views and CT, CT is reported to be more sensitive than radiology, particularly in large or giant breed dogs (which had osteosarcoma metastases) (Armbrust et al., 2012). Lymph node metastases are another topic of great interest in oncology, and in particular of intrathoracic lymph nodes due to the difficulty in radiographic detection. A study on the search for metastases to tracheobronchial lymph nodes in dogs with lung cancer reports that 5 out of 6 metastatic cases were highlighted in CT (sensitivity 83%), while none in radiology (sensitivity 0%) (Paoloni et al, 2006). A diameter of 12 mm or a maximum ratio of 1.05 between lymph node diameter and the corresponding vertebral body is considered the threshold above which the metastatic lymph node is considered (Ballegeer et al., 2010). The extreme usefulness of CT in finding metastases was demonstrated in a study of 1201 cancer patients, 27 (21 dogs and 6 cats) had muscle metastases, 2.2% of the total cases (2.08% dogs and 3.1% cats). Of these, 2 cases had metastases to the heart muscle (Vignoli et al., 2013). In a recent study, it was found that in a group of 61 dogs affected by hemangiosarcoma, 15 (24.6%) had skeletal metastases (Carloni et al. 2019), and 9 of 15 (60.0%). Dogs with muscular metastases showed lameness or reluctance to move and were referred for orthopaedic or neurological problems and not as oncological patients.
Another function of CT is to exclude concomitant diseases. The occurrence of different pathological conditions at the same time can significantly change the patient's therapeutic approach.
To increase the accuracy of CT, dynamic studies have recently been proposed, although still in the initial phase (Stehlik et al., 2020). A special study, helical hydro-CT (HHCT) was published on gastric cancers; in this study, the gastric administration of 30 ml/kg of water through an oro-gastric tube is used to dilate the stomach and better visualize the wall (Terragni et al., 2012).
This technique is particularly important in assessing the extent of the lesion and its operability. CT plays an important role in interventional radiology. It allows to perform guided sampling for cyto/histopathological examination with high diagnostic accuracy (Vignoli et al., 2004; Vignoli et al., 2007; Vignoli and Saunders 2011; Vignoli et al., 2021).

CT also plays a fundamental role in the treatment of tumours with radiotherapy. First, a positioning CT is done. Then the CT exam is imported into the treatment planning system ("treatment planning system" - TPS) and through the use of sophisticated software the plans themselves are drawn.
Finally, even in the veterinarian, CT is used to follow the results of the therapies. The information provided by these studies allows us to understand if the therapy is working completely or partially or if there is no response to the treatment and if it is advisable to modify it. It is also very important to check for post-treatment complications (Cancedda et al., 2014).

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COMPUTED TOMOGRAPHY OF SKELETAL DISEASES

Friday 13 September | 14:00 - 15:45 | MC 2 - Room C

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Computed tomography (CT) is a highly valuable imaging modality for diagnosing and managing skeletal diseases in dogs and cats. It provides detailed cross-sectional images, allowing for precise evaluation of bone structures and surrounding soft tissues.

Indications for Skeletal CT

Trauma: Assessment of complex fractures and dislocations (Riedesel, 2011). It should be considered that dogs and cats, for their size, must be always considered as polytrauma patients. Polytrauma is a severe injury involving two or more areas of the body (Kroupa, 1990). In small animal practice, most common polytrauma are road traumatic accidents (RTA), high-rise syndrome and bite wounds (Crowe, 2006; Dozeman *et al.,* 2020). Thoracic trauma is the prevalent injury in dogs and cats with evidence of pneumothorax and lung contusion while hemoperitoneum is reported as the most common abdominal injury (Dozeman *et al*., 2020). The clinical complexity and diagnosis of a polytrauma are therefore determined by the presence of injuries in more than one region; one study has reported that approximately 50% of dogs with thoracic lesions also presented skeletal fractures while other associated injuries affected the nervous system and abdomen (Kolata and Johnston, 1975).

Consequently, the use of only a single first-level diagnostic method is not sufficient for diagnosing trauma in all regions (Oliveira *et al.,* 2011; Fields *et al.,* 2012; Shanaman *et al.,* 2013). In human medicine, in the case of major trauma, the diagnostic protocol involving radiography of the chest, the cervical spine and the pelvis, and thoracic and abdominal echography is followed by total body computed tomography (CT) only in case of positivity to one of the previous exams (Scaglione, 2012).

According to the new Advanced Trauma Life Support (ATLS) guidelines, multi-slice CT represents the gold standard since it provides a fast and complete overview of the injuries; it enables the identification of effusions and lacerations of organs, and the use of a contrast medium allows the identification of active hemorrhage leading to immediate therapeutic intervention (Scaglione, 2012).

A recent article reported the usefulness of CT in trauma cases in dog and cat (Serra et al, 2021). The main limitation of the application of this method in veterinary medicine is represented by anesthesia which could limit the use of CT in critical patient. Eventually the study can be done without sedation/ anesthesia in case the patient is very depressed. For neoplastic lesions CT is still consdiered the gold standard in veterinary medicine, both for tumor identification and staging tumors (Tidwell & Johnson, 2013). In case of infectious diseases, such as osteomyelitis or septic arthritis CT has been described to be very useful (Wisner & Zwingenberger, 2015). Moreover in developmental disorders like the evaluation of congenital abnormalities and growth plate issues can be useful (Hecht & Adams, 2010). Degenerative conditions such as osteoarthritis, intervertebral disc disease, and spondylosis CT is valuable (Tidwell & Johnson, 2013). FInally, in the last years CT has been of paramount importance in the surgical planning: preoperative assessment for complex orthopedic surgeries (Wisner & Zwingenberger, 2015).

Advantages of CT over other imaging modalities

- High Resolution: superior detail of bone structures compared to standard radiography (Hecht & Adams, 2010).
- 3D Reconstruction: allows for three-dimensional views of the skeletal anatomy, aiding in complex fracture assessment and surgical planning (Wisner & Zwingenberger, 2015).The present author finds useful the 3D recostruction especially for facial adn rib trauma.
- Soft Tissue Contrast: better differentiation of soft tissue structures surrounding bones than X-rays (Tidwell & Johnson, 2013).
- Speed: quick acquisition time, making it suitable for trauma cases where rapid diagnosis is essential (Riedesel, 2011).

Common Skeletal Diseases Evaluated by CT

- Fractures:
  - Complex Fractures: CT provides detailed views of comminuted fractures and their relationships to joints (Riedesel, 2011).
  - Healed Fractures: evaluation of callus formation and alignment (Wisner & Zwingenberger, 2015).
- Bone Tumors:
  - Primary Bone Tumors: characterization and staging of osteosarcoma, chondrosarcoma, etc. (Tidwell & Johnson, 2013).
  - Metastatic Disease: detection of secondary bone involvement from other primary tumors (Wisner & Zwingenberger, 2015).
- Infections:
  - Osteomyelitis: identification of bone infection and involvement of adjacent soft tissues (Tidwell & Johnson, 2013).
  - Septic Arthritis: evaluation of joint infections and extent of bone erosion (Hecht & Adams, 2010).
- Degenerative Diseases:
  - Osteoarthritis: detailed assessment of joint space narrowing, osteophytes, and subchondral bone changes (Wisner & Zwingenberger, 2015).
  - Intervertebral Disc Disease: identification of disc herniation and spinal cord compression (Tidwell & Johnson, 2013).
- Congenital and Developmental Disorders:
  - Elbow Dysplasia: detection of fragmented medial coronoid process, ununited anconeal process, and osteochondritis dissecans (Hecht & Adams, 2010; Vignoli and Graham, 2022).
  - Hip Dysplasia: assessment of acetabular and femoral head conformation (Wisner & Zwingenberger, 2015; Vignoli and Graham, 2022).

Procedure

- Patient Preparation: animals are typically sedated or anesthetized to prevent movement during the scan (Tidwell & Johnson, 2013).
- Scanning Protocol: thin slice acquisition (1-2 mm) is standard for detailed skeletal imaging. Contrast agents may be used if soft tissue involvement is suspected (Riedesel, 2011).

- Image Reconstruction: multiplanar and 3D reconstructions are often performed to enhance diagnostic accuracy (Wisner & Zwingenberger, 2015).

Interpretation of Findings

- Fracture Details: CT can reveal fracture lines, displacement, and comminution that may not be visible on radiographs (Hecht & Adams, 2010).
- Tumor Characteristics: size, location, extent of bone involvement, and potential metastasis are assessed (Tidwell & Johnson, 2013).
- Infection Signs: presence of sequestra, involucrum, and periosteal reaction in osteomyelitis (Wisner & Zwingenberger, 2015).
- Degenerative Changes: detailed evaluation of joint degeneration and spinal changes (Riedesel, 2011).

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ULTRASOUND OF THE GASTROINTESTINAL TRACT

Friday 13 September | 17:00 - 18:45 | MC 2 - Room C

Massimo Vignoli

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Ultrasound examination of the gastrointestinal (GI) tract in dogs and cats is an important diagnostic tool in veterinary medicine. It allows for the non-invasive assessment of the stomach, small and large intestines, and associated structures, providing important informations in the diagnosis and management of the several GI diseases.

The indications for GI Ultrasound are:

- Vomiting and Diarrhea: chronic or acute episodes are common reasons for GI ultrasound (Penninck & D'Anjou, 2015).
- Weight Loss: unexplained weight loss warrants an investigation of potential GI causes (Barr, 2013).
- Abdominal Pain: ultrasound can help localize the source of pain (Nyland & Mattoon, 2015).
- Palpable Abnormalities: masses or distensions detected during physical examination (Barr, 2013).
- Suspected Foreign Bodies: particularly in cases of ingestion (Penninck & D'Anjou, 2015).
- Suspected Neoplasia: for evaluation of possible tumors (Nyland & Mattoon, 2015).
- Monitoring Chronic Conditions: such as inflammatory bowel disease (IBD) or postoperative states (Barr, 2013).

Preparation for GI Ultrasound

- Fasting: Animals are typically fasted for 8-12 hours to minimize gas and food content, improving image quality (Penninck & D'Anjou, 2015).
- Sedation: may be necessary to keep the animal calm and still (Barr, 2013).

Ultrasound Technique

- Patient Positioning: commonly in dorsal or lateral recumbency (Nyland & Mattoon, 2015).
- Probe Selection:hHigh-frequency linear or microconvex probes (7.5-18 MHz) are preferred for detailed imaging (Barr, 2013).
- Scanning Protocol:
    - Stomach: assess wall thickness, layering, motility, and contents.
    - Small Intestines: evaluate duodenum, jejunum, and ileum for wall thickness, layering, and motility.
    - Large Intestines: check colon and cecum for wall thickness and contents.
    - Mesenteric Lymph Nodes: Inspect for enlargement or abnormalities.
    - Peritoneal Cavity: look for free fluid or masses (Penninck & D'Anjou, 2015; Nyland & Mattoon, 2015).

Normal Ultrasound Findings

- Stomach:
    - Wall thickness: 3-5 mm
    - Five layers visible: mucosa, submucosa, muscularis, serosa, and submucosal interface (Barr, 2013).
- Small Intestines:
    - Wall thickness: 2-5 mm (duodenum thicker than jejunum and ileum)
    - Distinct layering with regular peristalsis (Penninck & D'Anjou, 2015).
- Large Intestines:
    - Wall thickness: 1-2 mm
    - Less distinct layering compared to small intestines (Nyland & Mattoon, 2015).

Common Abnormal Findings

- Foreign Bodies: hyperechoic objects with acoustic shadowing (Penninck & D'Anjou, 2015).
- Intussusception: telescoping of intestine, visible as concentric rings or a "target" pattern (Nyland & Mattoon, 2015).
- Neoplasia: irregular masses disrupting normal wall layering (Barr, 2013).
- Inflammatory Bowel Disease (IBD): thickened intestinal walls with preserved layering (Penninck & D'Anjou, 2015).
- Gastric Dilatation-Volvulus (GDV): dilated stomach with abnormal positioning and lack of motility (Nyland & Mattoon, 2015).
- Ulcers: focal wall thickening with crater-like appearance (Barr, 2013).
- Fluid Accumulation: anechoic areas indicating peritoneal effusion (Penninck & D'Anjou, 2015).

Advantages and Limitations

- Advantages:
    - Non-invasive and real-time imaging
    - No radiation exposure
    - Can guide fine-needle aspiration or biopsy (Barr, 2013).
- Limitations:
    - Operator-dependent
    - Limited by presence of gas or ingesta
    - May require sedation (Penninck & D'Anjou, 2015).
    - Most of the times not possible to diagnose a low grade lymphoma of the G-I tract in cats (Terragni et al., 2016).

Interpretation and Follow-Up

- Ultrasound findings should be interpreted alongside clinical signs, history, and other diagnostics (e.g., blood work, radiographs) (Nyland & Mattoon, 2015).
- Follow-up may include repeat ultrasounds, endoscopy, or surgical exploration based on initial findings (Barr, 2013).

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Where CT outperforms US ?

Friday 13 September | 17:00 - 18:45 | MC 2 - Room C

Michail N. Patsikas

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In small animal private practice there is an increasingly use of innovated digital techniques as digital radiography with artificial intelligence systems, ultrasonography with elastography and contrast enhanced protocols, multi-slices computed tomography (CT) and magnetic resonance imaging (MRI).
In the abdominal diseases US is the imaging method of choice because is easy, safe and accurate in the diagnosis. The main disadvantage of US is that the quality of the images is examiner dependent. However, CT is increasingly used in daily small animal practice. The quality of the CT images is not examiner depended and the contrast resolution is higher compared to US.
In a comparison of abdominal computed tomography and ultrasonography in sedated dogs less than 25 kg, there was no significant difference in lesion detection between CT and US. In dogs weighing greater than 25 kg, more lesions were detected with CT than with US demonstrating that CT outperforms US in overweighted and obese dogs (1)
In a study with sonographic measurement of tumors size in dogs, there was poor to fair intra and interobserver correlation between operators, verifying the disadvantage of operator depended technique (2). CT with the reconstruction techniques outperforms US in assessing the size and spatial relationship of an abdominal mass for surgical or radio-therapeutical planning (3).
CT outperforms US in constantly imaging all the abdominal lymph nodes as well as the intrapelvic nodes (sacral). CT may predict better than US the neoplastic invasion of the nodes based on contrast enhancement (4). CT is better to US in the evaluation of the response to treatment or progression of the nodal disease because the same sections could be repeated unchanged after weeks or months.
In the liver CT outperforms US in demonstrating the exact location and number of the nodules and the extrahepatic portosystemic shunts. In contrast to US CT shows pathognomonic findings in cases of splenic torsion with or without omental torsion. CT is better to US showing high sensitivity, specificity, and accuracy for vascular invasion and thrombus formation in cases adrenal masses. CT is more sensitive to US to demonstrate small size pancreatic tumors and is more precise than US to define the expansion of pancreatic necrosis, extra pancreatic disease, and vascular complications. CT is better to US in delineating the renal vasculature, evaluating the function of the kidney (arterial, nephrographic and excretory phase), calculation the glomerular filtration rate in dogs, demonstration ureteral obstruction and ectopic ureter, detecting small urethral calculi and confirming the lower urinary tract disruption.
US is an accurate method in the diagnosis of intestinal obstruction with high sensitivity (85%) and specificity (94%) (5), however, CT shows a 100% sensitivity and specificity in the detection of mechanical ileus and to define the exact site of obstruction.

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CLINICAL TUTORIAL: PRESENTATION AND DISCUSSION OF INTERESTING HEMATOLOGY CASES

Friday 13 September | 08:30 - 10:30 | MC 3.4 - Room D

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Dr. Argyrios Ginoudis
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In this session of interesting clinical cases, we will explore key clinical hematology cases in companion animals, focusing on the diagnostic approaches and challenges encountered in anemia, leukocytosis, and coagulopathies. The session will emphasize the importance of a structured diagnostic workflow, starting from patient history and clinical examination to advanced laboratory testing and imaging. A key highlight will be the essential role of blood smear examination, often underutilized but critical in identifying red blood cell morphology abnormalities, white blood cell differentiation, and platelet disorders. The talk will showcase the diagnostic value of blood smears in providing rapid and cost-effective insights that complement other laboratory findings.

Moreover, we will introduce and discuss novel diagnostic tests that offer enhanced accuracy and precision in identifying hematologic disorders. These cutting-edge tools, alongside traditional methods, will be evaluated for their potential to improve the diagnosis and management of complex hematologic cases. Through real-world case studies, we aim to provide practical knowledge on overcoming the diagnostic challenges faced by veterinarians in managing blood disorders, ultimately leading to better clinical outcomes for companion animals.

YOU ARE ONLY AS OLD AS YOU FEEL: BEHAVIOURAL PROBLEMS IN SENIOR CATS

Friday 13 September | 08:30 - 10:30 | MC 3.4 - Room D

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As the pet population ages, veterinary medicine increasingly focuses on geriatrics and the unique challenges associated with caring for older animals. Geriatrics is the branch of medicine that addresses health issues specific to old age, recognizing that aging is a natural biological process influenced by genetics and environmental factors, rather than a disease itself. In senior cats, cognitive dysfunction syndrome (CDS), or feline dementia, presents significant behavioural challenges that require specialized attention from us, the veterinarians. This paper explores the impact of aging on feline behaviour, common behavioural changes seen in senior cats, and effective strategies for managing these challenges to ensure a better quality of life.

Aging in cats involves a gradual decline in the ability to maintain homeostasis when faced with physiological and environmental stressors. The aging process is influenced by genetics, breed, lifestyle, and overall health status. Certain physical changes, such as greying fur or reduced activity levels, are generally considered normal aspects of aging. However, more significant changes may impact the cat's quality of life and require medical intervention.

Key changes associated with aging in cats include:

1) **Behavioural and Cognitive Changes:** Cognitive dysfunction syndrome (CDS) in cats, similar to dementia in humans, is a notable age-related change. Senior cats may display disorientation, altered social interactions, changes in activity levels, and disrupted sleep patterns. These behavioural changes are often mistaken for normal aging, underscoring the importance of early detection and management.

2) **Physical and Functional Declines:** Aging affects multiple body systems, leading to conditions such as osteoarthritis, dental disease, decreased renal function, and reduced sensory capabilities. Sarcopenia, or the loss of muscle mass, is common and can impact mobility and overall strength. Similarly, changes in the skin, coat, and weight often occur as cats age, impacting their health and wellbeing.

3) **Impact on Organ Systems:** Age-related changes are seen across various organ systems, including the cardiovascular, renal, gastrointestinal, and immune systems. For example, aged cats frequently develop chronic kidney disease (CKD), which affects up to 80% of cats aged 15–20 years. Cardiovascular changes may also occur, such as increased blood pressure or hypertrophic cardiomyopathy (HCM).

Challenges in Diagnosis and Management

One of the primary challenges in managing aging cats is differentiating between normal age-related changes and those due to disease. For example, behavioural changes such as

increased vocalization or inappropriate elimination may result from pain or cognitive dysfunction. Comprehensive diagnostic evaluations are essential to rule out underlying medical conditions.
The management of senior cats involves regular veterinary check-ups, early detection of disease, and proactive health care. Key strategies include:

1) **Regular Health Screenings:** Routine diagnostic tests, including blood pressure measurement, blood tests, and imaging, are crucial for early identification of age-related diseases.

2) **Behavioural and Environmental Modifications:** Adjustments such as providing easily accessible resources (e.g., food, water, litter boxes) and using environmental enrichment techniques can help maintain cognitive function and minimize anxiety.

3) **Pharmacological Interventions:** Medications like selegiline or dietary supplements rich in antioxidants and omega-3 fatty acids can support brain health and help manage cognitive dysfunction symptoms.

Integrating Geriatric Care with Behavioural Management
A comprehensive approach to managing aging cats integrates both medical and behavioural care. This includes establishing personalized health plans that address the unique needs of senior cats, focusing on prevention, early detection, and timely intervention. Such an approach helps mitigate age-related decline, enhances quality of life, and create stronger bonds between cats and their owners.

Conclusion
With an aging pet population, veterinary practices must adapt to the challenges of managing the complex health needs of senior cats. By understanding the unique aspects of feline aging and implementing a proactive approach to care, we can significantly improve the quality of life for older cats, allowing them to age with comfort and dignity. The ultimate goal is to ensure that senior cats are "only as old as they feel," enjoying their golden years to the fullest.

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OCULAR EMERGENCIES IN SMALL ANIMALS

Friday 13 September | 11:00 - 13:00 | MC 3.4 - Room D

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Ocular emergencies involve a range of acute eye conditions that require immediate attention and prompt treatment to prevent severe discomfort, potential loss of vision and even morbidity. General practitioners, as the first point of contact, often encounter these urgent situations, making their role crucial in early identification and management. A solid understanding of common ocular emergencies, their clinical presentations, and the appropriate immediate responses can significantly impact patient outcomes.

This introduction provides an overview of key ocular emergencies, recognizing the presenting signs, understanding the differential diagnosis and highlighting the critical actions needed to address them effectively.

Adnexa

Emergencies involving the eyelids are very common in clinical practice and require immediate attention in order to prevent infection, minimize scarring, and maintain proper eyelid function. This is crucial for protecting the eye and facilitating normal vision. These injuries can result from various causes, including blunt or sharp trauma, accidents, and animal fights.

An eyelid laceration may involve partial or full-thickness cuts through the eyelid tissue and there is often significant bleeding due to the rich blood supply of the eyelids. The trauma may extend to the eyelid margin, and potentially cause damage to deeper structures like the tarsal plate or canaliculi.

Under general anaesthesia and careful preparation of the wound with sterile saline, the edges are debrided. If the laceration is deep, a layered closure approach is important using absorbable 6-0 or 7-0 sutures for the deeper layers and non-absorbable sutures like 6-0 or 7-0 nylon for the skin layer. When treating eyelid trauma, proper alignment is crucial, especially if the laceration involves the eyelid margin. Figure-of-eight sutures are used to carefully approximate the edges. It is important to note that the eyelid should maintain its normal contour and that the patient can close their eye fully after the procedure.

Topical or systemic antibiotics for 7–10 days and an Elizabethan collar to prevent further self-trauma are advised for eyelid wounds. Skin sutures may be removed in 7-10 days. Prognosis is generally good if proper surgical apposition has been achieved and the wound is not infected. If an eyelid defect is left untreated this can result in an abnormal eyelid margin, which in turn will cause further irritation to the anterior surface of the eye. Despite the obvious eyelid symptoms that one cannot miss, a complete ophthalmic examination is necessary to rule out injuries to the lacrimal apparatus, orbit or deeper ocular structures (such as globe/scleral penetration, lens

luxation, retinal detachment) especially if marked chemosis or conjunctival hemorrhage are present.

Cornea

Corneal trauma occurs after disruption of the corneal epithelium with or without stromal loss. The sudden discomfort, severe discharge and redness of the eye are the most prominent clinical signs. Initial approach should be directed at determining and correcting the underlying cause of ulceration. A careful evaluation of the ocular structures is important in order to identify the underlying cause of the ulcer, such as entropion, ectopic cilia, KCS etc. Performing a slit-lamp examination helps us assess the size, depth, location of the ulcer and identify signs of infection, such as stromal infiltrates, hypopyon (pus in the anterior chamber), and endothelial plaques. Fluorescein staining is the gold standard for diagnosis.

If the ulcer is superficial (epithelial or <50% stromal loss) appropriate prophylactic treatment with antibiotics and anti-collagenase agents is essential. Cytology and culture and sensitivity are recommended in wounds that are already infected. Treatment of the reflex uveitis should also be considered with topical cycloplegics (e.g., atropine or cyclopentolate) to relieve pain from ciliary spasm.

If the ulcer is deeper or very infected, then various surgical options are advised (corneal grafting techniques). Corneal laceration or perforation accompanied by iris prolapse should be managed surgically as a same day emergency. If corneal surgery is not an option, a temporary tarsorraphy (6-0 suture) can aid the healing process. The commonly used third eyelid flap is not advised due to the subsequent difficulty in monitoring.

