**FELINE HYPERALDOSTERONISM**

**Case example**
Mischief, a 10-year-old neutered male domestic shorthair cat, was presented for poor appetite and lethargy over the previous 3 days. Mischief had been a healthy cat with no prior medical problems. The cat lived indoors and was current on recommended vaccinations. His diet consisted of good-quality dry and canned foods formulated for senior cats.

**Physical Examination**
On presentation, Mischief weighed 7.0 kg with no weight loss since his previous examination a few months previously and a body condition score of 4/5. Dehydration was estimated to be 5% to 7%. Generalized weakness and neck ventroflexion were noted. Pulse rate, breath rate, and rectal temperature were normal. Blood pressure measurement was 140/85. All other physical examination findings were normal including the neurological examination.

**Laboratory Results**
Complete blood count and urinalysis were unremarkable. Blood tests for feline leukemia virus antigen and feline immunodeficiency virus antibody were negative. See Table 1 for selected serum chemistry results.

**Table 1.** Selected blood test results for Mischief at presentation

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood urea nitrogen (mmol/L)</td>
<td>6.1</td>
<td>3.6–10.7</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>127</td>
<td>27–186</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>5.2</td>
<td>3.9–8.3</td>
</tr>
<tr>
<td>Potassium (mmol/L)</td>
<td>2.2</td>
<td>3.7–5.8</td>
</tr>
<tr>
<td>Sodium (mmol/L)</td>
<td>158</td>
<td>147-162</td>
</tr>
<tr>
<td>Total T4 (nmol/L)</td>
<td>17.3</td>
<td>10.0–60.0</td>
</tr>
</tbody>
</table>

Profound serum potassium deficits are associated with even lower intracellular potassium concentrations and aggressive treatment is required. Mischief was started on intravenous lactated Ringer’s solution with the addition of potassium chloride calculated to provide 5 mmol/kg over 24 hours. Serum potassium was monitored q8h. When the serum potassium was unchanged after 24h, a potassium chloride supplementation was increased to provide 8 mmol/kg/24 hours and oral potassium gluconate supplementation at 2 mEq q12h was started. Despite these measures, after 3 days of therapy, Mischief’s serum potassium remained less than 3.0 mmol/L.

**Further Investigation**

The refractory nature of Mischief’s hypokalemia required further investigation to identify its underlying cause. Common causes of hypokalemia in cats include:

- Chronic kidney disease
- Gastrointestinal disease
- Drug-induced (eg, diuretics, insulin)
- Postobstructive diuresis after treatment of urethral obstruction
- Hepatic disease
- Endocrinopathies (eg, hyperthyroidism, hyperaldosteronism, hyperadrenocorticism)
- Diabetic ketoacidosis
- Decreased intake (eg, prolonged anorexia)

Based on Mischief’s physical examination and initial laboratory data, common causes of hypokalemia such as chronic kidney disease, hyperthyroidism, and diabetic ketoacidosis were excluded. Abdominal radiographs were unremarkable. Abdominal ultrasound revealed a heterogeneous mass in the right adrenal gland measuring approximately 2.2 cm × 3.4 cm. All other abdominal organs were unremarkable. With the findings of hypokalemia refractory to treatment and a unilateral adrenal mass, a presumptive diagnosis of primary hyperaldosteronism (PHA) was made. While many cases of PHA are associated with both hypertension and hypokalemia, not all patients have both findings and some patients present without clinical signs referable to either hypertension or hypokalemia.\(^1\) Mischief did fit the typical age for cats with PHA (range 5–20 years, median age 13 years).

The adrenal mass was consistent with unilateral adrenal hyperplasia or neoplasia (eg, adenoma, adenocarcinoma, pheochromocytoma). Tests that can be used to support a diagnosis of PHA (when available) include measurement of plasma aldosterone and the plasma aldosterone-to-renin ratio.\(^1,2\) Recently, measurement of urinary aldosterone-to-creatinine ratio after suppression with oral fludrocortisone has been reported as a
practical confirmatory test for PHA. However, when an adrenal mass is identified, surgical excision and histopathology are necessary for a definitive diagnosis and planning medical versus surgical treatment.

**Treatment**

Potassium supplementation was continued and the aldosterone receptor blocker spironolactone (2.5 mg/kg, orally q12h) was started. When the serum potassium improved to 3.8 mmol/L, a board-certified surgeon performed a right adrenalectomy. No other abnormalities were found in abdominal organs. Mischief was maintained postoperatively on intravenous potassium supplementation. Serum potassium concentrations stabilized in the reference range by the third day postoperatively when potassium supplementation and spironolactone administration was discontinued.

Histologic examination revealed the adrenal mass to be a well-differentiated adenocarcinoma with no evidence of vascular invasion. The mass appeared completely excised.