Systemic nonsteroidal anti-inflammatory drugs (NSAIDs) will control the uveitis and ocular discomfort. Topical and systemic corticosteroids are contraindicated in complicated or infected corneal ulcers as they delay wound healing and increase collagenase activity.

Uvea

Inflammation of the uveal tract of the eye is called uveitis and can affect the iris, ciliary body, and choroid. It can lead to serious complications, including vision loss, if not promptly and properly managed. An emergency approach to uveitis involves a comprehensive history, focusing on onset and duration of symptoms (redness, pain, photophobia, blurred vision), any recent infections, systemic conditions, trauma, or previous episodes of uveitis.

If blood tests and further imaging results are unremarkable and no cause is identified, treatment with topical corticosteroids (e.g., prednisolone acetate 1%) every 1-2 hours is advised. Additional cycloplegic drops (e.g., cyclopentolate or atropine) help reduce pain from ciliary spasm and prevent the formation of posterior synechiae. Systemic corticosteroids can be used with caution if the uveitis is severe, posterior, or not responding to topical treatment and systemic infectious causes are ruled out.

Glaucoma

When the eye is inflamed and the ophthalmic examination via tonometry reveals a high intraocular pressure, glaucoma is diagnosed. Normal intraocular pressure ranges: dog 12–25 mm Hg, cat 12–27 mm Hg. Glaucoma is a painful condition that almost always leads to blindness. The primary goal is to reduce IOP as quickly as possible. All treatments for glaucoma (medical or surgical) work by one of two mechanisms. That is by either increasing aqueous outflow from the eye, or by decreasing aqueous inflow (i.e., production). The most commonly used glaucoma

drugs in veterinary medicine are: 1) adrenergics, 2) carbonic anhydrase inhibitors and 3) prostaglandins. These drugs must usually be used in various combinations to effectively lower and maintain a normal IOP. Often, systemic pain relief is required. Early recognition and immediate intervention are crucial for a favorable outcome. Surgical options are also available, in appropriate candidates (ECP, gonio valves etc).

A neuro-ophthalmic assessment (menace response, dazzle reflex and pupillary light reflexes) often provides prognosis for the eye. Failure to manage the high IOP and lack of reflexes in a blind eye indicate enucleation.

Orbit

Blunt or penetrating trauma to the eye may cause significant orbital trauma and proptosis. The later results when the globe is displaced forward and the lids contract behind it. This constricts venous return and the swelling and hemorrhage prevent the eye from returning to the orbit. This can lead to optic nerve stretching and permanent irreversible trauma and blindness. The traction can be so severe that can even affect the optic chiasm and the contralateral eye. The extraocular muscles may also be torn, resulting in permanent strabismus.

Prognosis depends on several factors such as the breed of the dog, the neuro-ophthalmic exam (direct or consensual pupillary light reflexes), findings on posterior segment exam, avulsion of extraocular muscles and facial fractures. Proptosis affects more commonly brachycephalic breeds with shallow orbits and wide palpebral fissures. A much greater force is required to proptose the globe in breeds with a deeper orbit. For cats, or species with complete bony orbits (i.e., cattle, horses) the force required is even bigger and prognosis very poor.

When dealing with a proptosis, assessment of the entire patient is very important to rule out any signs of cerebral edema or hemorrhage and respiratory or cardiovascular compromise. A complete ophthalmic examination should follow. Immediate ocular therapy should focus on keeping the globe moist; something that is often advised even during transport of the animal to the practice. Under general anaesthesia and preparation of the periocular tissues with dilute povidone-iodine and sterile saline, a lateral canthotomy is performed to facilitate globe replacement. Following globe replacement, a temporary tarsorrhaphy is performed by placing three or four horizontal mattress sutures of 4-0 or 5-0 with stents -to prevent eyelid tissue necrosis. It is very important to inset the needle through the opening of the meibomian glands. Misplacement of the sutures can lead to corneal trauma (ulceration). The sutures are left for approximately 2 weeks. Broad spectrum antibiotics and systemic anti-inflammatory corticosteroids are recommended at the time of surgery.

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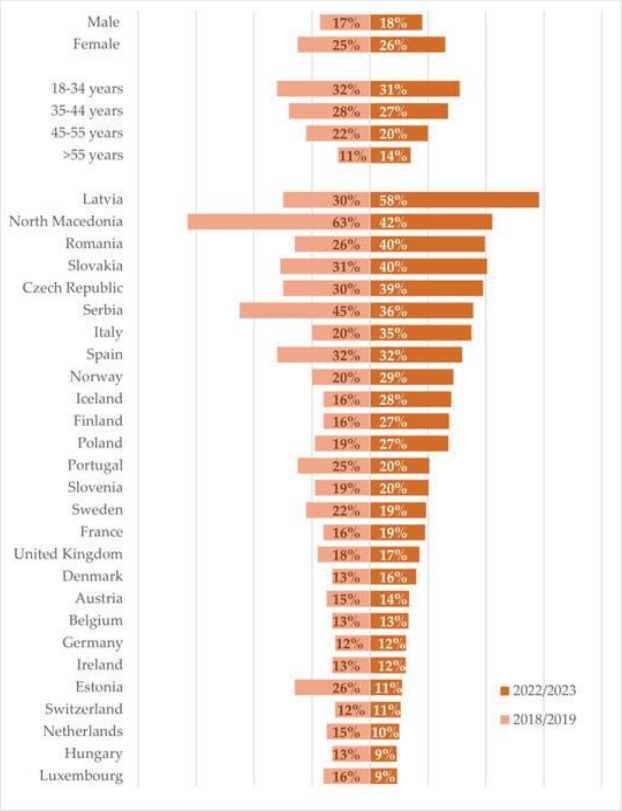
VETERINARIAN –CHASING A DREAM JOB? COMPARATIVE SURVEY ON WELLBEING AND STRESS AMONG EUROPEAN VETERINARIANS BETWEEN 2018 AND 2023

Friday 13 September | 14:00 - 15:45 | MC 3.4 - Room D

Mette Uldahl

1. Introduction

This pieces of research outlines the findings of the third FVE VetSurvey on mental well-being (MWB) and diversity, equity, and inclusion (DEI) in the veterinary profession (1). The survey assessed stress levels, well-being, and the effectiveness of various support programs within the profession, aiming to provide actionable insights for improving the working environment for veterinarians across Europe.



2. Material and Methods

The survey was conducted in 2018/2019 and 2022/2023 under the umbrella of the regular FVE led-VetSurvey, a This mixed methods study consisted of two cross-sectional online surveys. Participation was voluntary and not remunerated, and no question was compulsory, except for some of the demographic questions (e.g., gender, age) in 2018/2019. Some participants did not answer all questions, which led to different subtotals for each analysed question. The analysed questions in this study covered assessed demographics in relation to (i) self-reported stress levels on a scale from 0 (not stressed) to 10 (very stressed) in 2018/2019 and 1 (not stressed) to 4 (very stressed) in 2022/2023, (ii) whether respondents had to take time off for medical leave due to burnout, exhaustion, compassion fatigue, or depression, and (iii) measured wellbeing scores. For the latter, the standardized short seven-question Warwick–Edinburgh Mental Wellbeing Scale

(WEMWBS—© NHS Health Scotland, The University of Warwick and University of Edinburgh, 2006, all rights reserved) was used (2,3).

3. Results

Self-Reported Stress Levels by Country and Gender

Female veterinarians consistently reported higher stress levels than their male counterparts in both surveys. Stress levels varied significantly across countries, with veterinarians from North Macedonia, Bulgaria, Italy, and Slovenia reporting the highest levels in 2018/2019, and those from Denmark, Ireland, and the Netherlands the lowest. In 2022/2023, the highest stress levels were reported in Latvia, Lithuania, Greece, and Cyprus, while the Netherlands and Denmark maintained the lowest levels.

Medical Leave Due to Decreased Mental Well-being

Consistently, 22 resp. 23% of veterinarians required more than two weeks off work due to burnout, exhaustion, compassion fatigue, or depression. Female veterinarians reported taking medical leave more frequently than male veterinarians (29.7% vs. 18.4% in 2018/2019, and 26% vs. 18% in 2022/2023). Early-career veterinarians were more likely in need to take medical leave than their more experienced counterparts. The frequency of medical leave varied by country, with significant drops in North Macedonia and Estonia but increases in Latvia, Romania, Italy, and Iceland between the two survey periods (Fig. 3).

Figure 3. Percentages of veterinarians who took medical leave due to burnout, exhaustion, compassion fatigue, or depression of more than 14 days in the last three years by gender, age, and country.

Warwick-Edinburgh Mental Well-being Scale Results

The average WEMWBS score remained relatively stable between the two survey periods, with scores of 25 in 2018/2019 and 24.8 in 2022/2023. The order of best-ranked questions remained consistent, indicating stable well-being trends despite various crises.

4. Discussion

Factors influencing MWB are multidimensional. Younger veterinarians face different challenges than their more experienced counterparts, including adapting to new technologies and meeting evolving client expectations. Early-career veterinarians, particularly those managing family responsibilities, often struggle with balancing professional and personal lives. Recent graduates experience pressure to establish themselves in their careers, contributing to stress and anxiety, especially if their progress seems slower than expected. Women in veterinary leadership roles feel additional pressure to prove themselves, potentially leading to increased stress and mental health issues.

It has been shown previously that webinars and training sessions are effective in raising awareness and have a significant impact on mental well-being and DEI. Tailored approaches, such as helplines and peer-to-peer support groups, are beneficial for individual veterinarians in need. However, more research is needed to design universally applicable mental well-being scales and a scoring system to rate the effectiveness of support programs. Veterinary organizations should implement positive and inclusive role models and diverse examples from the profession from the beginning of veterinary training. Rewarding "great veterinary workplaces" that go the extra mile to create a positive environment can help raise awareness and improve workplace culture (4).

To curb the MWB/DEI burden, FVE, FECAVA and IVSA implemented holistic strategies along the veterinary career path. The joint FVE/FECAVA/IVSA Mental-wellbeing/DEI Working Group 2023-2026 established a hub providing tools, resources, training programs, and coaching to equip veterinary workplaces with necessary skills, offer grants for veterinary workplaces to apply for coaching or courses tailored to their needs, introduced an annual FVE award for 'GREAT Veterinary Workplaces', implemented a mentor/mentee program for early-career veterinarians and launched an outreach program for secondary schools called 'Vet for a Day'.

5. Conclusions

Veterinary MWB is complex and multifaceted, and impaired MWB can affect anyone, regardless of age, gender, or professional background. Our findings showed that despite multidimensional crises, the need for medical leave due to reduced mental health and MWB scores remained stable, with overall stress levels being consistently high. In particular, our results showed that early-career and female professionals are at higher risk, potentially due to the changed veterinary professional landscape, career development pressure, and professionals still developing coping strategies. Moreover, gender roles and expectations, stereotypes, and bias may play a role, as well as the need to manage multiple roles and responsibilities without appropriate support. All these aspects can be particularly demanding during early career stages. However, our results indicate that part-time work seems beneficial for veterinary MWB. Therefore, improving veterinarian wellbeing will be most successful by creating supportive veterinary workplaces that prioritize wellbeing, staff retention, and pay attention to the work/life balance. Despite many psychometric tools reported in the (veterinary) literature to measure MWB, there is a crucial need to define, in the near future, comparable and consistent standards for MWB assessments in healthcare professions. Broaden MWB and DEI within the veterinary profession to reflect societal needs, increase recognition and satisfaction, and attract and retain diverse teams is an imperative for a thriving profession as well as ensuring veterinary alignment with societal changes and modern developments in animal welfare and bonding.

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ROLE OF LEADERSHIP IN CREATING A POSITIVE WORKPLACE CULTURE

Friday 13 September | 14:00 - 15:45 | MC 3.4 - Room D

Patricia Colville

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Working within the veterinary profession is hugely rewarding and yet despite this, it is now recognised that cultural working environments can be linked to veterinary wellbeing concerns as noted in the paper discussed earlier by Ms Uldahl.

The link between leadership and organisational culture is firmly established in human medicine.

Every workplace has a culture. Culture is generally accepted as 'The Way Things Are Done Around Here'

Developing a positive workplace culture can help animal welfare, help individuals and teams and improve the business side of the practice through many facets, not least staff engagement and turnover. This is especially important at a time when there are recruitment pressures on the veterinary workforce. Culture, behaviour and values are inextricably linked and they all influence performance.
There is a common held view in human healthcare that a positive organisational culture is related to positive patient outcomes.

Every one of us is a leader; you don't need to have leadership in the title. There are different recognised leadership styles, and this aspect of veterinary practice is gaining greater focus, insight and evidence within the veterinary workplace.
Leadership is learned and can be improved and built on. We want to start by leading ourselves. Historically, a low priority has been given to veterinary leadership. Traditionally, we do not go to university to learn to be leaders – we go to learns to be vets and nurses, but the journey in human medicine suggests the roles are inseparable.
A Positive Workplace Culture improves, amongst other things (this list isn't exhaustive): teamwork; job satisfaction; collaboration; patient welfare; client satisfaction; and, business performance.

There will be various building blocks for Culture: values and beliefs; behaviours; systems and processes; health and wellbeing; individuals; and, communication styles. Everyone is responsible for the culture in the workplace. As leaders within your team, you want to shape that culture and not just let it happen to you and the team. Involving the team in working out what type of culture you want is the first step. What is that framework and how you hold each other accountable if an individual accidently steps out with that Cultural contract is important. Agree that at the start and embed it within the onboarding process. Set everyone up for success and with that in mind, consider how to develop psychological safety – when something doesn't go right (and no environment or team are perfect), how do we develop the safe space to question the processes, so the 'what' happened as opposed to 'who' made a mistake.

A large part of Leadership and Culture is communication – both verbal and behavioural. It is

important to consider the team you work within and adapt both communication style and frequency depending on size and the situation. Learn how to have those difficult conversations and how everyone can learn, develop and grow from them. Don't let them build up – you want it to become second nature and expected and there is team autonomy alongside accountability.

Let's work on designing your team/work Culture.

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TIPS FOR MANAGING STRESS IN A BUSY VETERINARY CLINIC

Friday 13 September | 14:00 - 15:45 | MC 3.4 - Room D

Elli Kalemtzaki,

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Working in a veterinary clinic can be incredibly rewarding, but it also comes with its own set of challenges. The fast-paced environment, emotional situations, and the responsibility of caring for animals' health can lead to significant stress[1].
In a study aiming at measuring the prevalence of severe mental distress and determining the level of wellbeing within the veterinary profession, two thirds of participants reported having feelings of depression, compassion fatigue, burnout, and anxiety within the last year.[2]
Veterinary practitioners often invest themselves deeply in the animals they care for, and this can overtime lead to emotional exhaustion and depletion. What are the consequences of dealing with patients and how can veterinarians manage their emotions? What should veterinarians do to act with professionalism and empathy while protecting their own mental wellbeing?
Here are some practical tips for managing stress in a demanding clinical setting:

1. Prioritize Self-Care

As healthcare professionals, you often spend a lot of time caring for others, but it's crucial to remember that taking care of yourself is equally important. Remember that self-care is a personal and individualized practice. Self-care is essential for maintaining physical and mental well-being. Adequate sleep, a balanced diet, and regular physical activity form the cornerstone of self-care practices.

Developing and implementing healthy coping mechanisms is crucial for stress management. Techniques such as mindfulness, meditation, and deep breathing exercises can help in calming the mind and reducing anxiety.
Exercise and movement improve quality of sleep, have been linked to improved mood and reduced feelings of anxiety and depression.[3]
Meditation can be a valuable tool for dealing with negative emotions in several ways. By cultivating a regular meditation practice, individuals can develop emotional awareness, improve emotional regulation, and gain a better understanding of their feelings. [4]
It's important to note that meditation is not a quick fix, and it may take time and consistent practice to see significant changes in emotional well-being.
Breathing exercises are a powerful tool for managing stress and promoting relaxation. When we are stressed or anxious, our body's "fight or flight" response can be triggered, leading to increased heart rate, shallow breathing, and tense muscles. By practicing specific breathing techniques, we can activate the body's relaxation response and counteract the stress response.[5]
Journaling can be an effective tool for managing negative emotions by providing an outlet for self-expression and self-reflection.[6]
Engaging in the act of writing itself can have a calming effect on the mind. Journaling can help reduce stress and anxiety by slowing down racing thoughts and promoting a sense of emotional release.

2. Effective Time Management

Time management is critical in a demanding clinical setting. Implementing a structured daily schedule and prioritizing tasks based on urgency and importance is essential. Utilizing organizational tools such as checklists, calendars, and time-tracking applications can aid in maintaining order and efficiency. Allocating specific time slots for various tasks helps in preventing the sense of being overwhelmed and ensures optimal task completion.

3. Delegate Tasks
Task delegation to competent team members is vital for workload management. Trusting colleagues and assistants with shared responsibilities not only distributes the workload more evenly but also promotes teamwork and collaboration within the clinic.

4. Maintain Clear Communication
Clear and open communication is essential for seamless clinic operations. Regular team meetings, briefings, and debriefings ensure that all staff members are aligned with the clinic's objectives and updates. Encouraging team members to voice concerns, share updates, and provide feedback fosters an environment of transparency and reduces stress.

5. Set Realistic Expectations
Setting realistic expectations for oneself and the team can prevent undue stress. Recognizing that perfection is not always attainable and learning to accept personal and professional limits is essential. Avoiding overcommitment to tasks that are not feasible within the available time and resources is crucial for stress management.

6. Foster a Positive Work Environment
A positive and supportive work environment significantly mitigates stress. Cultivating a culture of appreciation, where team members recognize each other's efforts and successes, is beneficial. Organizing team-building activities, celebrating achievements, and promoting camaraderie among staff fosters a supportive workplace atmosphere.

7. Seek Professional Support
When stress becomes unmanageable, seeking professional support from a therapist or counselor is advisable. Many veterinary clinics offer Employee Assistance Programs (EAPs) that provide access to mental health resources. Professional counseling can assist in developing effective stress management strategies and enhancing overall well-being.
Managing stress in a high-pressure veterinary clinic environment requires a combination of self-care, effective communication, and strategic planning. Prioritizing personal well-being, fostering a supportive work culture, and developing healthy coping mechanisms are crucial for stress reduction. By employing these strategies, veterinary professionals can maintain their well-being while continuing to provide exceptional care to their patients. The emphasis on self-care is as paramount as the care provided to animal patients.

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IMPLEMENTATION OF CHANGE STRATEGIES IN VETERINARY SETTINGS

Friday 13 September | 17:00 - 18:45 | MC 3.4 - Room D

Michail Zavlaris

DVM, PhD, Pg Cert VBM, B&A (L2), MRCVS – Manager of Anatomic Pathology, Finn Pathologists, The Veterinary Laboratory – Suffolk, UK.

The implementation of change strategies in veterinary settings holds the same challenges and characteristics as in any firm. Employees usually approach change with skepticism and they are cautious of its implementation[1]. Communicating change to teams and implementing a culture of ongoing and sustainable change is paramount in entrepreneurship. The key element to implement, organize, accomplish, and ensure an effective organizational change, is for leaders to use concise communication channels and engage employees in a mutual and well-understood objective. The latter tackles employees' skepticism, improves the understanding of the importance of change, makes processes more acceptable, and will drive an effective change implementation strategy[2,3].

Change management is the process that ensures a business responds to the environment in which it operates. Change implementation follows a dissatisfaction with present strategies or the company's position in the market[4]. To successfully apply change strategies, employees should be engaged in mutual work values and share the ethos of continuous development and improvement for a better or sustainable alternative future. The implementation of change strategies requires a detailed strategic plan and leaders should be aware that most likely employees will resist it. Individuals are often in fear and feel threatened as they see that their financial security might be jeopardized, they won't have a say in the processes, and their working conditions will be disrupted[1,5]. However, leaders can tackle these fears by installing a culture of ongoing improvement, sharing a common vision, being analytic on the reasoning behind the change, sharing a comprehensive plan, and encouraging participation[6,7].

The holistic approach, facilitates the implementation of change strategies as with this method managers can overcome resistance effectively[8]. This method avoids common blunders in implementing changes and helps to shorten the implementation times, whilst

enhancing engagement and commitment. Through this approach, leaders should support and encourage participation in working groups, adequately share progress and challenges, build a trusting culture, and be open to feedback. As a result, the company benefits from high employee compliance, their engagement in future projects, and improves success rates in implementing organizational changes.

Building bridges of clarity and mutual trust, and setting clear communication channels are the cornerstones of an effective change strategy implementation. A detailed planning of the change processes and finding alternative routes should systems not work as expected, keeps employees committed to the change objective. Ongoing bottom-to-top consultations amongst staff, sharing the perspective hazards if the change is not implemented, and highlighting the future benefits, can assist employees not to perceive change as a threat and make the implementation strategies successful.

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EVALUATE THE PERFORMANCE OF OUR VETERINARY CLINIC, FOCUSING ON THE USE OF KEY PERFORMANCE INDICATORS (KPIS)

Friday 13 September | 17:00 - 18:45 | MC 3.4 - Room D

Themis Charos

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Evaluate the performance of our veterinary clinic, focusing on the use of Key Performance Indicators (KPIs) as measurement tools. KPIs are measurable parameters that represent the achievement of a business's goals and provide a valuable tool for continuous improvement and the development of the clinic.
Initially, we will examine the treatment success rate as a KPI, which is an indicator of the effectiveness of our medical interventions. Analyzing this KPI allows us to understand how patients are being treated and the likelihood of their recovery.
Another important KPI is the recurrence rate, which shows the likelihood of problems recurring after treatment. This KPI is critical for assessing the long-term effectiveness of medical interventions and taking appropriate preventive measures.
In addition to medical outcomes, we also examine KPIs related to customer experience. Our customer service satisfaction rate provides information about their satisfaction with the services we provide and the potential need for improvements.
The customer churn rate is also a significant indicator of their satisfaction and can provide useful information about the quality of care provided.
In conclusion, analyzing these KPIs allows us to understand the performance of our veterinary clinic and identify areas where we can improve our services.
Continuous monitoring of these KPIs and taking action to improve our performance is essential to ensure high-quality and effective care for our customers.

"*OUCH, IT HURTS!*": DIFFERENT WAYS OF SHOWING PAIN

Saturday 14 September | 08:30 - 10:30 | Amphitheater N. Skalkotas - Room A

Gonçalo da Graça Pereira

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INTRODUCTION

Pain has a physiology component, also called nociception, which includes: transduction, transmission, modulation and perception (which is an affective or emotional component). The first process, transduction, has the purpose of turning noxious stimuli (thermal, mechanical or chemical) into an electric sign. Transmission is through synapses between first-order neurons and second-order neurons, which are located in the grey matter of the spinal dorsal horn. But all neurons are involved in the initial processes of modulation, processing and integrating pain, which is an organised response. Regarding perception, it is difficult to define exactly at which level of the Central Nervous System the nociceptive signal is perceived as pain, causing suffer. However, perception, as an emotional or affective component, is the result of the activity of several brain structures, which are:

1) Medulla oblongata, pons and mesencephalon
2) Reticular formation
3) Periaqueductal grey
4) Hypothalamus
5) Thalamus
6) Limbic system
7) Brain cortex

The system of neurotransmitters involved in pain is very complex. The same neuron can be influenced by different neurotransmitters and, at the same time, release others. At the same time, it can exist other connections with other neurons for many different neurotransmitters. For this reason, it is quite comprehensive that must exist a relation between stress and pain. In fact, stress modifies the concentration of neurotransmitters, which will influence the pain perception. There are many studies showing that chronic stress, which can be due to state of chronic pain, reduces serotonin levels, one of the pain inhibitory neurotransmitters. So, we should also consider that in stress situations, with low level of circulating serotonin, the perception of pain can also be higher. Thus, it is easy to understand this cycle relation between stress and pain. However, for behaviourist vets, what is really interesting to consider is that the reduction of the serotoninergic activity in the central nervous system is linked to various behavioural changes (such as tendency to show aggression, more impulsive – without previous warning signs, or ritualised behaviours). Understanding all these processes, it is clear to understand how pain can promote behavioural changes. Accurate history taking and good clinical examination is therefore essential.