**Follow-up**

At examination 1 month postoperatively, Mischief had normal serum chemistries, complete blood cell count, and urinalysis. Serum potassium was 5.0 mmol/L. Serum chemistries were monitored monthly for 3 more months and remained within reference ranges. At last examination, 10 months postoperatively, Mischief was stable with no recurrence of disease.

**Summary**

- Blood pressure should be measured routinely in sick cats.
- Hypokalemia that is poorly responsive to treatment should be investigated further.
- PHA in cats is likely more common than previously thought and should be included as a differential diagnosis in cats with hypokalemia and/or hypertension after other common causes such as chronic kidney disease are excluded.
- The diagnosis of PHA includes imaging of the adrenal glands and specific testing such as measurement of plasma aldosterone or plasma aldosterone-to-renin ratio when available.
- Unilateral adrenalectomy is the treatment of choice for confirmed unilateral primary hyperaldosteronism with high success rates and long-term disease-free times.

With thanks to the Specialty and Referral Services of Alta Vista Animal Hospital, Ottawa, Ontario for their role in Mischief’s care.

**References**


**CONGENITAL FELINE HYPOTHYROIDISM**

Hypothyroidism is the clinical syndrome associated with chronic deficiency in the secretion of thyroxine (T₄) and triiodothyronine (T₃). In feline medicine, spontaneous (congenital and adult-onset) and iatrogenic causes have been documented. The most common form of hypothyroidism diagnosed in cats is iatrogenic – as a consequence of treating hyperthyroidism. Only two reports of spontaneous adult-onset hypothyroidism are found in the literature; one cat was diagnosed with lymphocytic thyroiditis, and the other with idiopathic atrophy.

In human medicine, congenital hypothyroidism is relatively common, occurring in about 1 in 4,000 infants. Congenital hypothyroidism in cats is considered a rare disease as only a few cases have been described in the literature. This may be due to under-recognition and lack of awareness. All cases of congenital hypothyroidism described in cats have been primary, (i.e., defect at the level of the thyroid gland). There are no reports of pituitary (secondary) or hypothalamic (tertiary) forms of congenital hypothyroidism in cats.

**Etiology**

Congenital primary hypothyroidism can be divided into two main categories based on underlying pathology: thyroid dyshormonogenesis and thyroid dysgenesis. Thyroid dyshormonogenesis is a defect in any step of iodine uptake or thyroid hormone synthesis. Only a few cases have been described in the literature. A recessive mode of inheritance was proposed in a family of Abyssinian cats. (1) As in all forms of primary hypothyroidism, the low circulating T₄ concentrations lead to increased pituitary TSH secretion. Because the thyroid follicles remain intact in cats with thyroid dyshormonogenesis, the high circulating thyroid stimulating hormone (TSH) concentrations induce hyperplasia of the thyroid gland. Therefore, an enlarged thyroid gland (bilateral goiter) can sometimes be palpated in cats with this type of congenital hypothyroidism.

Thyroid dysgenesis is a developmental defect of the thyroid gland, sometimes resulting from TSH receptor abnormalities. In contrast to dysmorphogenesis, thyroid dysgenesis leads to hypoplasia or aplasia of the thyroid gland; this is a nongoitrous form of congenital hypothyroidism. A recessive mode of inheritance was proposed in a family of Japanese cats. (2) However, in most published cases of congenital hypothyroidism in cats, the underlying pathophysiology has not been investigated.
Clinical Signs
Thyroid hormone is necessary for the normal postnatal development of the nervous and skeletal systems in the kitten. Kittens are born clinically normal but changes become evident by 6-8 weeks of age. Clinical findings include disproportionate dwarfism (wide trunk, short limbs often with valgus malpositioning, short neck, sometimes kyphosis), central and peripheral nervous system abnormalities, and mental dullness. Other findings may include:

- Lethargy
- Bradycardia
- Inappetance
- Constipation
- Abdominal distension
- Delayed dental eruption

Physical examination findings often include:

- Macroglossia
- Large, broad skull
- Shortened mandible and ears
- Retention of the juvenile hair coat

Delayed epiphyseal maturation and dysgenesis in vertebral bodies and long bones are common and may contribute to lameness. In fact, some hypothyroid kittens are diagnosed when they are presented to a veterinarian for evaluation of constipation or lameness.

Diagnosis
Diagnosis of congenital hypothyroidism in cats is based on compatible medical history and clinical signs along with supportive laboratory data, especially in thyroid hormones. Radiology is also helpful to document skeletal abnormalities. Clinical pathology changes associated with congenital hypothyroidism include hypercholesterolemia (due to decreased hepatic metabolism and decreased fecal excretion), hypercalcemia (due to decreased renal clearance and increased gastrointestinal absorption), and mild normocytic, normochromic anemia.