PAIN AND AGGRESSION

Camps et al. (2012) published a case-report of 12 cases of aggressive behaviour caused by pain. Apart from this study there are no other studies showing the relation between pain and aggression. So, since the fact that pain can cause aggression is not always taken in account, we believe that pain-related aggression is underestimated. Due a disagreement

in the terminology used, some authors include pain-related agression in aggressive behaviour due to an organic cause. However, in the author's opinion, independently of the classification there are at least 2 emotional-motivational systems activated in this type of aggression, one is pain system and the other can be fear (anxiety) system. Both are negative emotions that should be the focus of our treatment.

The aggressive behaviour can be aroused through 3 different mechanisms:

1) Avoidance – the aggression comes when the animal try to avoid a particular handling or touch, which has been previously experienced. Learning is involved in the previous example, but learning can also be involved when a painful situation can become associated with a local or individual, becoming the target of aggression behaviour (later could be thized). The role of associative learning should not be underestimated and behavioural changes can be seen weeks or even months after an incidence of acute pain. It is also well described that in situations of pain (as the one caused by aversive training methods) can increase the chance of redirecting aggression towards another individual.
2) Stress – explained in the introduction
3) Reduction of physical activity – in farm and laboratory animals it was observed that a reduction of physical activity (due pain) is correlated with an increase of aggressive behaviour secondary to a decrease of serotoninergic activity.

PAIN AND COMPULSIVE BEHAVIOUR

As it was previously mentioned, chronic pain is a source of stress, which can trigger the appearance of a displacement behaviour (which with time can become compulsive if there are no improvements in the situation).

There are many diseases that can trigger a compulisve disorder secondary to pain. In Neurology we can find animals with lumbosacral stenosis presenting circling. Sensory neuropathies can lead to compulsive licking or even chewing a part of the body. Arthritis and tail fractures (or tail amputation that can cause neuromas) takes the animal to pay more attention into the painful area having the possibility of developing a compulsive behaviour. Any dermatology pathology that cause pruritus and/or pain can lead to compulsive behaviour as well. Another example that can be referred is the feline interstitial cystitis, which is very painful, leading the animal to present psychogenic alopecia.

PAIN AND FEAR

Mainly, there are 2 mechanisms through which pain can cause fear. The first is related with associative learning, where pain acts as an unconditional stimulus which induces a fear response. Apart from this learning process, there is another reason which is anatomically, chemically and functionally given as an explanation. The neurological pathways responsible for fear, anxiety and pain, are closely related!!! Which means that an animal that is experiencing pain, will create associations between the stimulus in the origin of the pain and the neutral stimuli (which will become a conditioned stimulus) that will help to predict a similar situation in the future.

The other mechanism only seams to be demonstrated in humans, where it has been widely demonstrated that when suffering from pain, like the other animals!, can generate and anxious response. These anxious humans have a large probability of presenting a pessimistic perception of the environment (also called pessimistic or negative cognitive bias). This perception will make that an initially neutral stimuli become potential (not real) source of pain. What will happen following is that this initially innocuous stimuli will be avoided (due to a reaction of fear at the prospect of them being able to cause pain) (Deghani et al., 2008). Despite the fact that there is a lack of scientific studies in this field in non-human animals, this process can take place in a similar way. In fact there are several

studies showing that non-human animals can show pessimistic or optimistic view of the environment (negative or positive bias, respectively). It was identified in dogs with separation related problems that have a negative bias, when compared with the average of the general population (Mendl et al., 2010). So, if pain that occurs in many pathologies can cause stress, it is expected that animals presenting pain can have a negative bias of the environment.

CONCLUSION

So, during a behavioural consultation, the vet should always include in its diagnostic protocol a medical check-up to rule out possible pathologies that are creating pain, leading to the presented aggresive behaviour. If any pain is found or even considered, an appropriate analgesic protocol must be putted in practice to ensure pain control, even before starting any emotional modification therapy.

Practical considerations:

- Investigate and treat underlying source of pain
- Use analgesic medication as appropriate and trial periods of medication where there is doubt about the relevance of pain
- Provide indirect means for the caregiver to move the animal, including house lines and food trails
- Avoid handling where possible and provide access to vehicles through the use of ramps (for dogs)
- Encourage exercise through short walks and make the experience inherently rewarding (for dogs)
- Tailor exercise and interaction to the individual situation of the case and where necessary limit intensity and/or duration of play
- Embark on specific counter conditioning programmes to establish positive associations with dilute forms of handling

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BEHAVIOURAL EUTHANASIA IN EVERYDAY CLINICAL PRACTICE

Saturday 14 September | 08:30 - 10:30 | Amphitheater N. Skalkotas - Room A

Dr. Christos I. Karagiannis

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Introduction

Dog owners who describe the dogs exhibiting more problematic behaviours are more likely to consider abandoning their pets compared to other owners. Behavioural problems in dogs and cats are among the most frequent, if not the main, reasons for pet relinquishment worldwide. In a recent study in dogs, aggressive behaviour towards people, especially toward adults living in the household, followed by aggressive behaviours towards other animals are the main drivers for behavioural euthanasia (1). Other studies as well, showed that behavioural problems are associated with poorer physical health and a reduced lifespan in dogs and can also lead to euthanasia (2).

Typically, owners decide euthanasia due to their pet's illness and suffering, feeling sorrowful but also reassured that they have made the compassionate choice. As veterinarians, we are frequently responsible for ensuring that our patients experience a peaceful and humane death. However, euthanasia due to behavioural issues poses a significantly more complex and conflicted scenario. Often, the animal is young and physically healthy, but euthanasia may be deemed necessary for welfare reasons due to behavioural problems that cannot be adequately managed or resolved, or because of risks posed to people or other animals, such as biting. Those behavioural problems can affect the welfare of both the household members and the animal, potentially weakening or even breaking the human-animal bond (3).

Behavioural euthanasia, the humane euthanasia of an animal primarily due to behavioural issues, presents a complex ethical and emotional challenge for veterinarians (4). This presentation aims to navigate this sensitive topic by exploring its multifaceted nature and providing a framework for veterinarians to guide owners through this difficult decision-making process.

Behavioural Euthanasia

Behavioural euthanasia focus on 1) alleviating animal's emotional or social distress rather than physical pain and/or 2) secure the safety of the pet owners or the greater society or other animals, e.g. in case of aggressive behaviours towards people or other animals. It is a last resort after exhausting all other options, including environmental modification, including rehoming the animal, behaviour modification and appropriate medication use.

Clinical Considerations

For veterinarians considering behavioural euthanasia, a thorough and objective assessment is crucial. This should include:

1) **Behavioural Evaluation and Risk Assessment:** A structured behavioural evaluation using validated tools helps assess the severity and nature of the problem for the animal and/or for people or other animals. This may involve owner questionnaires, direct observation sessions, and potential referrals to veterinary behaviourists.

2) **Differential Diagnoses**: As medical conditions like pain can manifest as aggressive behaviour or anxiety, medical conditions mimicking behavioural problems must be ruled out.

3) **Treatment Plan:**

    a. As an initial step in managing the problem, teaching the animal to use a crate or to wear a muzzle comfortably is crucial. The primary goal is to assist pet owners, alleviate the difficulties they encounter with their pet, and thereby gain time for the benefit of the animal. Concurrently, or as a subsequent step, it is essential to implement a comprehensive treatment plan that includes environmental and behaviour modification strategies, and, if appropriate, psychotropic medication. It is important to present and discuss various available options with pet owners to support them in the decision-making process.

    b. Exploring options like rehoming with experienced guardians familiar with the behavioural issues may be viable for some animals. However, careful evaluation is required to ensure a successful placement. It is advisable to recommend that owners temporarily board their dog for a few days to allow them time to contemplate their decision. In some instances, this absence may lead to owners realizing how much they miss the dog and renewing their commitment to working with it. Conversely, some owners may conclude that they can no longer tolerate the associated uncertainty and risk, leading them to decide against keeping the animal.

4) **Prognosis:** Veterinarians must realistically assess the likelihood of successful behavioural modification. Factors like the severity and frequency of the problem and the owner's capability to changing their pet's behaviour all contribute to the prognosis.

Ethical Considerations

Behavioural euthanasia raises significant ethical questions. These include:

1) **Animal Welfare:** Minimizing animal suffering, e.g. frustration, anxiety, fear, remains the primary ethical principle. When behavioural issues become unmanageable,

leading to a poor quality of life, euthanasia may be the most compassionate option for the animal.

2) **Human Safety and Well-being**: Behavioural issues that pose a significant safety risk to the owner or greater community cannot be ignored. The safety and well-being of the human element in the human-animal bond must be considered.
3) **Client Communication**: Open and honest communication with the client is paramount. Explaining the behavioural assessment findings, treatment options, and prognosis allows informed decision-making. Exploring the client's emotional state, support systems, and ability to cope with the challenges is crucial.
4) **Decision-Making Framework**

A structured framework serves as a valuable tool for veterinarians when facing the intricate decision-making process surrounding behavioural euthanasia. This framework typically includes (4):

a. Risk Assessment: Assessing whether the animal's behaviour causes considerable distress or presents safety risks to the owner, other animals, or the community.
b. Exhaustion of Treatment Options:
    i. Thorough exploration of all viable methods for behaviour modification, medical management and
    ii. Assessing whether the owner can realistically manage the animal's behaviour with ongoing training and support.
c. Assessment of Animal Welfare and Quality of Life: Determining whether the animal's quality of life remains unacceptably low despite intervention efforts.

Ultimately, while the decision to euthanize an animal rests with the owner, veterinarians are ethically obligated to provide unbiased information, facilitate the decision-making process, and offer support throughout all stages of this difficult decision.

Legal Considerations

It is important to verify that the individual requesting euthanasia is the legal owner and the sole adult with interest in or ownership of the animal. There are instances where individuals may act with malicious intent. In the case of a new client, the veterinarian may not have personal knowledge confirming that the dog is indeed theirs or that other family members or legal owners have consented to the euthanasia.

For rabies-controlled countries or low-risk countries, it is important to ascertain whether the dog has bitten anyone within the relevant rabies quarantine period, typically 10-14 days. Euthanizing a dog that should be quarantined without appropriate testing could result in legal liability.

Conclusion

Behavioural euthanasia poses a multifaceted and emotionally intricate decision within the field of veterinary medicine. Adopting a systematic approach that emphasizes animal welfare, ethical deliberations, public safety and transparent communication with the client facilitates a more informed and compassionate decision-making process. Ongoing research into veterinary behavioural medicine and enhanced client support mechanisms

will enhance our capacity to effectively address complex behavioural cases in veterinary practice.

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4. Pachel C.L Behavioral Euthanasia Considerations: Bringing the Conversation Out of the Shadows, Fetch DVM360 Conference, Kansas City, 27-30 August 2021

DOG NEUTERING AND BEHAVIOUR: WHAT DO WE KNOW?

Saturday 14 September | 11:00 - 13:00 | Amphitheater N. Skalkotas - Room A

Dr. Christos I. Karagiannis

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Many pet owners choose to neuter their dogs as a strategy to prevent or treat problematic behaviours, such as reducing aggressive behaviour. Behavioural problems can strain human-canine relationships, often leading to relinquishment or rehoming (1). As veterinarians, it is our responsibility to inform pet owners and set realistic expectations about their dog's behaviour post-neutering.

Neutering typically results in a significant reduction or elimination of behaviours associated with sex differences, such as roaming for mating, hormone-related aggressive behaviour e.g., male dogs fighting around a female in oestrus), and urine marking related to sexual communication. In males, the timing of neutering or the duration a behaviour has been present does not significantly impact the likelihood of modifying these unwanted behaviours (2).

Research consistently supports the impact of neutering on behaviours influenced by testosterone or oestrogen. However, studies examining behaviours not directly linked to these hormones yield mixed results. For example, neutering tends to reduce inter-male aggressive behaviours, but it can increase aggressive behaviours in both male and female dogs (3).

Other studies indicate that the age at which neutering occurs or the dog's breed may influence behaviour. For instance, in German Shepherds, neutering between 5 and 10 months of age was associated with increased reactivity towards unfamiliar people and dogs compared to intact counterparts (4). Furthermore, recent research found significant differences in aggressive behaviour towards other dogs between breeds, such as the "Huskies" type of dogs and the "Bulldogs." For more details about the "Huskies" and the "Bulldogs" breeds, please see the Kolkmeyer et al. 2024 study (5).

Studies comparing dogs neutered before or after 5.5 months show that early neutering may lead to increased noise phobias and sexual behaviours but lower incidences of separation anxiety, fear urination, and escape attempts. In the same study, male puppies neutered before 5.5 months were more likely to display aggressive behaviour towards family members and bark excessively (6). Conversely, a study on dogs neutered before or after 24 weeks found no increase in behavioural problems or return rates to shelters for those neutered prepubertally (7). In Vizslas, early neutering was associated with increased fear and anxiety-related behaviours, although sexual behaviours were not evaluated (8).

Interpreting the behavioural consequences of neutering is complicated by varying study designs and inconsistent results. For instance, the definition of aggressive behaviour varies widely among studies. Additionally, some studies may be skewed if neutering was

recommended as part of a behavioural treatment plan, potentially leading to higher numbers of spayed or neutered dogs with behavioural problems.

As new studies and information emerge regarding the effects of spaying and neutering on diseases and behaviour, the contemporary approach now involves a more personalized assessment. Evaluating the dog's lifestyle and specific circumstances is essential to determine the appropriate timing and necessity of neutering for each individual dog.

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"*I AM BEGGING YOU… DON'T LEAVE ME ALONE*": SEPARATION RELATED PROBLEMS IN DOGS

Saturday 14 September | 11:00 - 13:00 | Amphitheater N. Skalkotas - Room A

Gonçalo da Graça Pereira

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INTRODUCTION

Animal welfare can be seriously affected by separation related problems, being one of the most common behavioural problem (Overall, 2001, 2013; Bradshaw *et al* 2012). These problems can affect both dogs and cats, but are much more reported in dogs. The reason for that is related with all behaviour differences between both species, being cats much more subtile showing discrete signs or symptoms very different from what usually seen in dogs and even very different from case to case. The diagnose can be a challange in both species as many differential diagnoses must be considered. Treatment is dependent on the correct diagnose and many literature continue presenting approaches that can be very unproductive for the animal and its welfare. Despite the impact on animal wefare, the human-dog/cat bond bond can be disrupted leading to relinquishment of "healthy" animals or a decision to seek eutanasia (Salmon *et al*, 1998).

SIGNS

Dogs with separation related problems typically present excessive vocalization, destructive behaviour and/or elimination in the household, but during the caregiver(s)' absence or when can't have direct contact with the caregiver(s) (Pageat, 1998; Overall 2013). Althought these are the most common symptoms and also those that are annoying more the caregiver(s), there can be other less apparent and more subtiles, found both in dogs and cats, like anorexia, vomiting, diarrhea, changes in activity level, but also occuring only when left alone.

TREATMENT

Treatment includes making changes in the animal's environment (mainly to promote adequate stimulation – cognitive, physical and food enrichment, among others), psychopharmacology (to reduce anxiety level) and behavioural modification (to change emotional state to a positive one). The emotional change is the most important part of the treatment and the main goal is to: 1. Habituate the animal to be alone, and 2. Reduce the animal's "dependency" on the caregiver (Bowen & Heath, 2005; Sherman & Mills, 2008; Butler *et al*, 2011).

To achieve these two goals, the literature recommended several approaches, which currently are not recommended. Amat *et al* (2014) discussed that some of the approaches used in behavioural modification or behaviour therapy would be in contradiction to what is currently known about stress response. One important part is the predictability of the caregiver's departure and the other is the role of contextual fear in the treatment of this disease.

In the past it was said that one of the factors contributing to the anxiety response was the anticipation of caregiver's departure. Due an associative learning procedure, the animal associate several cues with the caregiver(s)' departure – like putting the shoes on, picking

up the keys, wearing the coat, among others – we can commonly see in the recommended behavioural therapy, in order to reduce the anticipatory anxiety, to do a desensitization to these departure cues (giving false cues or leaving the household without this cues). However, the effectiveness of this technique was never studied and many of us faced that were not supporting the treatment and, in many cases, the animal improved during a certain period (for instance during the weekend, when the guardian(s) spent more time in this part of the treatment), but returning to the same or worse, suddenly, when the caregiver had to return to the daily routine and stop the process (for instance, due the fact that returned to work).

For that reasons, Amat *et al* (2014), after reviewing several publications in different animal species, including humans, concluded that predictability reduces the anxiety associated with highly aversive stimuli. Guardian(s)' absense is considered by these animals as a highly aversive stimuli. For this reason, the new recommendation is to increase the predictability of the caregiver(s)' departure not only maintining the cues but moreover by adding a novel cue. The reseachers team from University of Barcelona suggested a piece of white cardboard placed in the exit door just before departure and removing it on the returning (Amat *et al*, 2014). Another recommendation is that this cue should be different from another one used during the fake departures, which can be used to gradually habituate the dog to stay alone. Instead of a white cardboard, a black one can be used. Amat *et al* (2014) recommended as well that when the animal is able to stay all by himself for sixty minutes without signs of anxiety, the cue used during the training sessions (here suggested the black cardboard) should be used to signal daily "non-training" departures (like going to work or others apart from training and not controlled).

Another recommendation that can be seen in the literature is that the animal should be left alone in a particular place in order to reduce the inconveniences coming from this behaviour problem (specially destruction). However this animals can suffer from contextual fear associated with this location, and this can be even worse if they have no predictability! For this reason, currently is recommended, whenever is possible, that during the gradual training of habituation to be left alone (fake departures), that location vary from that where the animal is being currently left alone. This location should be trained in advance to be seen as a safe-place for the animal.

Finally, another common recommendation is to ignore the animal a certain amount of time (usully differing from author to author) before leaving the house and when arriving. The main idea was not to "reinforce" inadequate behaviours. However, remember that these animals are under a very negative emotional state, and we will not reinforce negative emotions. Apart from that, when the animal is ignored, there can be animals that take 30 minutes to calm while other 15 minutes or 1 hour. And during this period, the animal is still under a high stressful period, because what he was desiring (the contact with the human being(s)) is being denied. For that reason, it is recommended to calmly greet the animal up on the arrival and ask him for a previously conditioned behaviour associated with a positive emotion (here we can use relaxation protocols or simply incompatible behaviours trained under positive emotional state). It is always important to remind that behaviour modification or therapy is changing the emotional state of the animal. When treating an animal with a behavioural problem, we are treating emotions!

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OPTIMIZING CAT TOILETS: DETAILS THAT MAKE THE DIFFERENCE !

Saturday 14 September | 14:30 - 16:15 | Amphitheater N. Skalkotas - Room A

***Gonçalo da Graça* Pereira**

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People can experience a reduction in stress by having cats as part of their social structure and cats can benefit due to the plentiful food, shelter and social interactions involved[1]. Both people and animals can benefit from a social relationship between species[2,3,4,5], but is the actual human lifestyle compromising the cat's welfare and quality of life? The major role of the veterinarians is to assure the well-being of animals "relieving suffering, whether it is related to physical or emotional pain"[6], as stated by Beaver and colleagues (2004). "Does it matter to the animal?" is the first question that should be asked when assessing any animal's quality of life. In 2007, a panel of experts proposed that a first step towards assessing a species quality of life and welfare would be the establishment of an ethogram and definition of the behaviours consistent with optimal quality of life for that individual species[7]. With this in mind, a complete understanding of feline behaviour is important when evaluating the cat's wellbeing. Correct interpretation of behaviour will allow seeing changes in behaviour that can be good indicators of fear, frustration, or pain[8]. Some behaviours may be so strongly motivated as to constitute a "need". Odendaal (1994) defined needs in terms of their effect on quality of life[9]. If a behavioural need arises, then it is important that the environment provided allows for that need to be met. Are this cat's behavioural needs being ensured currently in the majority of households?

Pet cats are now living in a restricted environment inside our houses with partial or complete deprivation of access to the outdoor environment. This outdoor environment is itself a coveted resource that, when limited, can lead to physical and behavioural disturbances. When monotonous, unchanging and unchallenging environments provide insufficient mental stimulation, animals show signs of boredom, often manifesting as abnormal behaviour patterns[10]. The absence of activity and environmental management are major causes of stress. Furthermore, cats living in a restricted environment may not have enough physical space to allow an acceptable flight distance thereby reducing the cat's opportunity to retreat. This situation is exacerbated by an increased density of cats living in the same home. Group housing of cats is seen in both shelter situations and in personal homes. Usually these cats are not related, are neutered and cannot migrate[11]. Wolfle (2000) suggested that for some social species (such as some rodents, dogs and non-human primates) companionship is often considered the most important need to achieve well-being[12]. But, in its wild nature, cats are solitary hunters[13]. In general, guardians promote the creation of social relations incompatible with the behavioural nature and needs of these animals, not ensuring, in most of the cases, conditions to address many of their basic instincts[14]. Cats organize their territory in a way that allows them to hunt, feed, rest and eliminate far from other cats[15]. The existence of protected isolation and elimination areas is crucial[13]. The space reduction affects each individual in a different way, according to their respective distance and isolation needs. The environment's balance can be disturbed by a poor distribution of required zones and resources (food, water, litter trays)[15]. The increase of interactions between cats can cause an increase in agonistic encounters and unwanted behaviours (as spraying, scratching and aggression)[16].

After identifying the major stressors that influence cat's welfare, one could think that guardians are evil. But a possible reason is totally different: caregivers simply don't know their cat's behavioural needs. Da Graça Pereira and colleagues (2014) in their study showed that caregivers had a lack of information about their cat's behavioural needs[17]. But, worse than this, another conclusion from the same study was that, when compared with veterinarians in certain categories of cat's behavioural needs, veterinarians and caregivers were at the same knowledge level[17]. So, there is a long way to change the life-style of cats, as we need to change scholar curricula and also give educative/informative training for caregivers[17].

One of the major stressors identified in cats are its toilets. And there are many details that make the difference by the cat's perspective. Some of the characteristics of a good litter tray are presented and during the lecture the author will show some signs to identify if the cat is enjoying its toilet or not. The available litter tray should have a size enough[15], in order that allow the cat to turn around inside, getting in and out without any problem. Usually is recommended to have at least one and a half the cat's size. The majority of cats prefer a thin (like sand) litter[18] and is recommended to have, at least, one litter tray per cat plus one extra or another possible rule is: "*a cleaned toilet for each cat, in enough number, giving the chance to all cats to use one, if they need it, at the same time*". This several litter trays should be dispersed by the territory and not all concentrated in the same room. Should be located in a place of easy access and quite, if possible with two diferent accesses to avoid the feeling of closure[15], and far from noise equipments as washing machines. Cats usually have prefer opened liter trays, with simple litter without any odour, but preference test can be performed, like giving the cat the option to choose what he prefer. Hygiene must be guaranteed according to the use of the litter tray, but must be the most clean as possible.

If we decrease the surrounding stress, improving quality of life and animal welfare[19] throught the implementation of therapeutic strategies that decrease the noradrenergic activation[20], surely we will decrease the risk and manifestation of pathologies (including behaviour and many others)[19].

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TRAVEL-RELATED PROBLEMS IN CATS: NEW INSIGHTS

Saturday 14 September | 14:30 - 16:15 | Amphitheater N. Skalkotas - Room A

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Travel-related issues in cats encompass a variety of behaviours that begin with the preparation for departure, such as avoiding the carrier and displaying aggressive behaviour towards the person attempting to place them inside. These issues persist during the journey itself, including vocalization, elimination, reactivity, vomiting, and excessive salivation while being transported. Furthermore, some cats may continue to experience these issues even after returning home, leading them to hide for hours. These behaviours can be associated with a history of negative experiences for the cat, e.g., veterinary visits or nausea during car travel, but this is not always the case.