Some reports suggest that kittens less than 12 weeks old should have serum total T₄ concentrations 2-3 times higher than normal adult cats. Therefore, some hypothyroid kittens may have serum total T₄ concentrations within the normal reference range for adult cats while others will be below the adult reference range. Non-thyroidal illness can also suppress total T₄ concentrations. In cases where the diagnosis is unclear, free T₄ (by equilibrium dialysis) and canine TSH assays may be used. Review papers have been published on diagnosis of hypothyroidism and should be consulted for more detailed information. (3,4)
Treatment and Prognosis

Kittens with hypothyroidism are treated with levothyroxine at 0.05-0.1 mg/cat, once daily. The dose can be adjusted based on clinical response and serial monitoring of serum total T4. Little data is available on prognosis. It is suspected that skeletal abnormalities may be reversible if the patient is diagnosed and treated early, but otherwise may persist. To reverse or ameliorate effects on the central nervous system, treatment must be initiated within the first few weeks of life to prevent mental dullness and impaired cognitive development.

References:
Idiopathic inflammatory bowel disease (IBD) is a common chronic enteropathy of cats that is immunologically mediated. Mucosal inflammation is most often found in the small intestine, but can involve any part of the gastrointestinal (GI) tract. The disease is most common in middle-aged cats, although cats of any age can be affected. Clinic signs are persistent or recurrent and include vomiting, small intestinal diarrhea, weight loss, and hyporexia. If the colon is involved, large bowel diarrhea may be present with blood, mucus, and tenesmus. Some affected cats also have inflammatory disease in the liver and/or pancreas. The cause of IBD is not fully understood, but research suggests genetic factors influencing the mucosal immune system, dietary factors, and enteric bacteria play important roles.

**Diagnosis**

Currently, the diagnosis is one of exclusion and requires intestinal biopsy to differentiate IBD from other disorders such as lymphoma and food-responsive enteropathy (Table 1). The diagnostic approach starts with a thorough patient history (including dietary history) and physical examination. Initial diagnostic testing (e.g., fecal analysis, complete blood count, serum chemistry profile, urinalysis, total T4, feline leukemia virus and feline immunodeficiency virus testing) is designed to confirm or refute the presence of primary GI disease. Further testing may focus on the GI tract, such as serum feline TLI and PLI, cobalamin, and folate. Advanced diagnostics that may be useful include imaging (radiography, ultrasonography) and biopsy (intestinal tract, liver, mesenteric lymph nodes, pancreas) via endoscopy, laparotomy, or laparoscopy. The preferred method of intestinal biopsy – endoscopic versus full thickness – is a subject of controversy. Recommendations have been published for maximizing diagnostic yield when performing GI endoscopy and should be reviewed by clinicians using this approach.\(^1,2\) The clinician should initially focus on ruling in or out parasitic causes, infectious causes, GI disease requiring surgery (such as a foreign body), exocrine pancreatic insufficiency, and non-GI disease. Once these disorders have been eliminated, the most common diagnoses for GI signs in the cat are idiopathic IBD, diet-responsive enteropathy, and alimentary lymphoma. While biopsy is used to diagnose IBD and lymphoma, the distinction between severe IBD and lymphoma is not always easy to make based on histopathology and may require immunophenotyping (B cell/T cell markers) or PCR (clonal expansion of lymphocytes) for confirmation.

**Table 1: Comparison of IBD, food-responsive enteropathy, and lymphoma in cats**
<table>
<thead>
<tr>
<th></th>
<th>IBD</th>
<th>Food-responsive enteropathy</th>
<th>Lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Signalment</strong></td>
<td>Mostly middle-aged cats</td>
<td>Young cats</td>
<td>Middle-aged to older cats</td>
</tr>
<tr>
<td><strong>Clinical signs</strong></td>
<td>Lethargy, weight loss, hyporexia, vomiting, diarrhea</td>
<td>Diarrhea +/- weight loss +/- cutaneous lesions</td>
<td>Lethargy, weight loss, hyporexia, vomiting, diarrhea, +/- icterus</td>
</tr>
<tr>
<td><strong>Clinical course</strong></td>
<td>Recurrent or progressive</td>
<td>Recurrent or progressive</td>
<td>Progressive</td>
</tr>
<tr>
<td><strong>Exam findings</strong></td>
<td>Normal or thickened bowel loops; abdominal pain if liver/pancreas involved</td>
<td>Often normal, cutaneous signs may be present</td>
<td>Normal or thickened bowel loops +/- palpable masses</td>
</tr>
<tr>
<td><strong>Diagnostics</strong></td>
<td>Rule out non-GI causes, FNA cytology mesenteric lymph nodes/masses, intestinal biopsy is definitive</td>
<td>Rule out GI parasites, perform dietary therapy trial</td>
<td>Rule out non-GI causes, FNA cytology mesenteric lymph nodes/masses, intestinal biopsy is definitive</td>
</tr>
</tbody>
</table>


**Treatment**

Treatment for IBD in cats remains empirical as data is lacking or inadequate. In humans and in dogs with IBD, quantifiable indices are used to measure clinical disease. An index has been suggested for cats – the feline chronic enteropathy activity index (FCEAI) – where the magnitude of the score correlates with the degree of inflammation. The index is used to assess response to treatment and to tailor medical therapy to the individual patient. It can be applied to patients with IBD or diet-responsive enteropathy.

Although grading systems have been proposed, no standardized histopathologic evaluation of biopsy samples has been validated for disease severity or outcome. Until pathologists can agree on a standard grading scheme, lesions are subjectively classified. In some cases (such as intestinal infiltration with neutrophils or macrophages), culture, special stains, or fluorescence in situ hybridization may be indicated. Results could determine which patients are best treated with antibiotics and/or probiotics.

Studies in cats with chronic lymphoplasmacytic enteropathy have found that most patients respond to treatment with diet, antibiotics, or immunosuppressive drugs. Sequential treatment helps determine which treatment will be most effective for the
individual patient. Using this approach, a diet trial is performed first for at least 7 days and response is assessed. Most cats will benefit from long term dietary therapy even if other treatments are necessary. The next step is a 14-day trial of metronidazole (15 mg/kg PO daily); if clinical signs improve, the dose is tapered by 25% every 2 weeks until it is discontinued. Cats that are non-responsive to diet and metronidazole are treated with oral prednisolone (2 mg/kg PO daily) alone or in combination with metronidazole. The prednisolone dose is tapered by 25% every 2 weeks to reach the lowest dose that controls clinical signs. Other immunosuppressive medication choices include chlorambucil (2 mg/cat PO every 72 hours) or cyclosporin (5 mg/kg PO daily). Some cats can be weaned from medications and maintain remission with dietary therapy alone. Cats with low serum cobalamin should be supplemented at 250 mcg/week SC for 6 weeks, then one dose after 30 days. The serum cobalamin is reassessed 30 days after the last dose. Some cats will require long term monthly cobalamin supplementation.

Not all owners are able to afford an optimal diagnostic investigation, including biopsies. Clinicians often must treat suspected IBD cases without diagnostic confirmation. These patients should be treated with the sequential therapy approach outlined above. Cats that have significant weight loss and watery small bowel diarrhea should be treated with cobalamin parenterally. Cats with signs of large bowel diarrhea may benefit from dietary fiber supplementation, such as ¼ teaspoon psyllium per meal. Patients that fail to respond to these treatments can be treated with prednisolone with the understanding that it may not be the best therapy should the patient have lymphoma or an infectious component.

**Prognosis**

Most cats with IBD respond well to treatment but some will fail due to compliance issues, severe disease, concurrent disease (such as hepatic or pancreatic disease, or hyperthyroidism), and misdiagnosis (especially cats that actually have lymphoma). Low serum cobalamin has been correlated with poor clinical response in cats with chronic enteropathy. A decrease in the FCEAI for a patient is associated with successful outcomes, as is a decrease in serum acid glycoprotein (an acute phase protein).

**References available on request**
Veterinary medicine has no mandatory reporting or investigation of anesthetic-related adverse effects, including death. Until recently, very little data was available to evaluate the risks of anesthesia for cats. A multi-center prospective cohort study in the United Kingdom from 2002-2004, the Confidential Enquiry into Perioperative Small Animal Fatalities (CEPSAF), has changed that. This study recorded patient outcomes after premedication and within 48 hours of the end of the procedure, and calculated the risks of anesthetic-related death for cats (n=79,178), dogs, rabbits, and other small mammals.

Cats have a higher anesthesia-related mortality rate than dogs; in fact, healthy cats were twice as likely to die compared to healthy dogs (see Table 1). Other studies have had similar findings. ‘Healthy’ and ‘sick’ are based on the American Society of Anesthesiologists (ASA) classification system. Comparable data suggests that mortality rates for humans in developed countries is less than 0.05%.

Table 1: Mortality rates in cats and dogs from the CEPSAF study

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Dogs</th>
<th>Cats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0.17%</td>
<td>0.24%</td>
</tr>
<tr>
<td>Healthy (ASA 1-2)</td>
<td>0.05%</td>
<td>0.11%</td>
</tr>
<tr>
<td>Sick (ASA 3-5)</td>
<td>1.33%</td>
<td>1.40%</td>
</tr>
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</table>


Most deaths, in cats as well as dogs, occur in the post-operative period. The most common causes of death in the CEPSAF study were cardiovascular or respiratory problems (57%), although the cause was unknown in 20% of feline patients. The most critical time is the first 3 hours after the end of anesthesia, when about 2/3 of all anesthetic-related deaths occur. Patients are often transitioning from 100% oxygen to room air during this time, while they are cold and shivering, which increases oxygen demand. This is especially risky for cats with cardiac disease and those with other illnesses. It is also the time when monitoring is at the lowest level as equipment has been removed and nursing staff may be distracted with other tasks. Finally, as cats regain consciousness, they may become aware of pain if it has not been adequately prevented or treated, leading to tachycardia and hypertension. Therefore, the immediate post-operative period should be one of diligent monitoring of feline patients.