In certain instances, the presenting complaint by the owners might be the cat's complaints during travel, which can manifest through excessive vocalization, reactivity, and/or defecation/urination in the carrier, but this can be just the pick of the iceberg. The cat can show signs of distress during 1) the preparation for leaving the house, 2) during the transportation and 3) after returning home, e.g. 60% of the cats that return from a veterinary visit exhibited ongoing distress upon return home (1)

Specifically,

4) Pre-travel
   i. Avoiding the carrier
   ii. Displaying aggressive behaviour towards the person attempting to place them inside

2) During travel
   i. Vocalization
   ii. Elimination
   iii. Reactivity – pacing and restlessness
   iv. Vomiting
   v. Excessive salivation

5) Post- travel
   i. Hiding for hours
   ii. Aggressive behaviour towards other cats in the house
   iii. Decreased appetite

Usually, a cat is introduced to its carrier on the first day of its adoption, on its way home, or on its first veterinary visit. If the cat associates its carrier, the journey with the car and other related stimuli with an emotional negative experience, e.g., anxiety or nausea in the car, or a physically painful, e.g., the first immunizations, the carrier or the car can become conditioned aversive stimuli.

In the case of certain cats, the recurrence of adverse experiences such as car rides can amplify their behavioural responses rather than diminish them, as seen in the process of habituation of the previous paragraph. These cats are getting sensitized in the stimuli of travelling and they learn that the related stimuli are negative and that is possibly the reason, why the manifestations of emotionally related and motion sickness-related behaviours in cats can occur even when the vehicle is stationary as well.

In the diagnostic process of travel-related problems, it is of utmost importance to differentiate between behavioural responses arising from distress associated with travel and those stemming from the consequences of travelling, such as a veterinary clinic visit or a history of punitive actions by the owner during the cat's confinement in a carrier. Consequently, it becomes imperative to thoroughly explore the progression of concerning behaviours and their evolution over time, influenced by both owner interventions and the cat's individual experiences.

Behaviours associated with distress during travel tend to exhibit persistence and stability as they become entrenched over time. In contrast, behaviours linked to the specific travel destination can exhibit changes in response to the cat's realization of its destination, e.g., when suitcases are positioned near the exit door.

Medical conditions which may present:

- Painful conditions that might cause a cat to become aggressive or to hesitate when it comes to moving and entering its carrier should be considered in the diagnostic process.
- Excessive vocalization can stem from various factors, including pain, endocrine disorders (e.g., hyperthyroidism), or intact females during oestrous, which might not be readily identified by an inexperienced owner.

Management of the problem

1) Measures aimed at stabilizing the problem

Stabilization involves the immediate management of the problem and has two important elements – preventing the problem from getting worse and safeguarding others. Containment of the problem should not be confused with a long-term solution and this needs to be communicated to the client. The general practitioner should be able to offer relevant advice until measures can be taken to resolve the problem in the longer term either locally or through referral.

2) Measures aimed at preventing behavioural problems from getting worse
   - If feasible, as a short-term measure, the cat should avoid travelling and should not be compelled to enter the carrier.
   - When travel is necessary, such as for a vet visit or due to the owner's relocation, the use of short-term anxiolytic medication 2-3 hours before travelling should be taken into consideration.
   - When travel is necessary, additional steps should be followed (adapted from Argüelles et al 2021) (2) :
     - Clean the carrier with enzymatic agents
     - Spray the carrier with pheromonal products based on F3 at least 30 minutes before placing the cat inside.
     - Stop any form of punishment, e.g., chasing or scruffing the cat, that takes place when the owner is putting the cat into the carrier, as it is likely to intensify the cat's stress.

- Spray the car with pheromonal products based on F3 at least 30 minutes before the carrier with the cat enters the car.
- Place, the carrier on the floor of the car behind the front passenger seat, and strapped in position.

Measures aimed at resolving the problem

1) Environmental changes

Changes to the physical environment that may be useful include:

- The provision of interactive enrichments to occupy the cat and reduce frustration in case that frustration plays a role in the cat's behaviour.
- Introducing a new carrier, such as one with a different colour or type, can be beneficial in situations where the problem may be habitual, for instance, when a cat tends to hide upon seeing the carrier.
- Breeds with brachycephalic features, such as Persians, Himalayans, and Exotic Shorthairs, often require larger carriers with enhanced ventilation, especially when embarking on extended journeys or flights.
- Transform the cat's carrier into a "safe area" for the cat: Put the carrier in a quiet corner of the house, place a soft towel/blanket inside, and remove the door of the carrier as a first step.
- The use of pheromonal products based on F3, to help create a 'safe area' in the cat's carrier.
- Spray the car with pheromonal products based on F3 at least 30 minutes before the carrier with the cat enters the car.
- Cats are sensitive to extreme temperatures. During travel, it's crucial to provide appropriate climate control in the vehicle or carrier to ensure comfort and safety.
- Management of the environment upon arrival. Place a plug-in of the synthetic pheromone analogue of the F3 fraction of the feline facial pheromone in the quiet room. Prepare the quiet room with food, water, a litter tray and familiar items for the cat and provide hiding place and leave the cat there for some hours or days if needed.

2) Behaviour modification exercises

- Teach the cat to remain calm inside its carrier through desensitization and counterconditioning.
- For car journeys, a similar approach of desensitization and counterconditioning is advised.
- Frustration tolerance exercises may assist in decreasing the cat's overall susceptibility to travelling.

3) Pharmaceutical Interventions:

The use of the majority of short-acting medications for travel-related problems in cats is off-label. The only authorized medication for this condition is pregabalin. Based on the author's experience, the timing of administration is crucial. It is important to administer all anxiolytic medications at least 2 hours before the cat encounters its first stressor. It's important to mention as well, that acepromazine, while not classified as an anxiolytic, can also induce disinhibition and repelling behaviours.

- Maropitant: In the case of cats exhibiting symptoms of motion sickness, maropitant can be prescribed 4 hours before the journey. Additionally, it is

advisable to fast the cat for 2–3 hours before the trip. Maropitant can be combined with anxiolytics.

- Analgesia: In the context of feline travel-related issues, particularly in senior cats, it is imperative to consistently contemplate the potential sources of acute or chronic pain. To mitigate the exacerbation of protective emotions during travel, the prescription of analgesics before travelling may be recommended to alleviate pain.

When to refer

- If progress ceases, the case should be fully re-evaluated medically prior to referral.
- If initial progress is disappointing, then more specialist help may be required.

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DIAGNOSTIC APPROACH IN DOGS WITH OTITIS

Saturday 14 September | 08:30 - 10:30 | MC 3 - Room B

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Otitis externa (OE) is defined as an inflammation of the external ear canal (vertical and/or horizontal ear canal) down to the tympanic membrane, while otitis media (OM), is the inflammation of middle ear cavity. Canine otitis is a syndrome, not a diagnosis, and it is the result of a primary disease, combined in most cases, with the presence of secondary infections and predisposing and/or perpetuating factors (Table 1). Otitis externa may be unilateral or bilateral, acute, chronic or recurrent.

Primary causes of OE are the main causative factors of otitis that may be combined with the presence of predisposing factors. Otodectic mange, hypersensitivities (food allergy, atopic dermatitis, contact hypersensitivity), foreign bodies, and less commonly ear neoplasia, hypothyroidism, keratinization disorders, or autoimmune skin diseases, are the main primary causes of OE. Primary otomycosis due to *Aspergillus* spp., *Sporothrix* spp., and dermatophytosis has been rarely reported. Atopic dermatitis is the most common primary cause leading to OE in dogs.

Predisposing factors increase the risk of OE, but their mere presence will not initiate ear canal inflammation, unless combined with a primary cause. Pendulous ears, excessive hair in the ear canals, stenotic ears and increased humidity, are considered the major predisposingcauses of OE in dogs.

Secondary causes are all the bacterial and/or yeast overgrowth and/or infection. In acute OE the most common are Gram-positive bacteria, usually *S. pseudintermedius* and *Malassezia* spp. yeasts, while Gram-negative microorganisms are usually found in chronic otitis. Secondary infections aggravate the existent inflammation and maintain the otitis, contributing to the development of progressive pathologic changes of ear canals.

Perpetuating factors are the result of progressive changes of ear structures and they occur in chronic otitis. Acute inflammation and edema are gradually followed, unless treated, by glandular hyperplasia, fibrosis, stenosis and occlusion of the ear canal. Chronic otitis may lead to calcification or even ossification of ear canal cartilage, OM and aural cholesteatoma. The presence of these changes favors proliferation of microorganisms and induces a vicious cycle that perpetuated otitis.

Otitis media is most commonly the result of chronic purulent OE. Primary secretory otitis media (PSOM) or otitis media with effusion (OME) is a form of a primary OM, not accompanied by OE, usually seen in Cavalier King Charles spaniels and brachycephalic dogsand is probably a result of scull anatomy and obstruction or malfunction of the auditory tube and of increased production of mucus in the middle ear.

Diagnostic investigation of otitis begins with a complete history. Important information including age of onset, chronicity, seasonality, presence of other cutaneous or systemic signs,previous treatments and response should be obtained. A clinical and dermatological examination should follow, since the external ear canal is an extension of the skin and OE is commonly a manifestation of a more generalized skin disease. Otoscopy is mandatory in all cases, as it offers vital information about the diameter of ear canals, the depth and extension of inflammation, the presence and the nature of the exudate, presence of foreign bodies or masses, and the integrity and appearance of tympanic membrane (TM). In cases where an adequate otoscopic evaluation is not possible due to chronic inflammation, it should be repeated after treatment with glucocorticosteroids, usually

prednisolone at 1-2mg/kg/24h, for 7-14 days. In cases where the amount of exudate does not allow adequate examination of TM, the dog should be examined under general anesthesia, in order to flush the exudate. Tracheal incubation is needed in all cases where OM is suspected, when TM is ruptured, and when myringotomy is planned, due to myringitis or TM bulging. For the latter procedure, after the flushing of external ear canal with warm sterile saline, very dilute chlorhexidine solution (0.05%) or Tris-EDTA, myringotomy is performed using a sterile catheter in the caudoventral quadrant of the TM, below the attachment of the manubrium of malleus. Ear canal parasitology and cytology would follow otoscopy in every case of otitis. Microbial culture is mandatory in all cases of OM and in rare cases of OE, especially when rods are identified in cytology and systemic administration of antimicrobials is considered. Ear samples for cytology and microbial culture should be collected from the deeper part of the horizontal ear canal after otoscopy for OE, for which in most cases no sedation is needed, while in cases of OM, samples are collected from the tympanic bulla (TB) through the otoscopic cone, with the dog under general anesthesia as previously described. After sampling from the tympanic bulla, a thorough flushing of the bulla is performed. Diagnostic imaging, usually computed tomography or magnetic resonance imaging, may be used to evaluate the ear canals and TBs in non-responding cases of chronic OE, in dogs suspect of OM, and in cases with neurological signs like peripheral vestibular syndrome or facial nerve paralysis, indicating inner and middle ear disease, respectively. Additional diagnostic tests including hematology, biochemistry, hormonal assays or biopsies for histopathology, may be needed in selected cases, depending on the suspected primary factors.

Table 1. Otitis pathogenesis

Otitis pathogenesis			
Predisposing factors	**Primary factors**	**Secondary factors**	**Perpetuating factors**
Conformation	Ecto-parasites	Bacteria	Progressive pathologic changes • epidermis • glands • dermis • ear canal • auricular cartilage • tympanic membrane
Excessive moisture	Foreign bodies	Yeast	
Trauma	Hypersensitivities		
Obstruction	Keratinization disorders Glandular disorders		
	Autoimmune diseases		
	Fungi		
	Neoplasms		Otitis media
	Other		Iatrogenic

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THERAPEUTIC STRATEGIES IN DOGS WITH OTITIS

Saturday 14 September | 08:30 - 10:30 | MC 3 - Room B

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Canine otitis is a multifactorial syndrome with many, and frequently concomitant, predisposing, primary, secondary, and perpetuating causes. For this reason, therapeutic management should be tailored to each patient and should be modified over time as the causes contributing to ear inflammation change during treatment. Unfortunately, there is a shortage of properly designed controlled trials to help clinicians to take evidence-based therapeutic decisions, and treatment guidelines are largely empirical. However, most veterinary dermatologists would agree that the main factors that should be considered when designing and, later-on, when modifying the therapeutic approach are: a) the presence of otitis externa only, of otitis externa and otitis media (and sometimes, also otitis interna) or of only otitis media; b) the extent and severity of the irreversible pathologic changes of the external ear canal (fibrosis) and its cartilages (calcification); c) the primary cause and whether it is treatable and fully reversible, necessitates long-term management or remains unknown.

The first parameter to consider in a dog with otitis externa is the presence or absence of otitis media/interna. Sometimes the answer to this question is easy from the first examination: dogs with acute otitis, without large amount of exudate filling the external ear canal, without edema obstructing the ear canal, without neurologic signs of otitis media/interna, and with clearly visible tympanic membranes of normal appearance are patients with otitis externa only. However, if one of the above conditions is not met, the definitive confirmation or exclusion of otitis media will be made after the administration of glucocorticoids (e.g., prednisolone at a daily dose of 1-2 mg/kg, orally, for 1-2 weeks), followed by deep ear flushing under general anesthesia, and, if necessary, by myringotomy and diagnostic flushing of middle ear cavity.

In dogs with **otitis externa** only, extensive pathologic changes of the ear canal and it's cartilages are typically absent, and medical management is attempted, with the aim to keep the ear canal clean and dry (at home ear flushing with a commercial ear cleansing/drying solution, and, if necessary, repeated deep ear flushing under general anesthesia in the Clinic), to treat inflammation (topical and, in severe cases, systemic glucocorticoids), to treat the secondary causes (bacteria and yeasts) that are present in the ear canal, and, to treat the primary cause(s). In cases of otitis externa, antibacterial treatment is usually topical and mainly guided by the results of cytology: aminoglycosides, fluoroquinolones, polymyxin-B, and silver sulfadiazine are typically effective against both Gram-positive cocci and Gram-negative rods; chloramphenicol, florfenicol and fusidic acid are effective against only cocci; and ticarcillin-clavulanic acid and tris-EDTA are used to treat infection by rods and especially by *Pseudomonas* spp. The results of *in vitro* antimicrobial susceptibility testing can even be misleading in these cases because the extremely high local concentrations of topically applied antibacterials may overcome the *in vitro* resistance of the organisms. However, in cases with severe purulent otitis that does not respond to topical treatment and there is a need for adjunctive administration of

systemic antimicrobials, the selection of the latter should be based on the results of *in vitro* susceptibility test. Yeasts, mainly *Malassezia* spp., are usually sensitive to all antifungals that are included in the commercial ear preparations, and administration of systemic antifungals is rarely, if ever, indicated. Treatment of the primary cause is necessary to achieve cure and avoid future relapses. Etiologic treatment may be straightforward and definitive (e.g., removal of foreign bodies, treatment of ectoparasites like *Otodectes cynotis*), simple but life-long (e.g., treatment of underlying hypothyroidism in a dog with chronic ceruminous otitis externa) or life-long and complicated (e.g., treatment of atopic dermatitis). The latter will be treated systemically (glucocorticoids, ciclosporin, oclacitinib, lokivetmab, and, perhaps, allergen immunotherapy) but in some cases ear canal inflammation persists despite the overall good control of the disease. In such cases, reactive (e.g., daily application until complete resolution of otitis) followed by proactive (e.g., intermittent application, such as 2 days per week, to avoid relapses) topical glucocorticoid (e.g., hydrocortisone aceponate) treatment is indicated.

In dogs with **otitis externa and otitis media/interna** a completely different therapeutic strategy is typically followed. An initial decision must be made if medical or surgical approach (total ear canal ablation-bulla osteotomy) will be selected. Dogs with end stage otitis and stenotic ear canals that do not open after a few weeks of prednisolone administration, with extensive calcification of external ear canal cartilages, with osteolytic lesions on computed tomography (or magnetic resonance imaging) indicative of severe osteomyelitis of bulla tympanica, or when long-term systemic glucocorticoids are contraindicated due to comorbidities, may be better served by surgery, especially if otitis is unilateral. In the remaining cases, medical treatment is initially attempted and is based on systemic administration of glucocorticoids, that are continued after the initial deep ear flushing and are discontinued only after complete control of middle ear inflammation and restoration of tympanic membrane; a glucocorticoid treatment duration of at least 2-3 months is to be expected but there are patients that need longer periods. At the same time, bacterial infection of middle ear cavity will be treated with systemic antimicrobials selected based on the results of *in vitro* susceptibility test of middle ear exudate; the latter is collected after the flushing of the external ear canal. Also, the already outlined treatment of otitis externa (ear cleansers, topical glucocorticoids, antibacterials and/or antifungals), should be implemented but without using ototoxic preparations, and whenever there is new accumulation of exudate in the ear, the deep flushing procedure under general anesthesia should be repeated. In these cases, if the primary cause of otitis is atopic dermatitis, the diagnostic investigation and management (other than systemic glucocorticoid administration) can start only after definitive treatment of otitis media.

In dogs with only **otitis media**, usually due to the so-called otitis media with effusion (OME) or primary secretory otitis media (PSOM) which is more common in Cavalier King Charles spaniels, myringotomy is performed to flush the middle ear and remove the accumulated mucus, and is followed by administration of oral glucocorticoids for a short period, and perhaps of mucolytics, like N-acetylcysteine or dembrexine, on a long-term basis, because they may delay relapses. Unfortunately, the latter are common in many dogs, and they necessitate either to repeat the above (myringotomy, glucocorticoids) or to perform permanent tympanostomy.

CANINE NON-INFLAMMATORY ALOPECIA: THE CLINICIAN'S APPROACH

Saturday 14 September | 11:00 - 13:00 | MC 3 - Room B

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In the dog complete or partial hair loss without any other cutaneous lesions is the clinical manifestation of non-inflammatory alopecia. Non-inflammatory alopecia is basically classified into congenital and acquired alopecia and etiologically can be or associated with a) hair cycle disturbance/arrest, actually a deregulation of hair follicles, b) a decreased formation or cytodifferentiation of hair follicles, also described as dysplastic follicular disorders and c) a true follicular atrophy. Non inflammatory alopecia is usually symmetric and distribution plus its extent, whether it is regionalized or generalized, varies depending on its cause, but generally head and legs present with normal hair coat in diseases with hair cycle arrest. This is not true for both effluviums and for dysplastic alopecias. Also, it should be mentioned that in chronic patients with Cushing's disease, at the final stage, hair loss may be evident all over the body including legs and head. Localized non inflammatory alopecia is presented by traction alopecia, post-rabies vaccination alopecia in small breed dogs, spot-on medication site reaction and scars (f.e. burns, trauma).
The major causes for an alteration of hair follicle cycle are endocrinopathies (hypothyroidism, hyperadrenocorticism, hyperestrogenism). Hyperadrenocorticism and hypothyroidism are the most frequent and alopecia is associated with other non-dermatological symptoms that can help the clinician during diagnostic approach. However, even if suspicion is high hormonal testing that is specific for each endocrinopathy is required to confirm diagnosis and to proceed with proper therapy. Other conditions that can cause hair cycle arrest are alopecia X, recurrent flank alopecia, telogen effluvium, anagen effluvium, post clipping alopecia and pattern baldness. Post clipping alopecia is the only one that may not be symmetrical.
Follicular dysplasia/aplasia is a group of genetic conditions that affect the formation of the follicle and/or the hair shaft, that appears at birth or at young age. Dysplasia is an alteration of the shape and structure of hair shaft resulting in hair growth disturbance and fragility. Diseases included in this group can be coat color-linked (f.e. color dilution alopecia, black hair follicular dysplasia and follicular dysplasia of red and black Doberman pincher, follicular lipidosis of Rottweiler) or non-color linked (f.e. follicular dysplasia of specific canine breeds). In this group of diseases certain breeds are reported to have a predisposition. Dogs with X-linked ectodermal dysplasia, a genetic disorder due to a mutation, present follicular aplasia (absence of the hair follicle unit) in areas of complete alopecia and dental dysplasia.
True follicular atrophy can be caused by ischemia due to cutaneous vasculopathies, dermatomyositis, traction alopecia, post-traumatic/scarring alopecia and post-injection or vaccination (mainly rabies vaccine) alopecia.
Suspicion over non inflammatory alopecia may raise by the presentation of hair coat (f.e. broken hairs, thin hairs, easy epilation, hair dilution) and distribution/pattern of alopecia together with the presence or absence of other findings and skin lesions during examination. Personal patient information is also important, in specific breed predisposition, sexual status and age, particularly age at the time of onset of skin lesions. Other historical data and physical findings will increase further the suspicion. A rank-ordered list of

differential diagnoses then is generated, and to reach final diagnosis the most appropriate tests (common skin tests and skin biopsy, dermatoscopy, complete blood count, serum biochemistry profile, urine analysis, hormonal function evaluation, imaging tests) will be ordered based on this reasoning list.

Below important points, reached by the history, the clinical and dermatological examination, for the diagnostic approach of canine non inflammatory alopecia.

Breed: Hyperadrenocorticism affects commonly Poodle, Maltese, Boxer, Boston terrier etc. Alopecia X affects primarily Nordic breeds, such as Pomeranians, Chows-chows, Samoyed but also some other breeds like Poodle. Hypothyroidism affects mostly large or giant breeds, such as Golden retriever, Dobermann, English pointer, English and Irish setter, Great Dane etc and other breeds such as Cocker Spaniel, Dachshund, Pomeranians. Predisposition has been reported for cyclic flank alopecia (f.e. English and French bulldog, Boxer, Schnauzer, Airedale terrier), pattern baldness (f.e. Dachshund, chihuahua, whippet, greyhound), breed-specific alopecias (f.e. Irish water spaniel, Portuguese water dog, curly coated retriever, Dobermann), color diluted alopecia (f.e. Dobermann pinscher, Yorkshire terrier, Dachshund), black hair follicular dysplasia (f.e. Large Münsterlander, Papillon, bearded collie, Yorkshire) and follicular lipidosis (f.e. Rottweiler). Mexican hairless, Peruvian dog and Chinese crested dog are common canine hairless breeds.

Onset age: History data, whether the hair coat was normal at birth or not, is important for congenital alopecia. Additionally in congenital alopecias hair loss may occur later during the first weeks of age, 1-3month old puppies, or later between 4months to 1year old. Breed specific follicular dysplasias occur commonly between 4-6months and 4years of age. Pattern baldness occurs typically between 6months to 2years of age. Flank alopecia can be seen at any age, and it has been reported in young dogs of 8months up to 11year old dogs.

Sex: Sexual status is important for hyperestrogenism cases due to testicular or ovarian neoplasms. There is no actual predisposition between male and female for the other non-hormonal alopecias, except for X-linked ectodermal dysplasia that affects mainly male dogs.

Seasonality is commonly witnessed with cyclic flank alopecia.

Spontaneous remission is commonly seen in anagen and telogen defluxion and in post clipping alopecia. Also, cyclic flank alopecia may not occur for one or more years and in some cases, it has been reported to have a permanent remission. In alopecia X hair regrowth may occur at sites of trauma to the skin, f.e at sites where biopsy was performed.

General signs and pruritus: PU/PD, polyphagia, muscle atrophy and sexual cycle disturbances are seen in Cushing's disease. Hypothyroidism is frequently associated with heat seeking/cold intolerance, weight gain, intolerance to exercise, lethargy/mental dullness, reproductive disorders, neuropathies etc. Pruritus is usually present in cases of secondary infections, f.e. Malassezia dermatitis and bacterial dermatitis. Calcinosis cutis can be pruritic, too.