Factors associated with risk of anesthetic death in cats include overall health status, subclinical disease, body weight, age, hypothermia, intravenous fluid use, anesthetic drugs and techniques, and duration of anesthesia (see Table 2):
**Overall health status**: Careful attention should be paid to a preanesthetic physical examination and patient history, stabilization of the patient, selection of anesthetic techniques, plans for monitoring, and post-operative care.

**Subclinical disease**: Some cats deemed to be ‘healthy’ in the CEPSAF study may in fact have had subclinical disease, especially cardiac disease. Clinics should establish pre-anesthetic laboratory testing protocols for feline patients based on age and other risk factors. Pre-anesthetic testing can range from simple blood and urine panels in young, otherwise healthy patients to more involved testing including blood pressure assessment, radiographs, or disease-based laboratory testing (e.g., total T4).

Subclinical cardiac disease is especially concerning. The prevalence of cardiomyopathy is about 15% in ‘apparently’ healthy cats and cardiac disease can be present in patients without cardiac murmurs or arrhythmias. The risk of hypertrophic cardiomyopathy increases with increasing age, male sex, certain breeds (e.g., Maine Coon, Ragdoll, Bengal, Persian), and presence of a heart murmur. However, good handling skills are necessary to perform adequate pre-anesthetic examinations on feline patients that are often very stressed. In one shelter study, multiple auscultations were required to detect a heart murmur in some cats. Cardiac biomarkers such as NTproBNP (Feline proBNP, IDEXX) represent an opportunity to detect occult cardiac disease and should be considered for higher risk patients and even older patients without a detectable heart murmur.

**Body weight**: Cats weighing less than 2 kg (4.4 lb) are at increased risk of death (15 times greater than cats weighing 2-6 kg [4.4-13.2 lb]). Reasons include the high surface area-to-body weight ratio of small cats predisposing them to hypothermia, and inaccurate calculation of drug doses if body weight is not accurately measured (instead of estimated). Obese cats are also at increased risk of death due to respiratory compromise, reduced cardiovascular reserves, and relative drug overdoses if calculations are not based on lean body weight.

**Age**: Cats older than 12 years are twice as likely to die compared with cats aged 6 months to 5 years, and the risk is independent of ASA status. This increased risk may be due to decreased respiratory and cardiovascular reserve, decreased ability to regulate body temperature, and age-related decrease in anesthetic drug requirements. Health screening of apparently healthy cats over 10 years of age reveals an increased prevalence of problems such as high blood pressure and kidney disease, so pre-anesthetic laboratory data will be helpful in senior cats to assess health status.

**Hypothermia**: Detrimental effects of hypothermia include increased intraoperative bleeding, increased risk of wound infection, increased oxygen consumption due to shivering in recovery, slower metabolism of drugs, delayed recovery, and decreased perfusion. Shivering may also contribute to increased sensation of pain in cats as it does in humans. The CEPSAF study found that temperature was monitored in only 1-2% of cats during anesthesia, and in only 11-15% of cats during recovery. Another study by Redondo and colleagues found that 97% of cats have a lower body temperature at the end of anesthesia than before. The greater the degree of hypothermia, the greater the risk of mortality (7% with severe hypothermia). Active warming techniques should be used to provide warmth either before premedication or at least at the time of premedication. In addition, chilling should be reduced by avoiding contact with cold surfaces and avoiding the use of cold surgical preparation solutions.
Intravenous fluids: The use of IV fluids increased the risk of death by a factor of 4 in both healthy and sick cats in the CEPSAF study. This is most likely due to inappropriate administration of fluid therapy. The blood volume of cats is about 60 mL/kg body weight compared to 80-90 mL/kg for dogs. Intraoperative fluids rates are often 10 mL/kg/hour and this rate is likely too high for cats. Current recommendations are a more conservative 3 mL/kg/hour as a starting rate for crystalloid fluid administration in cats. As well, infusion or syringe pumps or a Buretrol should be used to ensure accurate volume delivery. This is especially important since a percentage of cats will have undiagnosed cardiac disease and vascular overload could contribute to mortality.

Anesthetic drugs and techniques: Premedication provides sedation that makes cats easier to handle and less stressed, and it reduces the dose of induction and maintenance drugs.

Monitoring: Most of the reduction in the risk of anesthesia for humans is due to improved monitoring. In veterinary medicine, a trained nurse whose primary focus is management of the patient during anesthesia significantly reduces the odds of a complication. In the CEPSAF study, monitoring pulse rate and quality and monitoring pulse oximetry significantly reduced mortality.

Duration of anesthesia: A duration of anesthesia greater than 90 minutes increases the risk of mortality by a factor of 3 compared with durations less than 30 minutes. Therefore, it is important to ensure that all preparations are made in advance, that all drugs and equipment are on hand, and that procedures are performed efficiently. If several different procedures require anesthesia, it may be more prudent to perform them separately to reduce anesthesia time for each event.

Table 2: Key factors related to morbidity/mortality and how to mitigate the risk

<table>
<thead>
<tr>
<th>Factor</th>
<th>Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothermia</td>
<td>Measure body temperature regularly</td>
</tr>
<tr>
<td></td>
<td>Use passive and active warming early</td>
</tr>
<tr>
<td>Fluid therapy</td>
<td>Use syringe or fluid pump, or Buretrol for accurate measurement</td>
</tr>
<tr>
<td>Duration of anesthesia</td>
<td>Plan in advance, be efficient</td>
</tr>
<tr>
<td>Airway obstruction, tracheal rupture</td>
<td>Intubate carefully, do not overinflate the cuff</td>
</tr>
<tr>
<td></td>
<td>Use anesthetic masks for short procedures</td>
</tr>
<tr>
<td>Cardiovascular collapse, hypoxemia</td>
<td>Monitor pulse rate and rhythm, monitor pulse oximetry</td>
</tr>
</tbody>
</table>

A few topics require special mention. Respiratory obstruction is a more frequent post-anesthetic cause of death in cats than dogs. Tracheal injury can occur during intubation if the procedure is not done correctly. Intubation should be performed under the correct plane of anesthesia, with direct visualization of the larynx, and gently with patience. Topical local anesthetics such as lidocaine are helpful if used in appropriate metered aerosol doses. The correct size and length of endotracheal tube should be used for each patient. Endotracheal tube cuffs should not be overinflated; this is a cause of tracheal tears. For short procedures, intubation may not be required and an anesthetic mask can be used instead.
blindness has occurred in cats related to the use of spring-loaded mouth gags for dental procedures. This is due to cerebral ischemia caused by impaired blood flow in the maxillary artery when the mouth is held open under pressure. For this reason, spring-loaded mouth gags should not be used in cats.

References:
Payne JR, Brodbelt DC, Luis Fuentes V. Cardiomyopathy prevalence in 780 apparently healthy cats in rehoming centres (the CatScan study). J Vet Cardiol 2015;17(Suppl 1):S244–57.
Robertson S. Anesthetic-related morbidity and mortality in cats. In Little S, editor: August’s Consultations in Feline Internal Medicine, vol 7, St. Louis, 2016, Elsevier.
Clinicians are often presented with apparently healthy patients that have liver enzymes elevated above the reference interval on routine health screens. This raises the question – does the patient have liver disease? In order to answer the question, some key points must be remembered. One is that the liver has a great reserve capacity and clinical signs of hepatic disease may not appear until disease is advanced. Another is that the liver is often the victim of non-hepatic disease (especially diseases of the pancreas and gastrointestinal tract, and hyperthyroidism) so the entire patient must be evaluated to detect secondary reactive hepatopathies (Box 1). Finally, due to the way that reference intervals are established (typically the central 95% of the reference group), 2.5% of the population will have values above or below the reference interval for any given test. In general, 2-fold to 3-fold increases above the upper limit of the reference interval are considered mild, 4-fold to 5-fold elevations are considered moderate, and higher elevations are considered severe. Detection of a single mildly elevated liver enzyme on routine testing of an apparently healthy animal is insufficient for the diagnosis of hepatobiliary disease.

**Box 1: Common non-hepatic diseases that can elevate liver enzymes in the cat**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Condition</th>
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<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>Severe hemolytic anemia</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>Abdominal trauma</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>Systemic infections</td>
</tr>
<tr>
<td>Neoplasia</td>
<td></td>
</tr>
</tbody>
</table>

The prevalence of elevated liver enzymes in both healthy and sick cats is not well described. In one study of routine health screening of 100 apparently healthy cats 6 years of age and older, 6% had elevated ALT results with most being mildly elevated.[1] Only one cat had an elevated AST result. Data on ALP or GGT was not included in the study. By contrast, in a study of 1,022 samples from both healthy and sick dogs, elevated ALT was found in 20% and elevated AST in 12% of samples.[2]