Cutaneous signs: distribution and evolution of lesional spreading (for skin diseases with hair cycle arrest alopecia starts from friction areas and spreads all over the body, in Cushing's disease alopecia worsens over time), skin atrophy (a typical clinical sign of Cushing's disease, may also be seen in ischemic dermatitides) and skin pigmentation (commonly seen in alopecic areas with alopecia X, hypothyroidism and cyclic flank alopecia, but also a linear preputial erythema/hyperpigmentation is seen in male hyperestrogenism), hair coat color on lesional site (the presence of alopecia exclusively on black or red hair color will set the suspicion of color linked hair dysplasia) and quality changes (are seen in all hair cycling alopecias and in hair coat dysplasias). Milia, striae and calcinosis cutis and thin plus anelastic skin is seen in Cushing's disease. Comedones seen due to marked infundibular hyperkeratosis but are of little diagnostic value as they can be seen in all alopecias associated with hair cycle arrest. Lesions such as milia, striae and calcinocis cutis for Cushing's disease and tragic face due to myxedema for hypothyroidism have a

pathognomonic significance from a diagnostic point of view. But alopecia on the bridge of the nose and rat tail is not.

Attention in the list of differential diagnosis should be given to some inflammatory pilosebaceous diseases (f.e. alopecia areata and sebaceous adenitis) with minimal to no clinical signs of inflammation, especially during the terminal stage of their evolution, and to leishmaniasis that may look like alopecic diseases, and they can mislead the clinician during the diagnostic procedure.

In conclusion, in many canine patients with non-inflammatory alopecia diagnosis can be suspected through a detailed history and a thorough clinical and dermatological examination. However, diagnostic approach can be a diagnostic puzzle since many important points should be collected and all together with the results from skin tests, laboratory examinations and imaging tests will lead to final diagnosis.

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Welle Monika M., Canine noninflammatory alopecia: An approach to its classification and a diagnostic aid Veterinary Pathology 2023, Vol. 60(6) 748–769

CANINE NON-INFLAMMATORY ALOPECIA: THE PATHOLOGIST'S APPROACH

Saturday 14 September | 11:00 - 13:00 | MC 3 - Room B

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Hypotrichosis and alopecia refer to the partial or complete loss of hair in areas typically covered by hair. The mechanisms underlying alopecia include traumatic self-induced alopecia, alopecia due to folliculitis, hair follicle atrophy, hair cycle arrest, and hair follicle aplasia, dysplasia, or dystrophy. In some cases, these conditions may occur concurrently. Diagnosing alopecia can be challenging, prompting veterinarians to often rely on biopsies as part of the diagnostic process. A definitive diagnosis requires the integration of a detailed clinical history, a thorough physical examination (including blood tests), appropriate selection of biopsy sites, and detailed histologic findings (1, 2). This lecture will present evidence obtained from histopathological examinations that aid in differentiating pruritic and/or inflammatory alopecias from non-inflammatory ones.

Non-inflammatory alopecias include non-hormonal and hormonal types. In both categories, hair loss typically manifests symmetrically, affecting the trunk, neck, tail, ear flaps, and upper limbs. Non-inflammatory, non-hormonal alopecias in adult dogs are as prevalent in clinical practice as the three most common types of hormonal alopecias: hypothyroid, hyperadrenocortical, and hyperestrogenic alopecias. Non-inflammatory, non-hormonal alopecias generally do not cause itching or other symptoms unless complicated by secondary microbial infections (3). In contrast, hormonal alopecias are frequently accompanied by systemic clinical signs and laboratory abnormalities (e.g., seizures due to hyperlipidemia in hypothyroidism, hemorrhagic diathesis from bone marrow toxicity in hyperestrogenism, or diabetes mellitus in Cushing's syndrome) or concurrent skin lesions (e.g., dystrophic calcification, facial myxedema, or multifocal deep pyoderma in Cushing's syndrome and hypothyroidism) (4). These systemic symptoms and associated skin lesions often exacerbate the animal's overall condition, beyond the alopecia itself.

Histological features commonly observed in primary alopecic disorders include a predominance of telogen follicles, hairless telogen follicles, follicular atrophy, follicular dysplasia, follicles with excessive trichilemmal keratinization, and dystrophic follicles. These features are indicative of hair cycle disorders associated with arrest or impaired progression of the hair cycle (5). In cases of hormonal alopecias, a stereotypical histopathological pattern is often observed, necessitating differentiation between various hormonal dermatoses. However, histopathological findings from skin biopsies are often non-specific, making it difficult to distinguish between different hair cycle disorders. Potential diagnoses include hormonally induced dermatoses such as alopecia X, hyperadrenocorticism, hypothyroidism, hyperestrogenism, and cyclical flank alopecia, as well as primary alopecic disorders of unknown etiology (in animals without endocrinological abnormalities but exhibiting bilateral symmetric alopecia and histologic changes suggestive of a hair cycle disorder) (6).

Acquired non-hormonal alopecia in dogs - older than six months - is increasingly attributed to follicular dysplasias, which are associated with structural damage to the sebaceous follicular unit. This damage may or may not involve interruption of the hair follicle growth cycle, potentially leading to atrophy (structural/cyclical or mixed dysplasia). In cyclical dysplasia, the hair follicle growth cycle may be abruptly or gradually halted, with normal hair regrowth occurring in subsequent periods (2). Examples include cyclical flank alopecia, which may become permanent in certain breeds after one or more episodes, as well as hormonal dermatoses, alopecia X, telogen effluvium, post-chemotherapy (doxorubicin-induced) alopecia, and post clipping alopecia. In nearly all of these cases, most or all hair follicles are in the telogen phase, with many being empty (hairless shafts) (3, 6). Additionally, there is often a combination of atrophic or normal catagenic hair follicles, excessive keratinization of the hair canals, and diffuse orthokeratotic hyperkeratosis of the epidermis, frequently complicated by bacterial infections or seborrhea (4, 6).

In structural follicular dysplasias, the clinical presentation of alopecia is influenced not only by the dog's age at onset and the distribution of hair loss but also by the breed and hair type. In these cases, structural changes, including melanization of sebaceous glands and dysplastic hair follicles, weaken the hair shafts, causing them to deform and break easily. This explains the initial hair loss in areas subjected to rough grooming (e.g., brushing, combing, or the use of irritating shampoos) and frequent or continuous friction (e.g., from collars). As these structural changes are initially mild, hair may continue to grow, sometimes leading to spontaneous recovery. However, the newly grown hairs are often thinner and more fragile, resulting in recurrent hypotrichosis in areas prone to repeated friction. Over time, with recurring episodes, these structural changes progressively worsen (3, 4, 6).

This lecture will explore the histopathological findings in skin biopsies that help differentiate inflammatory from non-inflammatory alopecias and discuss the diagnostic value of histopathological examination in distinguishing among non-inflammatory alopecias.

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THE EMERGENCY PATIENT – EXAMINATION OF BLOOD SMEARS. COMMON ERYTHROCYTE AND LEUKOCYTE MORPHOLOGICAL ABNORMALITIES AND THEIR SIGNIFICANCE

Saturday 14 September | 14:30 - 16:15 | MC 3 - Room B

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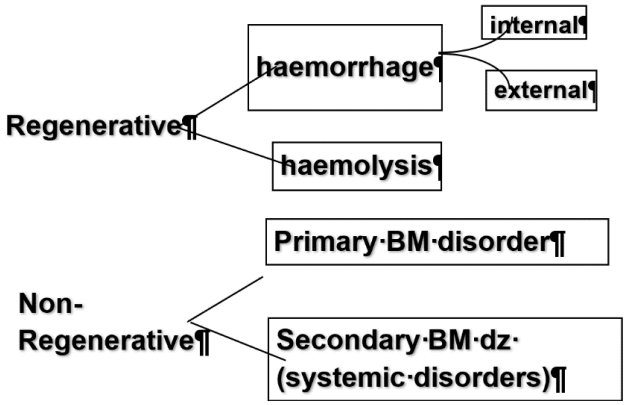
Accurate laboratory testing is vital when a patient is presented in the clinic as an emergency. External clinical pathology services are not available immediately and/or after hours. In-clinic haematology analysers are essential but do not provide complete haematological assessment. For this reason, examination of a blood smear should always be performed. The blood smear findings should be evaluated in conjunction with the results and graphics generated by the automated haematology analyser. The aim of the blood smear examination is to answer the following clinically relevant questions.

Is the anaemia regenerative? important question to answer for decision making especially when the Haematology analyser does not provide a reticulocyte count.

DECISION·MAKING¶



Blood smear examination: it takes 3-4 days for regeneration to become evident. Findings indicative of regeneration: *Polychromasia/reticulocytosis*, *anisocytosis*, ± *presence of nucleated red blood cells (nRBCs)*. Polychromatophils and reticulocytes are the same immature cells. *Polychromatophils* are larger than mature red cells and stain blue-red or grey with the haematology stains. The *nRBCs* are rarely seen in the peripheral blood of clinically healthy animals although very low numbers may be seen in dogs, particularly Schnauzers and Dachshunds. The nRBCs represent cells in earlier stages of erythrocyte development (less mature) than polychromatophils. They are normally present at <1 per 100 RBCs, have round to oval nucleus with very condensed chromatin and plenty of blue to reddish-blue cytoplasm. It is important to differentiate nRBCs in early stages of development from small lymphocytes; the nucleus in the nRBCs is perfectly round, their chromatin more coarsely granular and clumped and their cytoplasm darker and typically more extensive than in the small lymphocytes.

Is the anaemia an immune-mediated *haemolytic anaemia (IMHA)? Blood smear examination: detection of erythrocyte agglutination, spherocytes* and *ghost cells* are the findings which are indicative of immune-mediated erythrocyte damage and support a

diagnosis of IMHA. IMHA is an important cause of morbidity and mortality in dogs which also occurs in cats, although less frequently.
Agglutination appears as an unorganised 3-dimensional clustering of erythrocytes (resemble bunch of grapes) which is formed due to a strong cross-linking of antibodies on the surface of erythrocytes. *Spherocytes* are erythrocytes which appear perfectly round, commonly lack central pallor, more intensely staining (darker) and have smaller diameters than normal erythrocytes. It has been shown that the presence of ≥5 spherocytes/x100 oil field is very specific and should be considered supportive of a diagnosis of IMHA; 3-4 spherocytes/x100 oil field also may be consistent with IMHA provided no other cause of non-immune-mediated spherocytosis (e.g. snake envenomation, bee sting, zinc toxicity, histiocytic sarcoma) is identified. Presence of spherocytes in low numbers (< 3 spherocytes/x100 oil field) is usually a nonspecific finding. Spherocytes cannot be identified reliably in cats because the morphologically normal feline erythrocytes have no central pallor; for this reason, some normal erythrocytes which may appear more intensely stained and of smaller diameter can be misidentified as spherocytes. *Ghost cells* appear as remnant cell membranes (empty cells) which are created after intravascular immune-mediated erythrocyte lysis.

Is there evidence of active inflammation and/or immune-stimulation? Blood smear examination: The presence of a *left shift (immature neutrophils*) and *toxic neutrophils* are the most common findings indicative of active inflammation, while immune stimulation can be confirmed when *reactive lymphocytes* are seen in the circulation.
The *toxic neutrophils* exhibit morphological abnormalities which develop in the cells of the bone marrow, they represent maturation asynchrony between the nucleus and cytoplasm and occur due to accelerated neutropoiesis (shortened maturation time) driven by cytokines in response to intense inflammation. Toxic neutrophils can be mature or immature neutrophils, and they may be observed even with normal neutrophil counts and exhibit one or more of the following morphological features: ring-shape nucleus, cytoplasmic basophilia (due to increased amount of ribosomal RNA), cytoplasmic foaminess (due to prominent lysosomes) and presence of Döhle bodies (bluish, irregular aggregates of rough endoplasmic reticulum). In cats, Döhle bodies may be present without other signs of toxicity and sometimes can be seen in a low number of neutrophils of cats that are clinically healthy. In dogs, toxic neutrophils are usually associated with pyometra, parvovirus infection, acute kidney injury, peritonitis, immune-mediated haemolytic anaemia, disseminated intravascular coagulation, pancreatitis, septicaemia, and neoplastic disorders. In cats, the prevalence of toxic neutrophils is significantly higher in patients with sepsis, shock, panleukopenia, peritonitis, pneumonia, and upper respiratory tract infections.
Reactive lymphocytes are lymphocytes (in some cases as large as a neutrophil), with increased cytoplasmic basophilia and sometimes increased amounts of cytoplasm; some cells may also exhibit a prominent perinuclear clear zone or some small clear punctate cytoplasmic vacuoles; nucleoli are not present. Very low numbers of reactive lymphocytes can be found in clinically healthy animals but when are seen in increased numbers are indicative of nonspecific antigenic stimulation.

Is a Neoplastic process present? Blood smear examination: The presence of *blasts* or *unclassified cells* can be indicative of leukaemia (bone marrow neoplasia). When these cells are seen, additional investigation by a clinical pathologist is required. Typically, *Blasts or unclassified cells* have a single round, oval, indented, or convoluted nucleus, one or more prominent or indistinct nucleoli and variable amounts of lightly to markedly basophilic cytoplasm; these cells may be lymphoid or myeloid in origin but their appearance on routinely stained blood smears can be similar and therefore diagnosing the specific type of leukaemia is very difficult or impossible without special stains and/or immunophenotyping.

Is the patient Thrombocytopenic? Automated counts generated by the haematology analysers commonly underestimate platelet numbers ("false" thrombocytopenia) due to the presence of platelet clumps in the sample and overlap of platelet size with RBC size (platelets are counted as RBCs) especially in the cat and Cavalier King Charles Spaniel dogs. Blood smear examination to estimate platelet numbers/count is therefore essential.

Estimation of platelet numbers/count- Blood smear method:

1. First check for platelet clumps-if present, the automated platelet count is falsely low.

2. Then use the x100 oil lens and count the platelets in 10 fields on the monolayer of the blood smear.

3. Calculate the average number of platelets.

4. Multiply this average number by 20 (in the cat) or 15 (in the dog) to get the total platelet number ($x10^9$/L).

Any infectious organisms present? Blood smear examination: *ERYTHROCYTES* - the most commonly seen are *Babesia* (e.g. *B. canis*, *B. gibsoni*) and *haemotropic Mycoplasma (Haemoplasma*). Rarely, canine distemper inclusions may be seen. *Babesia*: intracellular parasite; large, pear-shaped, easily seen (*B. canis*) or small, round to oval to elongate, difficult to see (*B. gibsoni*); have a colourless to light blue cytoplasm and red to magenta coloured nucleus. Multiple organisms can be present inside one erythrocyte. *Haemotropic Mycoplasmas*: epicellular organisms appear as cocci and occasionally as rings or rods stained light to dark blue; can be seen individually or in chains. Four haemoplasma species (*M. haemofelis*, "*Candidatus*" M. haemominutum", "*Candidatus*" M. turicensis", "*Candidatus*" M. haematoparvum-like") have been detected in cats and two species (*M. haemocanis*, "*Candidatus*" M. haematoparvum) in dogs. It should be noted that microscopic examination is neither a sensitive nor a specific diagnostic test for the diagnosis of haemoplasmosis. PCR assays are the preferred diagnostic method for haemoplasma infection.

LEUKOCYTES - Organisms associated with circulating leukocytes or platelets are not as commonly seen as with erythrocytes. Even so, the organisms most commonly seen and clinically most useful are those of the *Ehrlichia*, *Anaplasma* and *Hepatozoon* species. Detection of *Ehrlichia* or *Anaplasma* morulae allows immediate diagnosis of ehrlichiosis or anaplasmosis, but these organisms may not be present in high numbers even in severely ill animals. Morulae of *Ehrlichia canis* (within monocytes or lymphocytes), *Ehrlichia ewingii* or *Anaplasma phagocytophilum* (within neutrophils or eosinophils) and *Anaplasma platys* (within platelets) appear as small, magenta to blue-purple coccoid structures. It should be noted that *E. ewingii* and *A. phagocytophilum* morulae are morphologically identical while *A. platys* in some cases may be difficult to distinguish from platelet granules. Gamonts of *Hepatozoon canis* are typically seen within neutrophils or monocytes and appear as large, oval to elliptical, light blue organisms.

Further reading

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MEDICAL MANAGEMENT OF THE CANINE PRIMARY IMMUNE THROMBOCYTOPENIA

Saturday 14 September | 14:30 - 16:15 | MC 3 - Room B

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Immune thrombocytopenia (ITP) is the most commonly occurring acquired primary hemostatic disorder in dogs, and a major cause of severe thrombocytopenia in dogs. It may be a primary (non-associative) disease (pITP) or secondary (associative) to various underlying triggers, such as neoplasms, medications or infectious diseases. Immune thrombocytopenia results from a combination of humoral and cell-mediated attack on platelets in the blood and/or megakaryocytes in the bone marrow (BM), and likely inappropriately low thrombopoietin concentration, ending up in significantly shortened platelet life span and severe thrombocytopenia. Autoantibodies target various epitopes on the surface of platelets, more commonly of the glycoprotein IIb/IIIa complex. Uncommonly, ITP may occur concurrently with other hematologic immune-mediated diseases, such as immune-mediated hemolytic anemia (Evans syndrome), neutropenia or as a component of a multisystemic disease (systemic lupus erythematosus).
Canine pITP affects more commonly young adult dogs, with several breeds being overrepresented (e.g., Cocker Spaniel, Old English Sheepdog, Poodle). Clinical presentation of dogs with pITP is variable and bleeding tendency is not associated with the severity of thrombocytopenia. The typical presentation is the surface bleeding (usually when platelets drop below 30,000/μL), manifested as mucosal and cutaneous petechiae-ecchymoses, epistaxis, retinal/scleral bleeding, hyphema, melena/hematochezia, hemoptysis and hematuria. Systemic clinical signs (e.g., lethargy, fever, lymphadenomegaly, loss of body weight) or cavitary bleeding are infrequently seen in pITP. Apart from thrombocytopenia, dogs with pITP may experience anemia (hemorrhagic and/or immune-mediated) and neutrophilic leukocytosis. Bone marrow evaluation is not indicated in the initial work-up, unless the dog has unexplained cytopenias or is refractory to treatment. Positive platelet/megakaryocyte-associated antibody testing by direct assays implies an immune component in the pathogenesis of thrombocytopenia, but it is not definitely diagnostic of ITP (low to moderate positive predictive value, high negative predictive value) and therefore, routine measurement of antibodies is not recommended. None of the above examinations is specific for pITP, which remains a diagnosis of exclusion, once other identifiable causes of thrombocytopenia have been reasonably ruled out, by preforming serologic and/or molecular testing for endemic infectious diseases (e.g., canine monocytic ehrlichiosis, anaplasmosis, leishmaniosis) in conjunction with diagnostic imaging. In addition, coagulation (prothrombin time or activated partial thromboplastin time) or fibrinolysis (D-dimers) testing to differentiate patients with consumptive (disseminated intravascular coagulation) or toxic (anticoagulant rodenticide poisoning) coagulopathies from patients with primary ITP is recommended.
Severely thrombocytopenic dogs should be cage rested, carefully handled and blood sampled, and preferably orally medicated to minimize bleeding tendency. Antifibrinolytic drugs (aminocaproic acid or tranexamic acid) can be considered for life-threatening

bleeding. Glucocorticoids, including prednisolone (2 mg/kg, PO, daily), or dexamethasone (0.2-0.3 mg/kg, IV, daily), constitute the cornerstone of treatment in canine pITP. There is no evidence that dexamethasone is more effective compared to prednisolone in canine ITP. Glucocorticoids have a rapid onset of action, interfering with the macrophage removal of platelets (by downregulating Fc receptor expression), impairing the platelet-antibody binding affinity and increasing platelet production. Once a safe and stable platelet number is reached (e.g., >100,000/μl), slow tapering is initiated (20-25% reduction of the total daily dose every 3-4 weeks). Although there is currently insufficient evidence that the combination of glucocorticoids with adjunctive immunosuppressive agents is associated with a better initial outcome and less chances for relapse compared to treatment with glucocorticoids alone, many clinicians use a second immunosuppressive drug, for its steroid-sparing effect, in life-threatening bleeding (e.g., melena), when hematologic recovery is not timely achieved (i.e., within 7 days) or in case of relapse during glucocorticoid tapering. Azathioprine (2 mg/Kg, PO, SID for 2 weeks, and every other day thereafter), mycophenolate mofetil (MMf,10 mg/Kg, PO, BID), cyclosporine (5-10 mg/Kg, PO, SID-BID), or leflunomide (2-4 mg/Kg, PO, SID) have been used in conjunction with glucocorticoids or rarely as single agent treatment (MMf) in the canine pITP. There is no evidence that any adjunctive immunosuppressant is superior compared to the others. In addition, the best strategy of tapering (slow *vs* abrupt discontinuation) for these drugs has not been clarified. The long duration of immunosuppressive treatment (frequently in excess of 6 months), and the potentially serious complications that may occur (e.g., secondary infections) should be timely and thoroughly discussed with the owners.

Acute management of ITP may also be improved with the adjunctive use of vincristine (0.02 mg/kg, IV) or human intravenous immunoglobulin (hIVIG, 0.5-1 g/Kg, IV, in 6-12 hours), indicated mostly in dogs with life threatening bleeding. Vincristine presumptively increases platelet numbers by accelerating thrombopoiesis and megakaryocyte fragmentation, and by reducing platelet destruction and antibody formation-binding with platelets, while hIVIG acts by blocking the Fc receptors of phagocytic cells, impairing platelet clearance. These drugs have been shown to be equally effective in hastening thrombocyte count recovery (median time: 3-5 days), compared to prednisolone alone (median time: 7 days) and shortening duration of hospitalization. Vincristine may be preferred over hIVIG due to lower cost and ease of administration. There is no clinical or laboratory evidence that platelets released after the administration of vincristine have any functional impairment. It is also important to remember that vincristine should be used very cautiously in breeds with high frequency of ABCB1 gene mutation (e.g., collie, Australian shepherds) and hIVIG might be used instead. In addition, vincristine and cyclosporine are competitive P-glycoprotein substrates and should therefore be used cautiously if administered concurrently, even in dog breeds with no high incidence of ABCB1 gene mutation (acquired P-gp dysfunction). If cyclosporine treatment is considered, initiation should be delayed for several days after the administration of vincristine.

Romiplostim, a novel thrombopoietin receptor (TPO-R) agonist, is currently used in the treatment of refractory ITP in humans. Romiplostim binds to the extracellular domain of TPO-R of platelets and megakaryocytes, increasing platelet output. The rationale for the use of TPO-R agonists, extrapolated mainly from human ITP, is that thrombocytopenia is partially attributed to inappropriately normal TPO levels with regard to the severity of thrombocytopenia. This is likely due to the shunting of opsonized platelets away from the liver-located Ashwell-Morell receptor (e.g. by platelet destruction in the spleen), failing to trigger TPO production. Data originating from two retrospective case series and a case report (totaling 24 dogs with refractory pITP), indicated that romiplostim administered in a dose ranging from 3-15 μg/Kg, SC, for a variable number of daily or weekly sessions, meaningfully increased and sustained platelets numbers in 22/24 dogs, on an average of 4-6 days, without noticeable adverse events. Given its very high cost and limited accessibility, romiplostim might be a safe option for refractory ITP cases, or in dogs intolerant to immunosuppressive treatment.

Splenectomy has been infrequently reported in dogs with ITP. A few small retrospective case series have indicated successful outcome after splenectomy (reduction or discontinuation of immunosuppressive drugs), but the uncontrolled design and the inconsistent implementation of splenectomy (early or late in the course of the disease) do not allow the drawing of firm conclusions. Splenectomy may be considered in refractory ITP cases, or in dogs intolerant of the immunosuppressive treatment, on the understanding that post-splenectomy relapses may still occur.

Severe hemorrhagic anemia should be addressed with whole blood or packed red blood cell transfusions. Platelet-containing products (e.g., fresh whole blood, platelet-rich plasma, platelet concentrates), may be considered in dogs with severe bleeding. Although platelet number increase is expected to be minimal and transfused platelets may be rapidly cleared from the circulation, there is still the possibility of a clinically relevant and life-saving increase, until the immunosuppressive drugs to take effect. Although gastroprotectants are not routinely indicated in ITP, their administration may be considered in cases of melena, on the understanding that sucralfate and proton pump inhibitors may reduce absorption of some immunosuppressants.

Therapeutic plasma exchange may rarely be considered in dogs refractory to medical treatment, although a definitive therapeutic benefit over the conventional treatments has yet to be substantiated.

Prognosis in canine ITP is good to guarded, with the fatality rate ranging from 10-30% in dogs with severe bleeding tendency. Dogs with melena, or high serum BUN concentration or low hematocrit on admission, and likely those with amegakaryocytic thrombocytopenia have a decreased probability of survival. A recently established bleeding severity score on admission (DOGiBAT bleeding assessment tool) correlated with transfusion requirement and duration of hospitalization, as opposed to platelet numbers. Relapses occur in 10-45% of the treated dogs, usually within six months of diagnosis. Rapid tapering of immunosuppressive treatment or an occult comorbidity might precipitate a relapse in the clinical setting. Dogs that have already relapsed once, are more likely to experience further relapses in the future. There is no evidence that indefinite administration of immunosuppressive treatment or adjunctive immunosuppressants may lower the chances for relapse.

Vaccine-associated ITP is rare in dogs. In dogs with pITP, the risk of vaccination adverse events (e.g., triggering of a ITP relapse) should be weighed against the risk of infectious disease exposure and compliance with national/local legislation. Measuring titers for canine distemper virus, canine adenovirus and canine parvovirus as surrogate markers for protection can be considered, so as to maximize core vaccination intervals. Immunosuppressive drugs should have been ideally discontinued or minimized.

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FELINE HEMATOLOGY: MIND THE DIFFERENCES!

Saturday 14 September | 16:45 - 18:30 | MC 3 - Room B

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Feline haematology exhibits several distinctive features compared to canine haematology. Understanding these differences is crucial for accurate diagnosis and effective treatment in veterinary practice.

Red blood cells:
One of the most noticeable differences between the two species lies in the red blood cells (RBCs). Feline RBCs are smaller and display more variability in shape compared to those of dogs. This phenomenon, known as anisocytosis, is relatively common in cats, and together with the same process happening to platelets, it may generate problems for impedance haematology analysers to provide a correct measurement of haematocrit (HCT) and platelets concentration (PLT). Another distinctive feature is the central pallor. Feline RBCs typically have a less pronounced central pallor than seen in dogs, making not possible to identify spherocytes when these are present when suspecting immune mediated haemolytic anaemia. Feline red blood cells also contain eight oxidizable sulfhydryl groups that make haemoglobin more prone to oxidation. This element, together with the minor ability of the spleen (non sinusoidal) to remove Heinz bodies from the circulation, makes feline red blood cells more prone to oxidative damage and haemolytic anemias, and explains why the presence of a few Heinz bodies within RBCs is a common finding. Additionally, the lifespan of red blood cells differs between these two species. Feline RBCs have a shorter lifespan, lasting about 70 days, whereas canine RBCs can live for 100 to 120 days. This shorter lifespan in cats can influence how quickly changes in RBCs production or destruction are reflected in their blood work. Reticulocytes, which are the indicator of regeneration, are present in two forms in the feline species; aggregate reticulocytes mature into punctate reticulocytes within 12-24 hours. Punctate reticulocytes, however, can remain in circulation for up to 10-14 days. The percentage of aggregate reticulocytes is a more accurate indicator of recent bone marrow activity and response to anaemia. Healthy cats typically have a lower baseline reticulocyte count compared to dogs. This is partly due to the presence of punctate reticulocytes, which are not counted in routine reticulocyte counts.

White Blood Cells:
When it comes to white blood cells, there are notable differences between cats and dogs. Morphologically, eosinophils and basophils show significant differences between the two species. In cats, eosinophils have rod-shaped granules that tend to be orange to red/pink and often fill the cytoplasm. Feline basophils contain numerous light lavender granules, which are significantly more numerous and

paler than those seen in dogs. Selected feline breeds (e.g., Siamese, Birman) may also contain characteristic reddish granulation within the cytoplasm. Regarding leukograms, the major difference between the two species is related to the fight-or-flight response. Neutrophilia tends to be much higher in cats under this condition due to the presence of a larger marginated pool of neutrophils. Concurrent lymphocytosis may also be observed. Mastocytaemia is rare and, in felines, is commonly associated with the presence of mast cell tumors, whereas in canines it is a less specific finding.

Platelets:
Platelet numbers and morphology also differ between cats and dogs. Cats generally have smaller platelets that are more prone to clumping. This clumping can make it challenging to obtain an accurate automated platelet count, and spurious clumping is the most common cause of thrombocytopenia in cats. In fact, a UK retrospective study showed that the prevalence of genuine thrombocytopenia in the feline population was only 5.9%. Recent studies have demonstrated that the addition of a small quantity of 10 µL of Amikacin (250 mg/dL) to a 0.5 mL EDTA tube prevents platelet aggregation in feline venous blood samples and does not cause clinically relevant changes in other hematologic measurements.

Infectious agents:
It is uncommon to encounter infectious agents in blood smears, and microscopy examination has low sensitivity for diagnosing infectious disorders. However, it is fairly specific, and their presence confirms infection. The exception is *Mycoplasma spp*., which are rarely present on blood smears and can be confused with stain precipitate or other contaminants, making PCR the most accurate method for diagnosis. Other infectious agents that can be observed within blood smears of feline blood include among other *Babesia sp*. *Mycoplasma sp.* and *Cytauxzoon sp*.

Recommended readings:

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DIAGNOSTIC APPROACH TO MEDIASTINAL MASSES IN DOGS AND CATS

Saturday 14 September | 16:45 - 18:30 | MC 3 - Room B

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The mediastinum, and particularly the cranial and medial portions, are frequently affected by pathological disease in both dogs and cats, and include processes ranging from inflammatory to neoplastic in nature. Thymoma and lymphoma are the two most common neoplasms observed at this level. Diagnosis can often be achieved by cytology, but may sometimes require further investigation including flow cytometry, PARR or histopathology coupled with immunohistochemistry. The distinction between these two conditions is extremely important from a clinical perspective, as the treatment options and prognosis are very different. Thymomas are commonly treated by surgery and, if completely excised, patients can have very long survival times. On the other hand, mediastinal lymphomas are treated with chemotherapy and, especially if they are high-grade, survival is short, often less than a year.

Thymoma is a neoplasm of the thymic epithelial cells most commonly seen in adult/older dogs and cats. Clinical signs may vary and are mainly associated with a space-occupying lesion. Paraneoplastic syndromes such as myasthenia gravis, megaoesophagus and hypercalcaemia may occur. Most thymomas are clinically benign and surgery is considered curative in most cases. Cytologically, it is characterised by a mixed population of epithelial cells (neoplastic component, usually without signs of atypia) and lymphoid cells (usually small lymphocytes, but a mixed cell population may be seen). Granulated mast cells may also be noted. Different subtypes have been described depending on the proportion of epithelial and lymphoid cells. These does not seem to have a clear prognostic value.

Mediastinal lymphoma is a specific subtype of lymphoma that has been described in both dogs and cats. In cats, it appears to be more common in young animals, especially those that are FeLV and FIV positive. In both species, these forms are mostly high grade and have a poor prognosis even when treated with chemotherapy. Cytologically, they are characterised by a monomorphic population of lymphoid cells, mostly of medium to large size. Mitotic figures are often seen and tend to be numerous.

When a definitive diagnosis via cytology is challenging further diagnostic investigations may be considered and may include:

Histopathology and immunohistochemistry: This can be performed after mass excision or as an endoscopic biopsy. If sufficient tissue is available, epithelial cells, if present, are easier to see than on on cytology, making it easier to differentiate between thymoma and lymphoma. If necessary, this technique can be combined with immunohistochemistry (IHC) to determine whether the lymphoid cells all express the same phenotype (supportive of lymphoma) or mixed T and B lymphocytes (in which case thymoma or a reactive event is more likely). Cytokeratin can also be used to confirm the epithelial origin of certain cells.

Flow cytometry: This technique is widely used in dogs, where it has been shown that finding

>10% of lymphoid cells co-expressing two lymphoid T-cell markers (CD4 and CD8) is supportive of thymoma. In lymphoma, the vast majority of lymphoid cells express either CD4 or CD8, depending on the cells from which the neoplastic clones arise. In cats, this approach has been shown to be ineffective, as lymphomas co-expressing CD4 and CD8 are common and there is therefore a large overlap with thymoma. The limitations of these techniques relate to the need to obtain a new sample and follow specific laboratory guidelines. In addition, there are not many laboratories offering this type of test and as this type of sample is very time sensitive, it is important that the sample arrives as soon as possible and ideally the sample is tested within 24 hours from collection.

The PARR test is a clonality assay that uses DNA samples from cells and PCR primers that target the B and T cell receptor gene segments in lymphocytes, and is used to distinguish monoclonal (likely neoplastic) from polyclonal (reactive) populations of lymphoid cells. The advantage of this technique is that it can be performed on any sample type, including pre-stained smears, and has no time limitations. However, both false negative and false positive results can occasionally occur, therefore it is considered a confirmation and not a first line diagnostic test.

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CANINE OCULAR MANIFESTATIONS OF INFECTIOUS DISEASES; A KEY SIGN TO EARLY DIAGNOSIS

Saturday 14 September | 08:30 - 10:30 | MC 2 - Room C

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Several ocular signs have frequently been related to systemic diseases, but their variability and non-pathognomonic nature make cause-and-effect association challenging to confirm. This review aims to describe the ocular manifestations of the most frequently seen in the everyday practice canine infectious diseases, along with some insights into their etiopathogenesis, differential diagnosis, and treatment.

Canine monocytic ehrlichiosis (CME) is an important tick-borne infectious disease in the dog with worldwide distribution, caused by the gram-negative and obligatory intracellular bacterium *Ehrlichia canis*. CME has a quite variable clinical picture, whereas ocular signs may be seen in all phases and usually accompany the other clinical manifestations of the disease. Bilateral anterior uveitis is the most frequent presenting warning ocular condition, characterized by blepharospasm, photophobia, lacrimation, conjunctival congestion, corneal edema, deep corneal vascularization, pupillary hemorrhages, hyphema, aqueous flare, ciliary flash, multifocal nodules within the iris stroma and iris hyperpigmentation. The less common posterior uveitis is usually expressed by chorioretinitis, serous or hemorrhagic retinal detachment, retinal atrophy, choroidal, retinal or vitreal hemorrhages, and optic neuritis. Secondary glaucoma, as sequelae of chronic uveitis, cataract, necrotic scleritis, orbital cellulitis, and panophthalmitis may result in many cases. Diagnosis of ehrlichiosis involves the direct visualization of morulae in peripheral blood smears, detection of *E. canis* antibodies, or PCR amplification of *Ehrlichia* spp. Oral doxycycline or tetracycline combined with anti-inflammatory therapy (topical and systemic glucocorticoids) and mydriatics-cycloplegics are the gold standard in treating natural disease.

Canine leishmaniosis (CanL) is quite common and endemic in many parts of the world where it is caused by *Leishmania infantum*, a diphasic protozoan parasite transmitted by *Phlebotomus* sand flies. Ocular disease is bilateral or unilateral and quite common in CanL (16% - 80%), appearing as severe anterior uveitis and characterized by uveal and corneal edema, miosis, fibrin formation in the anterior chamber, and multiple nodules within the iris stroma. Posterior uveitis, if present, is characterized by multifocal chorioretinitis with small hyperreflective foci, retinal detachment, and hemorrhage in the tapetal fundus. Blepharitis, conjunctivitis, keratoconjunctivitis sicca, or a combination thereof have been also associated with CanL. Diagnosis of CanL is quite difficult if it is based only on clinical signs, but is usually confirmed by measurement of blood serum specific antibody titers, as well as lymph node, bone marrow, spleen, and/or cutaneous cytology and histopathology. Antileishmanial treatment combined with glucocorticosteroids or non-steroidal anti-inflammatory agents and topical mydriatics–cycloplegics to control anterior uveitis, is the treatment of choice.

***Canine Dirofilariosis* (heartworm disease)**, enzootic in some countries, is vectored by several mosquito species. The causative agent *Dirofilaria immitis* is the most frequently reported intraocular nematode in the dog. Eyes are included in the aberrant/occasional tissue localization of the parasite. Affected dogs usually present with ocular discharge, blepharitis, conjunctivitis, mild corneal opacity, photophobia, anterior uveitis, and/ or visualization of the worm in the anterior chamber. Diagnosis will be based on direct visualization of the parasite, usually found in the anterior chamber, and further confirmed by immunological (antigen-based ELISA) and parasitological (Knott's modified) tests. Surgical removal of adult worms from the anterior chamber by limbal incision and control of uveitis are highly recommended.

Onchocercosis may represent an important ocular disease of dogs with zoonotic potential and widespread geographical distribution. It is caused by *Onchocerca lupi*, which is considered responsible for the canine cases in Europe. Two clinical forms of the disease, the acute and the chronic, have so far been described. In the acute disease severe conjunctivitis, conjunctival congestion, chemosis, protrusion of the nictitating membrane, mild to severe periorbital swelling, exophthalmos, blepharitis, serous to mucopurulent ocular discharge, diffuse corneal edema, corneal ulceration, anterior and/or posterior uveitis, accompanied by variable ocular discomfort have been noticed. In chronic cases, the worms typically reside within subconjunctival nodules or cyst-like formations in the retrobulbar space causing exophthalmos and occasionally protrusion of the adnexa. In rare instances, the worms may invade the anterior chamber accidentally. Surgical excision of as many of the periocular nodules and cysts as possible, along with filaricidal treatment with melarsomine, ivermectin, doxycycline, and control of uveitis could be considered as a treatment option.

Canine Thelaziosis is due to the nematodes *Thelazia callipaeda* and *Thelazia californiensis,* commonly named eyeworm, causing ocular disease of variable severity in many mammalian species and humans. The most common and characteristic clinical sign is persistent mucopurulent to purulent conjunctivitis, accompanied by blepharospasm, excessive lacrimation, corneal opacities, and ulceration. After a careful examination, milk-white parasites can be visualized in the conjunctival fornix, under the nictitating membrane, and within the conjunctival and lacrimal sacs. Mechanical removal of parasites after the instillation of local anesthetics along with antiparasitic treatment can be effective.

Toxocara canis infection is responsible for ocular aberrant migration of larvae to the eye, leading to severe granulomatous posterior uveitis and retinal degeneration. Establishing a definitive diagnosis is challenging since either ophthalmoscopic or histopathologic observation of *T. canis* larvae could differentiate this syndrome from other causes of chorioretinitis.

Ocular toxoplasmosis in dogs due to *Toxoplasma gondii* infection can cause anterior uveitis, multifocal retinitis, choroiditis, extraocular myositis, scleritis, optic neuritis, and keratoconjunctivitis. A diagnosis of toxoplasmosis is usually based on serologic tests. Even though toxoplasmosis may be a self-limiting disease requiring no therapy, in case of active intraocular inflammation, systemic therapy is usually advised.

Infectious Canine Hepatitis due to Canine Adenovirus Type I, is an uncommonly recognized infectious disease with a worldwide distribution, developing mild to severe clinical signs. The most characteristic and noticeable ocular lesion, mainly seen in young animals, is corneal

stromal edema masking deeper examination of the eye. Blepharospasm, miosis, hypotony, and aqueous flare can be noticed sometimes, 1–2 days before the corneal edema manifests. Moreover, glaucoma, a significant ocular sequela of CAV-1, results in many cases in blindness. Therapy of CAV-1 is symptomatic and similar to that for other forms of anterior uveitis, while hypertonic salt solution or ointment might help in reducing corneal edema.

Canine Distemper **(CDV**) is related to infection by a single-stranded RNA Morbillivirus in the Paramyxoviridae family, infecting a wide variety of families of animals. Acute ocular signs of CDV are usually associated with bilateral conjunctivitis with serous to mucopurulent ocular discharge. The causative agent is difficult to incriminate in case of no obvious other signs of the disease (respiratory and gastrointestinal). Lacrimal adenitis causes severe reduction of tear production, as well as encephalitis, resulting in dehydration of the cornea and KCS. An incidental finding is the multifocal, non-granulomatous chorioretinitis, more often noticed in the peripheral to the mid-peripheral non-tapetal fundus. Acute vision loss and mydriasis due to CDV optic neuritis are the most severe clinical ocular symptoms. The above ocular signs are indicative but not definitive for the diagnosis of CDV infection. PCR or virus isolation tests represent the diagnostic tools to confirm clinical cases. Treatment is mainly symptomatic for KCS and optic neuritis, while vaccination is crucial to preventing CDV.

Veterinary practitioners should be aware of the variability of the ocular manifestations of canine infectious diseases and recognize them as early signs of an underlying cause, allowing them to succeed in a more precise early diagnosis as well as more effective treatment.

Keywords: Canine infectious diseases, ocular manifestations, veterinary ophthalmology, zoonoses.

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FELINE OCULAR MANIFESTATIONS OF INFECTIOUS DISEASES: A KEY SIGN TO EARLY DIAGNOSIS

Saturday 14 September | 11:00 - 13:00 | MC 2 - Room C

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This presentation emphasizes in the direct association between infectious diseases and ocular manifestations in feline patients, underscoring the important role of ocular signs in facilitating early diagnosis and intervention. A general practitioner should recognize and moreover focus in ocular pathology as an indicator of systemic infections, providing most valuable insights into underlying disease processes, thus guiding therapeutic strategies.
The most important and frequent viral pathogen for its ocular manifestations is ***Feline herpesvirus type 1 (FHV-1).*** Symptoms include dermatologic lesions, involving the facial skin, conjunctivitis, keratitis, ulcerative keratitis with pathognomonic dendritic ulcers, stromal keratitis, and uveitis. Periodic reactivation of latent *FHV-1* occurs after normal stress conditions, without, or with a variety of symptoms, and systemic corticosteroids should be avoided, as they are responsible for the "round trip theory". "Persistent state" and "post-herpetic disease" are related to a variety of clinical syndromes. Diagnosis is rather challenging, with virus isolation being the gold standard. Treatment involves supportive care along with antivirals, acting as virostatics, depending on the viral stage and host's immune response. In any case, aggressive treatment of *FHV-1*-related disease may limit the disease's progression and reduce the frequency and severity of recurrences.
Feline Leukemia Virus (FeLV) has long been implicated in feline ocular diseases, yet less than 2% of those with clinical *FeLV* infection present with ocular symptoms. The virus does not cause primary ocular disease, with the early stages of lymphoma may resemble to any other uveitis, although the iris presents irregular, as the disease progresses. Dyscoria or anisocoria develops due to neoplastic infiltration or virus-related neurological effect. If the serum antigen ELISA test is positive, an antibody immunofluorescence test can confirm the infection, or the ELISA can be repeated in 3 months.
Feline Immunodeficiency Virus (FIV) causes chronic immunosuppression in cats and can lead to various types of chronic uveitis. Ocular inflammation may result from direct viral damage or secondary opportunistic infections of the eye. Keratic precipitates tend to be rare and few when present and cats infected with *FIV* are about five times more likely to develop lymphoma or leukemia, compared to non-infected cats with potential ocular involvement. The primary clinical diagnosis method has been the detection of serum antibodies against *FIV* through ELISA, with positive results confirmed by Western blot analysis.

Feline Calicivirus (FCV) is a non-enveloped RNA virus, widely prevalent in cat populations, accounting for the 90% of upper respiratory infections in domestic cats, along with the *FHV-1*. The virus causes epithelial necrosis, with typical oral ulcerative lesions, mild respiratory disease with sneezing and serous nasal discharge. *FCV* should be considered highly unlikely in cases of conjunctivitis without oral ulcers. Virus detection is via PCR tests on swabs from the oral cavity, subcutaneous scrapings, and blood. Therapeutic options are limited, and all healthy cats should be vaccinated against *FCV* with modified vaccines. Lifelong

immunity is unlikely in infected cats due to the continuous mutations of the RNA virus genome.

Feline Coronavirus (FCoV) biotype, termed feline infectious peritonitis virus ***(FIPV),*** is the etiologic agent of ***FIP***. Infections have been frequently associated with ocular manifestations in later years, more common in the non-effusive ("dry") form of the disease, with diffuse and severe corneal edema, "mutton fat" keratic precipitates, severe anterior uveitis, pyogranulomatous chorioretinitis, retinal vasculitis, and inflammatory retinal detachments. Diagnosing *FIP* in living cats is challenging. The current gold standard for diagnosis is immunohistochemistry, on effusions or lesions, to detect *FCoV* antigen in infected macrophages, which is considered 100% predictive of *FIP*. Supportive therapy aims to suppress inflammation, typically with corticosteroids, and antiviral treatment using nucleoside analogs, such as GS-44152, which showed efficacy, and protease inhibitors. These treatments as monotherapy or combined, are under evaluation.

Chlamydia felis is recognized as the most significant bacterial agent and major cause of conjunctivitis. Infection is usually unilateral, more common in kittens and young cats, and characteristic symptoms include blepharospasm, serous or purulent ocular discharge, and chemosis. Conjunctivitis is non-ulcerative, and keratitis is absent. PCR is considered the most reliable method for confirming the initial infection and the chronic disease. Treatment of choice is the systemic administration of doxycycline, which provides rapid improvement in clinical symptoms and possibly removal of the microorganism from the eye and the body.

Species of the genus *Mycoplasma spp*. are traditionally implicated in cat conjunctivitis, but their role as exclusive pathogens is debatable, as they are found in the conjunctival and upper respiratory tract flora of all cats. Clinical symptoms of ***Mycoplasmosis*** are non-specific and include unilateral or bilateral conjunctivitis with serous or mucopurulent discharge, hyperemia, and chemosis. Conjunctival pseudomembranes may appear and in cases of concurrent *FHV-1* infection, corneal stromal ulceration, neutrophilic cellular infiltrates, and keratomalacia may occur. Diagnosis by cytological examination is unreliable, and PCR positive results are of unclear clinical significance. Treatment with tetracyclines and fluoroquinolones is effective against most *Mycoplasma* strains and should be continued for at least 2 weeks, although desired duration for systemic infections is undetermined. Conjunctivitis responds to topical tetracycline treatment four times a day.
Bordetella bronchiseptica, a Gram- negative coccobacillus, is an important cause of respiratory disease in cats, but also implicated in conjunctivitis, with high prevalence in shelters and breeding colonies. It is highly contagious, with varying severity of clinical signs, from sneezing, conjunctivitis with serous or mucopurulent ocular discharge, to bronchopneumonia, that can be fatal. It is confirmed by aerobic bacterial culture and PCR assays performed on nasal and oropharyngeal swabs. Systemic antibacterial treatment is usually reserved for kittens less than 6–8 weeks of age, patients with respiratory disease lasting longer than 7–10 days, or those with signs of bronchopneumonia. Doxycycline is the antibiotic of choice, given at 5mg/kg orally, every 12 hours for 21 days. Topical treatment is only supportive and not specific. Pet cats do not require vaccination.
Conjunctivitis in ***Bartonellosis*** is unsubstantiated or insignificant, while uveitis, attributed to ***B.henselae*** and ***clarridgeiae,*** can occur**.** The diagnostic value of antibody titers for clinical infection is limited. Resolution of clinical symptoms generally occurs after antibiotic therapy with doxycycline, at a dose of 50 mg every 12 hours for 21 days, while topical corticosteroid treatment is ineffective.
Parasitic infections, including ***Toxoplasmosis*** can be of great importance. ***Toxoplasma gondii*** is a well-documented cause of chorioretinitis and anterior uveitis in cats, being a zoonosis. The common symptoms of the systemic disease are chorioretinitis, characteristic hypo-reflective lesions in the tapetal fundus and raised white infiltrates in the non-tapetal area. The definitive diagnosis is made by finding the microorganism in ocular tissues, and

as far as serology is concerned, a high IgM titer indicates a recent infection. IgG antigens may remain for two years or more, making a positive result that includes only these of low diagnostic value. Symptomatic treatment of anterior uveitis consists of topical corticosteroids and mydriatic-cycloplegic drugs, being effective in seropositive cases that present only with anterior uveitis. The antibiotic of choice is clindamycin hydrochloride, at a dose of 12.5 mg/kg twice daily, for 14-21 days.