The most commonly elevated liver enzymes in apparently healthy cats are the leakage enzymes, ALT and AST. Elevations are associated with damage (reversible or irreversible) to the hepatocyte membrane, allowing leakage of the enzymes from the cytoplasm. Elevations in ALT are most sensitive for inflammation, necrosis, and primary neoplasia and less sensitive for lipidosis, metastatic neoplasia, and portosystemic vascular anomalies. The half-life of ALT in cats is only 3-6 hours (compared with 2.5 days in the dog) so a return to normal values after acute insults occurs rapidly in the cat. ALT can be elevated due to *in vitro* hemolysis and lipemia.
AST is derived from both liver and non-hepatic sources (skeletal and cardiac muscle) so elevations are considered to be more sensitive but less specific for hepatic disease. One must bear in mind, however, that diseases of muscle are not common in cats and evaluation of serum creatine kinase will assist in discriminating the source of the AST elevation. Hemolysis can cause significant increases in AST. As for ALT, the half-life of AST is shorter in the cat (1.5 hours) than the dog (12 hours); serum AST will return to normal more rapidly than ALT. In primary liver disease, ALT and AST typically increase together, and may be accompanied by increases in ALP and/or GGT, as well as hypoalbuminemia and decreased BUN. Care must be taken in the interpretation of ALT and AST as they do not identify the disease origin and the magnitude of elevations is not a reliable indicator of disease severity. Evaluating ALT and AST every 3-5 days can be helpful in determining whether a disease process is resolving or persistent pathology exists.

ALP and GGT are hepatocyte membrane-associated enzymes and elevations are associated with cholestasis (stimulated by impaired bile flow). ALP is found in hepatocytes that line bile canaliculi and sinusoids and is also present in bone; mild elevations are common in growing animals. GGT is also present in the kidney and pancreas but increases are most commonly associated with cholestasis or biliary hyperplasia. While elevations in ALP and GGT can be induced by corticosteroids in dogs, this does not occur in cats. Phenobarbital is less likely to induce elevations in ALP in cats than in dogs, but has been reported. The half-life of ALP in the cat is only 6 hours (in contrast to 66 hours in the dog) and cats have less hepatocellular ALP than dogs so that elevations are usually considered significant in the cat. GGT may be a more sensitive indicator of hepatobiliary disease in cats as the half-life is longer than ALP. When ALP and GGT are roughly equally proportionately increased, the diagnosis is likely to be one of either pancreatitis, cholangitis, or extra-hepatic bile duct obstruction. In hepatic lipidosis, ALP is typically increased 5-10 fold while GGT is either normal or increased only 1-2 fold.

Investigation of elevated liver enzymes in the apparently healthy cat
Given that so many non-hepatic diseases can cause increases in liver enzymes, it is critically important to rule in primary hepatic disease before invasive procedures such as liver biopsy are planned. A systematic investigative approach is outlined in Figure 1. The first steps when an elevated liver enzyme is encountered in an asymptomatic patient are to verify the value and to rule out spurious increases in enzyme activity due to lipemia and hemolysis.

Figure 1: Algorithm for the approach to elevated ALT/AST in apparently healthy cats (adapted from Webster CRL. Interpretation of serum transaminase levels in dogs and cats. Clinicians Brief, Nov 2005, pp 13-18). SBA = serum bile acids
A thorough physical examination and medical history are important – is the patient truly healthy and asymptomatic? A few key points should not be overlooked in the medical history, such as history of toxin exposure and drug/supplement administration (Box 2), evaluation for hyporexia, and evidence for polyuria/polydipsia. The physical examination should include careful evaluation of the thyroid gland and assessment for jaundice, which can be subtle in the early stages.

**Box 2: Some drugs associated with hepatotoxicity in cats**
- Acetaminophen
- Anabolic steroids
- Diazepam (oral)
- Ketoconazole
- Megestrol acetate
- Methimazole

Results of other laboratory evaluations may also be incorporated in the initial evaluation. Five tests on routine biochemistry panels can be used to assess liver function: cholesterol, bilirubin, glucose, albumin, and BUN. However, they are most likely to be affected in cats with clinical signs of hepatic disease. If no obvious explanation for the abnormal liver enzyme can be found, there are two courses of action. A more in-depth diagnostic evaluation can be undertaken, starting with serum bile acids, or the liver enzymes can be re-evaluated in 2-4 weeks.
Serum bile acids are often used to test hepatic function (in non-icteric cats). There are some caveats to the use of bile acid testing. One is that while increases are associated with hepatic insufficiency, the magnitude of increase cannot be used to assess severity of disease or the type of dysfunction. The second is that paired (12-hour fasting and 2-hour post-prandial) samples are usually recommended, but obtaining post-prandial samples in cats is difficult. Single fasting samples can sometimes give false normal results but if a single bile acid test is abnormal, it does indicate liver dysfunction. An alternative to serum bile acid evaluation is evaluation of urine bile acids with a single sample. Cats with liver disease (especially cholestatic disease) have increased urinary bile acid excretion. Urine bile acids are measured 4-8 hours post-prandial and compared in a ratio to urine creatinine. The post-prandial urine sample can be collected at home, or the cat can be fed at home and brought to the hospital for sample collection. In one study of 54 cats with hepatic disease, 17 cats with non-hepatic disease, and 8 normal cats, the results of a single post-prandial urine bile acid test were highly correlated with health status.[3] Urine bile acid:urine creatinine ratios greater than 4.4 are considered evidence of hepatic dysfunction.