Feline Leishmaniasis is a zoonotic disease transmitted through an intermediate host. Transmission occurs through sandflies, and although dogs are considered the primary reservoir of the protozoan, cats have shown natural resistance to the disease. Ocular symptoms are common and characterized by blepharitis, conjunctivitis, and keratitis. Diagnosis is based on serological detection of Leishmania antibodies. Quantitative PCR can be useful in skin biopsies and lymph node aspirations from affected animals, usually showing a high parasite load. Treatment is empirical, based on known therapeutic protocols for dogs, usually oral monotherapy with allopurinol and maintenance with subcutaneous injections of meglumine antimoniate.

Cryptococcus neoformans or ***C.gattii*** associated with environments containing high amounts of nitrogen, such as bird droppings. Ocular symptoms of ***Cryptococcosis*** include chorioretinitis with granulomatous inflammation and retinal detachments, anterior uveitis, exophthalmos and possibly optic neuritis, in case the CNS is involved. Treatment with various systemic antifungals can be successful. Therapy should be continued until the antigen test is negative or for 2-4 months after the clinical symptoms have resolved.
As a conclusion, feline ocular manifestations of infectious diseases may serve as crucial diagnostic tools for early detection and management of systemic infections. By recognizing the diverse array of ocular signs associated with infectious diseases, veterinarians can promote and accelerate the diagnostic process, alleviate disease progression, and optimize clinical outcomes for their feline patients.

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FELINE CLINICAL CASES, ASSESSMENT AND DIAGNOSTIC PATHS

Saturday 14 September | 11:00 - 13:00 | MC 2 - Room C

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Several cases will be discussed interactively, as a clinical tutorial, in terms of refreshing the key points from the "Ocular Manifestations of Feline Systemic Diseases".

Disease identification and complexity, concurrent infections, differential and challenging diagnosis will be presented, as to the means of proper management in case of feline infectious diseases correlated to ocular symptoms.

GALLBLADDER MUCOCELE IN THE DOG. INDICATIONS FOR CHOLECYSTECTOMY.

Saturday 14 September | 08:30 - 10:30 | MC 3.4 - Room D

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Gallbladder mucocele (GM) is defined as a pathological distension of the gallbladder due to the accumulation of large amounts of thick, gelatinous bile and mucus within its cavity [1,2]. Gallbladder mucocele is considered as the most common pathological condition of the biliary tract and the most common indication for cholecystectomy in the dog. The pathophysiology of the disease appears to be multifactorial and is not well understood. It was recently found that the gallbladder epithelium undergoes an increased secretory activity resulting in mucus production and generation of gelatinous, viscous bile [3]. Gallbladder mucocele is considered as a disease of great importance, since the gradual concentration of viscous bile inside the gallbladder can cause: 1) obstruction of the common bile duct 2) ischemic necrosis due to the pressure exerted on the wall of the cyst or bile duct, which results in rupture and the choleperitoneum 3) cholecystitis and 4) systemic inflammatory reaction syndrome [4-6].
The disease affects older dogs of any sex and breed [1]. The clinical signs in dogs varies and can be related to other concurrent diseases of the biliary tract, to the severity of the disease (subclinical - clinical) and can also be unclear [1,7]. In general, in most dogs the symptoms are acute with a median duration of 4 days and a range of 1-730 days [7]. Laboratory findings vary depending on the severity and chronicity of the condition and the presence of concurrent diseases [1]. There are usually changes in general blood test, increased activity of liver enzymes, increased concentration of total bilirubin, lipids, urea nitrogen and creatinine [4,7]. Ultrasonography is the method of choice for the diagnosis of GM [1,8]. The distinction between GM and bile sludge is important, since sludge is found in clinically healthy dogs without biliary pathology [9]. The ultrasound examination can also demonstrate the presence of a rupture of the gallbladder wall, an important finding that requires an emergency surgical treatment of the condition [4,5]. The sensitivity and specificity of ultrasound diagnosis were found to be 56% and 91%, respectively [5].
Treatment of GM can be surgical or conservative. Conservative treatment can be applied in dogs with GM without obstruction in the common bile duct or in the absence of gallbladder rupture, in asymptomatic dogs where GM was an incidental finding or when surgical treatment is not an option [2]. Conservative treatment includes choleretic agents, hepatoprotectors and special diet. Antibiotics could be added to conservative treatment if infection is suspected [2]. Surgical management of GM is cholecystectomy and is indicated in dogs with symptoms from the biliary tract, those with evidence or suspected common bile duct obstruction, and those with moderate-acute clinical presentation [2]. Cholecystectomy is performed through a median laparotomy or laparoscopically. The patency of the common bile duct must be checked before cholecystectomy via laparotomy. Dissection and ligation of the cystic duct must be done carefully because of

its, not infrequently, friable nature. Intraoperatively, in cases of obstruction of the common bile duct the diagnosis is made by ultrasound (diameter > 4-5 mm) and laboratory (high concentration of total bilirubin) examinations and it is recommended to restore its patency by catheterizing the bile duct either through cholecystotomy or retrogradely, through catheterization of the major duodenum papilla after enterotomy. Piegols et al. (2021) showed the occurrence pancreatitis post catheterization and duct lavage independent of the method of catheterization in 252 dogs after cholecystectomy for GM [10]. Cholestasis predisposes to infection so it is recommended that, if infection is suspected, broad spectrum antibiotic therapy should be initiated that is active mainly against E.coli and Enteroccoccus spp. until culture and susceptibility testing results are available [1,2,5]. The most common intraoperative and postoperative complications of cholecystectomy for GM include fever, regurgitation, hypotension, rupture or perforation of the gallbladder and peritonitis, pancreatitis, sepsis, and death [10]. Dogs with GM and gallbladder rupture resulting in peritonitis had a 2.7-fold higher mortality rate than those without rupture and peritonitis [5]. Prognosis is generally better for dogs that survive in the immediate post-operative period [5].

In conclusion GM is currently the most common indication for cholecystectomy in the dog. Dogs with bile sludge should be monitored regularly with ultrasonography since sludge can lead to GM. Common bile duct catheterization, when required, should be done via cholecystectomy because retrograde catheterization is associated with pancreatitis. Cholecystectomy should be performed prophylactically in cases of GM with subclinical or mild symptoms as the efficacy of conservative treatment has not been clearly evaluated. Early intervention is associated with reduced mortality rates.

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NEUROSURGICAL EMERGENCIES: WHEN DO I OPERATE?

Saturday 14 September | 08:30 - 10:30 | MC 3.4 - Room D

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Summary text
Neurosurgical emergencies in dogs and cats necessitate prompt and precise intervention to prevent irreversible damage and improve outcomes. Intervertebral Disc Disease (IVDD), trauma, neoplasia, atlantoaxial instability, and hydrocephalus are neurological conditions requiring surgical management. Clinical and neurological examinations, supported by advanced imaging techniques such as MRI and CT scans, are crucial for accurate diagnosis and effective surgical planning. Indications for surgery include progressive neurological deficits, severe pain unresponsive to treatment and acute onset of severe symptoms. Postoperative care, including pain management, physical rehabilitation, and monitoring for complications, is critical for successful recovery. Early and intensive physiotherapy can significantly improve functional outcomes. Surgical intervention based on these criteria can effectively manage neurosurgical emergencies, enhancing the quality of life for affected dogs and cats.

Main text
Neurosurgical emergencies are quite common in clinical practice, and veterinarians are called upon to manage them as they require prompt and precise intervention to prevent irreversible damage and improve outcomes. Recognizing when surgical intervention is necessary is crucial for veterinarians to ensure the best possible prognosis for their patients.

Common Neurosurgical Emergencies

Intervertebral Disc Disease (IVDD)
Intervertebral Disc Disease is a common condition in both dogs and cats, characterized by the degeneration and herniation of intervertebral discs, leading to spinal cord compression. IVDD can present acutely, often necessitating emergency surgery. Clinical signs include pain, ataxia, and even paralysis. Surgery is typically indicated in cases with severe neurological deficits, non-responsive to conservative management, or in cases with rapid progression of symptoms.

Trauma
Traumatic injuries to the spine, peripheral nerves or skull, such as those resulting from vehicular accidents, falls, bite wounds or projectiles can lead to fractures, luxations, hematomas and nerve transection. These injuries often require immediate surgical intervention to stabilize the affected area, decompress neural tissues and repair transected nerves. Indications for surgery include unstable fractures, significant displacement of vertebral bodies and progressive neurological deterioration.

Neoplasia
Tumors affecting the brain the spinal cord or the peripheral nerves, can cause a variety of neurological signs depending on their location and size. Rapid growth or significant mass effect causing compression of neural structures necessitates surgical removal or debulking. MRI and CT scans are essential for diagnosis and surgical planning. Surgery is often indicated when the tumor is accessible and causing severe or progressive symptoms.

Atlantoaxial Instability

This condition is particularly seen in toy and small breed dogs and results from congenital or acquired abnormalities of the atlantoaxial joint, leading to spinal cord compression at the cervical region. Surgical stabilization is recommended for animals showing signs of pain, ataxia, or paralysis, as conservative treatment often fails to provide long-term relief.

Hydrocephalus

Hydrocephalus, an abnormal accumulation of cerebrospinal fluid (CSF) within the brain, can be congenital or acquired and it is most commonly seen in toy breeds. Clinical signs include dome-shaped skull, behavioural changes, and seizures (less common). Surgical intervention, such as ventriculoperitoneal shunting, is indicated in cases with severe clinical signs that do not respond to medical management.

Diagnostic Tools

Accurate diagnosis of neurosurgical emergencies involves a combination of clinical and neurological examination and advanced imaging techniques. Plain radiographs are valuable for the initial assessment of trauma cases, as they help identify fractures. However, they are less effective for soft tissue evaluation compared to MRI and CT. MRI is the gold standard for imaging the central nervous system, providing detailed images of neural tissues, intervertebral discs, and other soft tissue structures. It is particularly useful in diagnosing IVDD, neoplasia, and inflammatory conditions. CT scans offer excellent visualization of bony structures, making them ideal for assessing fractures, luxations, and bony tumors. CT myelography can also be used to evaluate spinal cord compression.

Indications for Surgery

Progressive Neurological Deficits

One of the primary indicators for surgery is the presence of progressive neurological deficits that do not respond to conservative management. Rapid progression of symptoms often suggests significant neural compression or damage, warranting immediate intervention.

Severe Pain

Pain that is not alleviated by medical treatment is another strong indication for surgery. This is often seen in cases of IVDD, trauma, and neoplasia where mechanical compression or instability is the cause of pain.

Acute Onset of Severe Symptoms

Sudden onset of severe neurological signs, such as paralysis, warrants immediate surgical evaluation. Conditions like acute IVDD herniation, traumatic fractures, and atlantoaxial luxation can cause rapid deterioration and require prompt surgical decompression and stabilization.

Surgical Procedures

Decompression Surgeries

Procedures such as hemilaminectomy, dorsal laminectomy, and ventral slot are used to relieve pressure on the spinal cord and nerves. These surgeries are commonly performed for IVDD, neoplasia, and certain trauma cases.

Stabilization Surgeries

Stabilization techniques, including internal fixation with plates, screws, pins and polymethacrylate are used to treat fractures, luxations, and conditions like atlantoaxial instability. These procedures restore stability to the affected area, preventing further injury.

Tumor Removal

Surgical excision or debulking of tumors in the brain or spinal cord can alleviate symptoms and improve quality of life. Complete removal is ideal, but partial removal may be performed if complete excision poses too much risk.

Shunting Procedures

For conditions like hydrocephalus, ventriculoperitoneal shunting is performed to divert excess CSF from the brain to the peritoneal or pleural cavity, reducing intracranial pressure and alleviating symptoms.

Postoperative Care

Postoperative care is crucial for successful recovery and includes pain management, physical rehabilitation, and monitoring for potential complications such as infection or recurrence of symptoms. Early and intensive physiotherapy can significantly improve functional outcomes.

Conclusion

Neurosurgical emergencies in dogs and cats require immediate intervention to prevent permanent neurological damage and improve recovery. Recognizing the signs that indicate the need for surgery, such as progressive neurological deficits, severe pain, acute onset of symptoms is essential. Advanced diagnostic tools like MRI and CT scans play a pivotal role in identifying the underlying cause and guiding surgical planning. With the right approach, veterinarians can effectively manage these emergencies, improving the quality of life for their patients.

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EARLY DIAGNOSIS AND MANAGEMENT OF HIP DYSPLASIA IN DOGS: BETTER BE SAFE THAN SORRY

Saturday 14 September | 08:30 - 10:30 | MC 3.4 - Room D

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Hip dysplasia (HD) in dogs is a heritable developmental disorder characterized by an abnormal formation of the coxofemoral joint. The pathogenesis of hip dysplasia is multifactorial, mainly involving genetic predisposition and various environmental influences. The disease manifests in genetically predisposed animals exposed to environmental (nongenetic) factors that promote the expression of the genetic weakness. The earliest sign of canine hip dysplasia has been defined as hip joint laxity. Over time, abnormal joint biomechanics contribute to secondary degenerative joint disease, including cartilage degeneration, synovial inflammation, bone remodeling, and osteophyte formation. Every dog is born with normal hips. If congruity between the femoral head and the acetabulum is maintained, the coxofemoral joint will continue to develop normally. The earliest signs of hip dysplasia are seen at about four weeks of age. The ligament of the femoral head, acting as the primary stabilizer of the joint at that time, increases in volume and suffers small partial tears and hemorrhage, leading to joint inflammation and increased synovial fluid volume—this finding, together with lengthening of the ligament of the femoral lead to joint subluxation. The earliest radiographic signs of hip dysplasia are seen at seven weeks of age, including joint incongruity and an abnormal conformation of the dorsal acetabular rim. Ongoing subluxation, stretching of the joint capsule, and further lengthening of the ligament of the femoral head at the age of 8-12 weeks lead to a worsening of the radiographic signs and cartilage degeneration. The most susceptible areas for cartilage damage due to uneven distribution of weight-bearing forces are the femoral head and the dorsal acetabular rim. The time window to prevent the development of degenerative joint disease that eventually leads to osteoarthritis is very narrow (16-20 weeks of age).
Research on canine hip dysplasia genetics continues, but progress has been sluggish compared to expectations. For this reason, veterinarians need to focus on the dog's phenotype to identify dogs with lax hips who may already suffer or are susceptible to developing joint degenerative changes. Joint laxity (clinical and radiographic) appearing before degenerative and structural changes is the key to the efforts to prevent the progression of the disease.
Early diagnosis, ideally between 12 and 20 weeks of age, is based on the dog's signalment, physical and orthopedic examination, and, most importantly, radiographic findings/measurements. It is essential to understand that one must not wait for clinical signs to screen a young dog for hip dysplasia. The owner of dog breeds at risk of developing hip dysplasia should be informed about the early screening at the time of the first vaccination. The reason is that early acute clinical findings, such as lameness, exercise intolerance, and pain of the hindlimbs, are thought to result from extreme joint laxity. Joint laxity leads to capsular strain and inflammation as dogs age, resulting in periarticular fibrosis. This stage of the condition commonly leads to decreased or absent clinical symptoms.
The most common clinical signs include muscle atrophy of the hind limbs, hip or spinal sway movement, bunny hopping, lameness, and pain on palpation (especially during joint extension and abduction). The Ortolani test may be performed in the awake animal, but it is usually very painful. The animal is then evaluated in deep sedation. In young dogs, a

positive Ortolani sign is the most reliable clinical feature of hip dysplasia. It should be negative in all dogs 12-16 weeks. The angles of subluxation (AS) and reposition (AR) of the joint can be measured with a designated goniometer. After clinically evaluating joint laxity, objective radiographic measurements are performed.

The most widely performed radiographic views include the standard ventrodorsal (VD) extended view, the frog VD view, the distraction view, and the dorsal acetabular rim (DAR) view. The VD extended view is evaluated for signs of joint incongruity (femoral head coverage/Norbert angle), abnormality of the morphology of the acetabulum, and early signs of degenerative joint disease (subchondral bone sclerosis, morgan line, acetabular cupping, femoral head flattening and osteophytes). In the frog VD view, the acetabular depth/filling and coverage of the femoral head are evaluated. Unfortunately, the VD extended view lacks sensitivity to diagnose laxity as it masks joint incongruity due to the wind-up phenomenon. Distraction-based radiographic techniques have been developed to improve the identification of hip joint laxity. For example, the distraction view of the PennHip evaluates non-weight-bearing laxity and provides a predictive index for the development of osteoarthritis. The index can be measured with two different distraction devices (PennHip distractor - DI and Vezzoni modified Badertscher distension device-LI). Both methods were shown to be equally reproducible. In general, a distraction index (DI) or laxity index (LI) below 0.3 is linked to physiological laxity and a favorable outcome regarding the risk of osteoarthritis development. An index ranging from 0.3 to 0.7 indicates an abnormal laxity, whereas an index exceeding 0.7 correlates with excessive laxity and is associated with an unfavorable prognosis. It is essential to know that breed variations exist, and numerous publications concerning the DI can be found in the literature. Finally, the DAR view measures the DAR slope and can evaluate whether the DAR is preserved or shows pathological changes.

Treatment options depend on the severity of clinical signs, degree of joint laxity, and radiographic findings. Shortly, conservative treatment includes NSAIDs, weight management, physiotherapy, polysulfated glycosaminoglycans, and Omega-3 fatty acids-rich diet. Surgical preventive methods include juvenile pubic symphysiodesis (JPS) and double pelvic osteotomy (DPO). Surgical therapy procedures can be preventive, restorative, or palliative. Juvenile Pubic Symphysiodesis (JPS) and double pelvic osteotomy are preventive methods. Dogs with severe clinical signs, femoral head and acetabulum erosion, acetabular filling, radiographic signs of osteoarthritis, and a difference between AR and AS of more than 15° are no candidates for preventive procedures. Total hip replacement (THR) is the restorative method of choice, while femoral head and neck excision (FHNE) is a palliative procedure. More recently, custom-made implants to improve femoral head coverage have been used. Joint laxity and pain scores improved in most cases. On the other hand, force plate analysis showed no improvement, and osteoarthritis scores increased. Treatment recommendations should always be individualized for each dog, and owners' expectations and financial aspects should also be considered.

- Age: 4-5 months
  - Mild joint laxity, no clinical symptoms→ Conservative treatment
  - Mild-moderate joint laxity, no clinical symptoms→ conservative treatment or JPS
  - Moderate joint laxity, with/without clinical symptoms→ JPS
  - Moderate- severe joint laxity, with symptoms→ conservative, DPO or THR later
  - Severe joint laxity, with clinical symptoms→ conservative, THR or FHNE later in life, depending on symptoms
- Age: > 5-6 months
  - Mild joint laxity, no clinical symptoms→ Conservative treatment
  - Mild-Moderate joint laxity, no clinical symptoms→ conservative treatment or DPO
  - Moderate joint laxity, with/without clinical symptoms→ conservative treatment or DPO
  - Moderate- severe joint laxity, with symptoms, no osteoarthritis→ conservative, DPO or THR later in life

- Severe joint laxity, with clinical symptoms and signs of osteoarthriris→ conservative, THR or FHNE later in life, depending on the severity of symptoms

Early diagnosis of hip dysplasia in dogs is crucial for implementing effective management strategies and minimizing disease progression. Identifying the condition early in life allows for interventions to restore joint congruity, slow or prevent osteoarthritis development, and improve the dog's quality of life. Moreover, early screening of hip dysplasia can guide breeders and provide valuable information in choosing which dog should be selected as a breeding dog.

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VACCINATION GUIDELINES IN THE DOG AND CAT: MAXIMIZING THE BENEFITS AND MINIMIZING THE ADVERSE EVENTS

Saturday 14 September | 11:00 - 13:00 | MC 3.4 - Room D

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Vaccinations are an integral part of a comprehensive preventive health care program aiming to significantly minimize the incidence (e.g., canine infectious hepatitis, feline leukemia virus), or nearly eradicate (e.g., rabies) major canine and feline infectious diseases and the associated morbidity and mortality. Vaccination practices in companion animals are currently re-evaluated globally, with a two-fold objective: firstly, to strengthen "herd immunity", which depends not only on how well an individual pet has been vaccinated, but mostly on the proportion of animals vaccinated against vaccine-preventable diseases in a certain population. Secondly, although the frequency of post-vaccinal adverse events has been very low, reasonably reducing the "vaccine load" per animal to minimize the potential for their occurrence, is beyond any doubt. Vaccination protocols update has also been affected by the accumulating evidence that the duration of immunity offered by several (mostly attenuated) vaccines is much longer than previously thought.

The major changes that have recently been incorporated in the canine and feline vaccination guidelines include: 1) the classification of vaccines into *core and non-core* vaccines, on the clear understanding that the definition of "core" and "non-core" may vary among different geographic areas. Core vaccines should be administered, if possible, to every dog and cat, regardless of their lifestyle. Vaccines conferring protection for canine parvovirus-2 and its variants (CPV), canine adenovirus (CAV), canine distemper virus (CDV), feline parvovirus (FPV), feline calicivirus (FCV)/herpesvirus-1 (FHV) fall into this category worldwide. Rabies vaccination is considered as core in countries stipulated as such by the law. Non-core vaccines are those intended for dogs and cats having a geographic location and/or a lifestyle that entail a reasonable risk of exposure to certain infectious agents not considered as core (e.g. canine leptospirosis, feline leukemia virus). Importantly, in countries where leptospirosis is endemic and effective vaccines are available, vaccination may be recommended for all dogs, while vaccination against FeLV may be considered as core in cats aged less than a year, and in adult cats with outdoor access. Vaccines with insufficient scientific evidence for their efficacy or safety (e.g. for canine coronavirus or feline infectious peritonitis) are generally considered as *not recommended*. 2) the first booster vaccination of puppies and kittens after the completion of the basic immunization schedule (16 weeks of age or older) with attenuated core vaccines is recommended to be given at the age of 6 months and then triennially, rather than annually.

For the pet dogs admitted for vaccination earlier that the age of 16 weeks, current guidelines suggest vaccination against CPV, CAV and CDV starting at the age of 6-8 weeks and then every 3-4 weeks until the age of 16 weeks or older. For rabies, the first vaccination is generally not given earlier that 12 weeks of age, unless otherwise required by the national/regional legislation. Termination of the primary vaccination schedule before the age of 16 weeks is strongly discouraged, to ensure that maternally derived antibodies will have been waned, allowing for the vast majority of puppies to be actively immunized.

Dogs admitted after the age of 16 weeks, two vaccine doses administered 3-4 weeks apart are recommended, but even a single dose of attenuated vaccines is expected to immunize the majority of dogs. The first booster for dogs vaccinated for the last time at 16 weeks of age, is at or shortly after the age of 26 weeks of age, to close the window of vulnerability for the minority of dogs that failed to get immunized earlier because of the persistently high maternal immunity. Subsequent vaccinations with attenuated vaccines should be given no more frequently than triennially, including the most commercially available rabies vaccines. If vaccination for leptospirosis is deemed necessary, two initial vaccinations must be given to effectively immunize the dogs, followed by yearly boosters, as they confer immunity that does not usually exceed one year.

Vaccines against canine leishmaniosis (CanL) are available in some endemic countries and are considered non-core. Generally, vaccines against CanL do not reliably prevent the infection and therefore even vaccinated dogs may serve as reservoirs for the infection and continue to transmit it. Instead, vaccinations reduce (but not eliminate) the possibility for the occurrence of clinical disease, representing an additional preventive tool for the disease, in dogs at increased risk of the disease due to breed predisposition, living outdoors and/or living in a highly endemic areas, in the context of repellents and insecticides. The protocol for the only commercially available vaccine for CanL in Greece (LetiFend, Leti, Spain) includes the administration of one primary vaccination dose, followed by annual boosters.

For the pet cats admitted for vaccination earlier that the age of 16 weeks, current guidelines suggest vaccination against FPV, FCV and FHV starting at the age of 6-8 weeks and then every 3-4 weeks until the age of 16 weeks or older. For rabies, the first vaccination is generally not given earlier that 12 weeks of age, unless otherwise specified by the national/regional legislation. Termination of the primary vaccination schedule before the age of 16 weeks is strongly discouraged, to ensure that maternally derived antibodies will have been waned, allowing for the vast majority of kittens to be actively immunized. For cats admitted after the age of 16 weeks, two vaccine doses administered 3-4 weeks apart are recommended, but even a single dose of attenuated vaccines is expected to immunize the majority of cats. The first booster for cats vaccinated for the last time at 16 weeks of age, is at or shortly after the age of 26 weeks of age, to close the window of vulnerability for the cats that failed to get immunized. Cats vaccinated as outlined above, maintain efficient immunity against FPV for several years, but immunity against FCV and FHV is not long lasting; therefore, although low risk cats may be vaccinated every three years, cats at high risk of exposure (e.g., boarding catteries) may necessitate revaccinations every 1-2 years. Rabies boosters are also given typically every three years. In areas endemic for the FeLV, all cats less than one year of age should be vaccinated twice, starting at 8 weeks of age, and then annually if they retain a high risk of exposure (or every 2-3 years in cats with low risk of exposure).

Serologic testing may facilitate vaccination-related decision making in the clinical setting. In dogs, detection of antibodies for CPV, CAV and CDV, is a strong indicator of protection from disease. In cats, this applies for the FPV, but not for the FCV and FHV. An owner may wish to assess for the presence of protective immunity following the completion of the initial puppy core vaccination series. As a rule, lack of seropositivity four weeks after the completion of the initial puppy series at 16 weeks of age, indicates the absence of protective immunity justifying revaccination. Failure again to achieve seropositivity four weeks after the new vaccination is a reasonable evidence that the puppy may be a non-responder and incapable of mounting protective immunity against any or all of the tested agents. Similarly, veterinarians might wish to be able to offer their clients an alternative strategy to routine core vaccination at 3-yearly intervals. In the latter setting, a seronegative or a seropositive result justifies vaccination or extension of the booster core vaccination interval to more than 3 years, respectively.

In conclusion, the fundamental concept of the updated canine and feline vaccination guidelines, is to encourage the vaccination of as many animals as possible with the core vaccines, and to consider non-core vaccines after careful assessment of the animal's lifestyle and the local prevalence of infectious diseases.

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INTERPRETATION OF CARDIAC BIOMARKERS IN CLINICAL PRACTICE

Saturday 14 September | 11:00 - 13:00 | MC 3.4 - Room D

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In general, biomarkers are commonly used in veterinary practice as functional indicators of biological processes in different organs, and their use is of integral importance to clinicians. Biomarkers that are considered reliable share common characteristics as sensitivity and organ specificity, and should provide information about diagnosis and prognosis when evaluated during the course of the disease. Cardiac biomarkers are increasingly used in veterinary medicine, even though they are still not included in general biochemical profiles of most patients. The most frequently used cardiac biomarkers in veterinary medicine are natriuretic peptides, suggesting myocardial stress, and cardiac troponins, which hint at underlying myocardial injury.

Brain Natriuretic peptide (BNP) is produced in the heart of humans and small animals, and acts as a hormone affecting different organs. Its production is activated upon the development of volume overload and cardiac dilation. More specifically, atrial and ventricular stretching, resulting from various heart conditions, contribute to the production of the peptide, which in turn causes vasodilation and diuresis. This mechanism compensates the renin – angiotensin – aldosterone (RAAS) system, which is activated when cardiac dilation and reduction of blood supply to tissues occur. The measurement of this protein cannot distinguish between different heart conditions, but its elevation can be used as indicator of cardiac remodeling and dilation, regardless of whether the cause of the heart disease is congenital or acquired. The activation of this system in heart conditions can be quantified with measurement of pro-BNP, precursor protein of BNP. Specifically, proBNP is converted in the N-terminal fragment of b-type of BNP (NT-proBNP), which shows great stability in blood plasma and serum, and in C-terminal fragment (C-BNP) which is quickly metabolized, and thus rarely used. Atrial natriuretic peptide (ANP) is similarly produced (from proANP to NT-proANP) and metabolized, but there is currently less scientific information about the use of this protein or its precursors as a biomarker of cardiac disease in animals.

There are many studies, especially in canine mitral valve disease and its different clinical stages, that have shown a good agreement between not only the confirmation of disease with higher NT-proBNP concentrations, but also a correlation between its blood levels and disease severity. Evidence has shown that longitudinal quantification of the NT-proBNP helps with the follow-up of patients, proving it as a reliable prognostic tool. In Dobermann Pinchers it can be used as a biomarker in the occult stage of the disease, even though echocardiography and Holter recording remain the golden standard in the diagnosis of this cardiomyopathy.

Both NT-proANP and NT-proBNP have been used in distinguishing cardiac related dyspnea from primary respiratory disease in cats. NT-proBNP has also proved beneficial into discriminating cats with cardiogenic pleural effusion from non-cardiac causes. In the preclinical stages of feline cardiomyopathies there have been conflicting reports, obtained from different studies, with some evidence suggesting effective discrimination

between asymptomatic cats and healthy controls, and others reporting no meaningful difference between these populations. As a result, point-of-care echocardiography or a full cardiologic examination remain the method of choice for screening of clinically healthy cats for cardiomyopathy.

In both dogs and cats, measurements of NT-proBNP are affected by systemic diseases, particularly chronic kidney dysfunction, systemic arterial hypertension and feline hyperthyroidism. When these conditions are medically treated or controlled, studies suggest that the blood concentration of the above biomarker is decreased or normalized.

Cardiac troponins involve 3 myocardial intracellular proteins, cardiac troponin I (cTnI), troponin T (cTnT) and troponin C (cTnC). In healthy animals, acting together, their role is mandatory to cardiac contraction and their concentrations in blood are negligible or low. Troponins have isoforms in skeletal muscles but in cardiology the cTnI and cTnT cardiac isoforms are mainly used. After cardiac injury occurs, cTnI is released from cardiomyocytes into bloodstream and its circulating levels remain high from hours to weeks, depending on the cause and progression of myocardiac damage. In humans, cTnI is used in the diagnosis, as well as prognosis, of myocardial infarction, as these patients show acute elevation in serum concentration. Infarctions are rarely observed in dogs and cats, which usually suffer from more chronic cardiac diseases. There is ample evidence in veterinary literature that cTnI and cTnT are elevated in various congenital and acquired heart diseases.

The increases of troponin blood levels in chronic cardiac diseases are usually low to moderate. A possible explanation given, is that myocardial injury is a continuous process in most heart disease, with remodeling and dilatation of the heart muscle playing an important role in the release of intracellular troponins in the bloodstream. It has also been observed that severe systemic disease, systemic inflammation, neoplasia, intoxication and other systemic disorders may affect levels of troponin, with increases in concentrations varying from low to severe. Possible causes of such an increase in extra-cardiac diseases include microthrombosis, endotoxins, hypoxemia, tachycardia and oxidative stress. Whether in these conditions myocardial injury precedes or results from such systemic disorders remains unknown, but results should be carefully interpretated when assessing the possibility of primary cardiac disease in severely ill patients.

Unfortunately, there is no evidence that troponins can be used in distinguishing between different heart diseases and elevations from extracardiac causes, even though the levels of the circulating concentrations are better at aiding in the evaluation over the course of the disease, with cTnI being the better marker for short-term and cTnT for long-term prognosis.

In canine mitral valve disease, a correlation has been frequently observed between the severity of the disease and the circulating cTnI. At the same time, dogs presenting with CHF symptoms and increased cTnI concentration had shorter survival times. In dilated cardiomyopathy (DCM) in Dobermanns, troponin I measurement is recommended in addition to Holter and echocardiography. Furthermore, it has been found that in DCM Dobermanns and Great Danes, increased levels of cTnI were predictive of shorter long-term survival and increased risk of sudden cardiac death.

In cats with respiratory symptoms, cTnI has been used to distinguish between cardiac and other causes, but there is significant overlap in blood levels, thereby reducing this biomarker's utility in clinical practice. Hyperthyroidism can increase cTnI in cats, but its specificity in differentiating between this endocrinopathy and primary cardiac disease is generally low. Both cTnT and cTnI have been shown to provide reliable prognostic information in HCM, with their blood level increase associated with shorter survival time.

Cardiac troponins have also been found to increase with age and renal disease, as well as in cases of acute pancreatitis. As a result, cTnI elevations in suspected cardiac patients with concurrent disorders should be carefully interpretated.

C-reactive protein (CRP) is an inflammation marker that is commonly used in small animal practice. It has been shown that significant increases in CRP correlate with CHF

symptoms in dogs with mitral valve disease, but its specificity is generally low, and other causes of systemic or localized inflammation should be ruled out before its concentration can be of value in cardiac disease.

The aforementioned biomarkers can be very helpful in clinical practice, especially when the availability of echocardiography is limited, but their utility is better suited in providing only supporting evidence, as well as in the long-term follow-up evaluation of heart failure and cardiac disease. It is rare in clinical practice that a single cardiac biomarker elevation will provide diagnosis and prognosis, but in cases of myocarditis in both dogs and cats (cTnI), symptoms of acute heart failure (NT-proBNP and cTnI), pleural effusions in cats (NT-proBNP and cTnI) and even cardiac neoplasia (cTnI), these biomarkers can assist or at the very least raise suspicion of underlying cardiac disease. Novel biomarkers that have been evaluated in humans for cardiovascular disease, such as copeptin, pro-adrenomedullin, interleukin-6 and many others, are seldom used in veterinary practice since evidence in their utility in companion animals is still limited.

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ADMINISTERING ANALGESIA TO ANIMALS WITH COEXISTING DISEASES OR PATHOLOGICAL CONDITIONS

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There is insufficient evidence for the safe use of analgesics in cases where other conditions coexist in addition to the condition for which they are used. Moreover, there are shortcomings in relation to the co-administration of different drugs with analgesics. This deficiency exists not only in veterinary medicine but also in medicine. Most reports in the literature concern the administration of a combination of drugs in healthy laboratory animals. We are interested not only in perioperative use but also in chronic administration. Chronic kidney disease (CKD) is the most commonly recognized form of kidney disorder in dogs and cats, and in the majority of cases, it represents an irreversible and progressive condition. The estimated prevalence of CKD in dogs and cats is 0.5–1.0% and 1.0–3.0%, respectively. It is more prevalent in older animals, with a rate as high as 80% in the geriatric cat population. The primary drug-elimination pathways are liver metabolism and renal excretion. For this reason, patients with impaired renal function may require an adjustment of the usual drug dosage regimen, not only to overcome serious adverse reactions due to excessive drug accumulation but also to avoid treatment failure. In 70% of cases of osteoarthritis in cats, chronic kidney disease is also present. Inflammatory diseases such as gingivitis, osteoarthritis, etc. need to be treated with anti-inflammatory drugs.

The minimum effective dose of meloxicam for chronic administration in cats is reported to be 0.035 mg/kg. In cats with renal failure of severity up to IRIS 3 (i.e. blood creatinine up to 5 mg/dl) the oral administration of meloxicam at a dose of 0.02 mg/kg daily for more than 6 months did not affect their lifespan. In cats with relatively stable renal function i.e. IRIS gravity up to 2 (creatintine 2.8 mg/dl), oral administration of meloxicam 0.02 mg/kg/24 h continuously for 6 months did not impair renal function. Notably, in IRIS 2/3 (creatinine < 5 mg/dl) cats, a single administration of 10 mg/kg gabapentin gave blood levels higher than those of healthy cats given 20 mg/kg. The earliest indication of impaired renal function in the cat is anorexia. Caution should be given in cases with stomatitis where water consumption is unstable. Water intake should be confirmed in order not to impair renal function and the occurrence of anorexia should be differentiated from anorexia due to the dependence of the gingivitis. Dogs with osteoarthritis that need to be given non-steroidal anti-inflammatory drugs often (in Greece where leishmaniasis is common) suffer chronic renal failure. Interestingly, most of the relevant data concerning safe NSAID use in the literature are in healthy dogs. Thus, in healthy dogs, Agiotensine Converting Enzymes inhibitors and NSAIDS administered for 7 days did not affect renal function as they did not affect renal function when given for 28 days. Furthermore in healthy dogs no (severe) harm was caused by administration of meloxicam and prednisolone in contrast to ketoprofen and prednisolone which impaired renal function. Additionally, in dogs with cancer of mammary glands, administration at a therapeutic dose of carprofen for 90 days did not impair renal function.

Finally, a modification of the NSAIDs regimen is proposed similar to that of the lactam antibiotics, i.e. a reduction proportional to the increase in creatinine. Although not ideal for inflammation (it has no such effect), paracetamol is consider safer than NSAIDs. On the other side, coxibs (exclusive inhibitors of COX-2 action) are not safer. Opioids, when considered necessary, appear to be relatively safe for renal function.

In the absence of Hepatic Failure, elevated ALT and ALP are not a contraindication to the administration of NSAIDs. Recall that an increase in liver enzymes does not indicate liver dysfunction. Ascites, jaundice, hypoalbuminemia, increased ammonia and bile acids in the blood indicate liver dysfunction. NSAIDs are not hepatotoxic, if they cause hepatotoxicity this is due to an idiosyncratic reaction. In liver dysfunction the likelihood of digestive disorders increases (decrease in metabolism - increase in blood levels of NSAIDs - side effects). There is no dosage regimen modification guideline. With regard to the digestive tract, CAUTION should be given to the use of NSAIDS as the enzyme COX-2, which they suppress, contributes to the healing of the gastric mucosa. When carprofen first appeared on the veterinary market, 20 years ago, an article was published in which a 20-day course of carprofen in 21 Labrador dogs with osteoarthritis resulted in hepatotoxicosis. On thorough investigation a histologically idiosyncratic reaction was considered. Seven of them also showed changes in renal function but azotemia was seen in only 2 of them. After this report nothing similar was observed. In contrast, administration for 2 months to healthy dogs with osteoarthritis no hepatic or renal impairment was observed. Experimentally, liver perfusion impairment was observed when 30 μg/kg fentanyl iv was administered to dogs under general anaesthesia with isoflurane in dogs. However, it should be noted that this amount of fentanyl is much higher than that administered once in clinical practice. Cats with heart disease are often predisposed to thrombosis and some are given prophylactic treatment such as clopridogrel. However, there is no contraindication to the use of NSAIDs, although it should be noted that the use of coxibs will upset the balance of prostanoid synthesis towards a predominance of thromboxanes and the possibility of thrombosis. Although there are no veterinary guidelines, there are studies in healthy dogs showing that treatment with meloxicam at the doses tested minimally affected platelet function in dogs with osteoarthritis. Treatment with carprofen decreased clot strength and platelet aggregation. Clot strength was increased after treatment with coxibs (deracoxib). Furthermore, in healthy dogs, the administration of an ACE inhibitor (a drug very commonly prescribed to dogs with cardiovascular disease and not only) together with NSAIDs and furosemide for only seven days did not affect renal function.

THE USE OF SYMPATHOMIMETIC DRUGS IN DOGS AND CATS

Saturday 14 September | 14:30 - 16:45 | MC 3.4 - Room D

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Hypotension is a significant cardiovascular complication during general anesthesia in dogs and cats. Many anesthetic drugs compromise cardiac function, affect vascular tone, and alter vascular volume. Additionally, numerous animals hospitalized in intensive care units experience severe hypotension due to underlying diseases impacting cardiovascular function. Sympathomimetics (SPM), are frequently administered in veterinary anesthesia and intensive care to support cardiovascular function by imitating the function of the sympathetic nervous system. SPM include natural catecholamines (epinephrine, norepinephrine, dopamine), synthetic catecholamines (isoproterenol, dobutamine), and synthetic non-catecholamines (ephedrine, phenylephrine). These agents are vital for maintaining hemodynamic stability and ensuring adequate tissue perfusion in critically ill or anesthetized patients. The pharmacological properties of these drugs, including their pharmacokinetics and pharmacodynamics, are crucial for their effective clinical application. Key drugs such as dobutamine, a selective beta-1 agonist, and dopamine, which has dose-dependent effects, are instrumental in enhancing myocardial contractility and cardiac output. Vasopressors like norepinephrine, primarily an alpha-adrenergic agonist, are essential for managing hypotension, particularly in septic shock, due to their potent vasoconstrictive properties. Epinephrine, a non-selective agonist, is frequently used in emergencies such as anaphylaxis and cardiac arrest for its broad adrenergic effects. These drugs are mainly administered via intravenous (IV) infusion for precise titration, though intraosseous route may be an alternative when IV access is difficult. Despite their therapeutic benefits, SPM may cause adverse effects such as tachycardia, arrhythmias, hypertension, and tissue ischemia, requiring careful monitoring. A thorough understanding of the pharmacological properties, clinical applications, and potential side effects of sympathomimetics is essential for optimizing outcomes in critically ill or anesthetized animals.

PAIN SCALES IN DOGS

Saturday 14 September | 14:30 - 16:45 | MC 3.4 - Room D

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The last two decades several pain measuring tools have been developed worldwide for the identification and measurement of pain in dogs. These tools, also known as "Pain Scales", are being used by the veterinarian or by the owner at home environment. Scientific research conducted by veterinarians with the collaboration of statisticians and in some cases dog owners in order to evaluate the validity and reliability of these instruments through data study, statistical analysis and comparison of the results with objective criteria. It is necessary for a pain scale to measure correctly, objectively and specifically pain (not any similar emotion) which is confirmed by the validity testing.
Two of the most prevalent validated pain scales that measure acute pain (including perioperative pain) are Glasgow Composite Measure Scale (GCPS) and Glasgow Measure Pain Scale-Short Form (GMPS-SF). The last is more reliable and sensitive in detecting different pain volumes. Moreover, it is simple and quick in use, it is not affected by coexisting mobility disorders and there is a limit of score above which analgesic plan is needed.
Canine Osteoarthritis Staging Tool (COAST) and Liverpool Osteoarthritis in Dogs (LOAD) are both validated pain scales for chronic pain induced by osteoarthritis. COAST excels LOAD as it focuses on grading osteoarthritis and identifying the predisposing factors and early stages of the disease. Additionally, COAST is applied both by the owner and veterinarian allowing more information of the pain status of the dog. Canine Brief Pain Inventory (CBPI) is a pain scale for evaluation of pain due to bone neoplasia, but in some cases it can be used for measuring chronic orthopedic pain. For the study of chronic pain induced by a variety of chronic conditions and its impact on dog quality of life scientists created "Health Related Quality of Life" pain scale (HRQL). The assessor should take into account the possibility of false negative and positive results and in particular HRQL cannot exclude the presence of pain but can be used as an alarm signal for the possible presence of pain in animals.
At this point it would be useful to be mentioned that the last few years many promising pain assessment instruments have been developed. For instance, HRQL-SF is a pain scale for the assessment of chronic pain induced by many conditions and it is available in a short electronic questionnaire which is filled by the owner and the results are being sent instantly. Helsinki Chronic Pain Index (HCPI) has been studied upon chronic osteoarthritic pain but it can also be used for variable conditions of chronic pain. It is validated in Finnish but validation in English is expected to be done in the near future. Canine Orthopedic Index (COI) is a non-validated pain instrument created for osteoarthritic pain although it seems to be sensitive in alterations of clinical condition of the animal. Cincinnati Orthopedic Disability Index (CODI) consists of two parts: The first part is a personalized questionnaire for each dog created by the collaboration between the veterinarian and pet owner who observes his dog on a daily basis and may identify some signs of pain based on his own dog behavior. The second part is filled by the veterinarian including his professional evaluation. Canine Oral and Maxillofacial Pain Scale (COPS-C) is a scale for chronic and acute oral & maxillofacial pain which has been validated only in Italian. COPS reliability is questionable because of intrinsic and observer bias and also inability to discriminate

between existence or absence of pain. Despite this, we should take into consideration that it is a first attempt to study this kind of pain.

In conclusion, the scientific field of identification and evaluation of pain in animals is imperative to be studied further. The aim is the development of new validated and reliable pain scales specified in each medical condition and type of pain. It has been proved that pain has a detrimental impact on the healing process but also in animal emotional and psychological state. Therefore, there is an ethical obligation of the veterinarian to serve and guard animal welfare.

PAIN SCALES FOR CATS

Saturday 14 September | 14:30 - 16:45 | MC 3.4 - Room D

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Recognizing pain in animals is a challenge, as they cannot speak and cats are particularly prone to hiding their pain and not showing what they experience .Moreover, cats do not visit veterinary clinics as frequently as dogs do, resulting in a lack of familiarity with a hospital environment. The transportation process (e.g. ,in a carrying cage) adds additional stress and anxiety .For this purpose, an attempt has been made to establish tools for its assessmentof pain, such as pain scales. There are many pain measurements scales registered for cats. For post-operative/acute pain ,four(4) scales are used. For oral cavity pain, two (scales) are available .For chronic pain ,which includes musculoskeletal pain and osteoarthritis pain ,seven (7) scales are used. There are also special questionnaires for chronic pain due to specific chronic diseases. For post-operative/acute pain, the Feline Grimace Scale (FGS) is considered the best for this animal species because it is based on the cat's facial expressionsand body language, and can be performed quickly ,easily ,and at a distance from the animal without the need to handle or stress it. The Glasgow Feline Composite Measure Pain is also widely used and has been developed by Aristotle University of Thessaloniki, as it can be applied quickly and reliably in a clinical setting. The overall score serves as an indicator for the need for analgesic medication. Regarding oral cavity pain, the COPS-C/F (Composite Oralmaxillofacial Pain scale – canine/feline) questionnaire is used for both veterinarians and owners. For chronic musculoskeletal pain and osteoarthritis pain, the FMPI (Feline Musculoskeletal Pain Index) questionnaire is used, with its short form being the most studiedtool for this category and being reliable and easy to complete by the owner.

RABBIT PAIN ASSESSMENT SCALES

Saturday 14 September | 14:30 - 16:45 | MC 3.4 - Room D

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Despite being an increasingly popular pet in the last years, the available tools for pain assessment are still few for rabbits.

In general, pain recognition in rabbits is a challenge for the clinician, not just because in nature they constitute prey species, but also because they are especially susceptible to stress. Thus, behaviors that indicate stress can be mistakenly evaluated as pain manifestations. The difficulty of recognizing signs of pain in rabbits is even more significant when the clinician is not familiar enough with the species. Hence, pain assessment scales can be useful tools as they are more objective and reliable criteria.

Four pain assessment scales have been evaluated so far for the acute pain of the rabbit that can be integrated and applied by the clinician in everyday veterinary practice. Those scales evaluate the facial expression of the animals (Rabbit Grimace Scale & CANCRS), changes in physiological parameters (CANCRS), and behavioral changes (Rabbit Pain Behavior Scale & Bristol Rabbit Pain Scale) through standard questionnaires. The final scores obtained from these questionnaires indicate the level of pain experienced by the animal when the scale was applied. Based on the results the clinician can be facilitated in making decisions concerning the administration of analgesia and the general treatment of the rabbit.