Abnormal liver enzymes should not be ignored in the apparently healthy patient, but care should be taken not to convict a patient of liver disease too hastily. In fact, elevations in liver enzymes are more often associated with non-hepatic disease. A step-wise approach can be taken to investigate elevated liver enzymes in a systematic manner, reserving invasive procedures for those animals with evidence of hepatic dysfunction.

References
One of the most common problems in cats presented to veterinarians is anorexia. Since anorexia is a non-specific clinical sign that can be associated with a variety of underlying disorders, the clinician may find it challenging to diagnose and treat affected cats. Effective intervention requires an understanding of common causes and management options.

Anorexia is the loss of appetite for food. Another useful term is hyporexia, which can be defined as a reduction in appetite.¹ Both situations are important in feline medicine. The distinction is useful both for descriptive purposes and because totally anorexic patients often require more aggressive diagnostic and therapeutic intervention, including assisted feeding. In order to understand if a cat or kitten is consuming adequate nutrition, guidelines for daily caloric intake should be noted. For adult cats, the starting point for daily resting energy requirement (RER) is calculated by the equation \[30 \times \text{body weight in kg} + 70\]. Multiplying by an illness factor is no longer recommended as it has been associated with higher complication rates.² The amount fed should then be adjusted according to monitoring of body weight (BW) and body condition score (BCS). The daily caloric intake should also provide a minimum of 5 g protein/kg body weight and this may be met when using recovery or convalescence diets due to their high fat and protein content. For kittens under 2 kg (4.4 lb), it is more accurate to use the equation \[70 \times \text{BW (kg)}^{0.75}\] to calculate RER.

The detrimental effects of anorexia/hyporexia are well known. Metabolic changes include increases in glucose, lactate, cortisol, glucagon, and norepinephrine as well as increased proteolysis leading to loss of muscle while fat may be preserved. Immune function and wound healing are impaired and morbidity and mortality are increased. Hepatic lipidosis can occur in older obese cats that have become anorexic due to a stressful experience or concurrent disease. It is associated with acute and rapid weight loss (40-60%), depression, and icterus; muscle mass is lost while abdominal & inguinal fat is often retained. This disease requires aggressive nutritional management.

There are many potential causes for hyporexia/anorexia. An attempt should be made to prevent hyporexia/anorexia when possible, and to find a specific cause when it is identified. In addition to loss of appetite due to disease, some common causes include:

- **Diet change**: Cats are affected by many qualities of food, such as the taste, smell, format (canned, dry, semi-moist), kibble shape, kibble size, mouth feel, etc. Cats are notorious for developing fixed food preferences that are often shaped by early experience. Food acceptance and intake can also be affected by environmental factors, such as the feeding location, timing of feeding, type of bowl, presence of other animals or people, etc. Food should always be fresh and stored appropriately. Poor quality or spoiled diets may cause anorexia, vomiting, and diarrhea.

- **Stressors**: Many external stressors cause changes in feline behavior such as anorexia/hyporexia, vomiting, diarrhea, etc.³ Stressors may also have wide ranging effects on cat behavior, such as suppression of normal behaviors (e.g., resting, grooming), and increased vigilance and hiding.
Undesirable physiologic responses to stress include hyperglycemia, decreased serum potassium, increased serum creatinine phosphokinase, lymphopenia, neutrophilia, erratic response to sedation and anesthesia, immunosuppression, hypertension, and cardiac murmurs. Examples of stressors include change in diet, change in caretakers, change in daily routine, unnatural day/light cycles, lack of interaction with caretakers, cold ambient temperatures, noisy environments, presence of other cats and dogs, unfamiliar caretakers, unfamiliar environment, and lack of environmental resources (e.g., places to hide, perch, etc.). Many hospitalized cats suffer from hyporexia/anorexia. Some veterinary hospital cages are small and inhibit normal behavior because they lack places for cats to perch, hide, and scratch. Small cages also make it difficult to separate food and water from the litter box. Food intake is adversely affected when less than 2 ft. of triangulated distance between litter box, resting area, and food/water bowls is available. Cats housed in cages with 11 sq. ft. of floor space were significantly less stressed than cats with 5.3 sq. ft. of space in one study. For cats, vertical space is just as important as horizontal space. Places to hide are very important for cats; one study found that the ability to hide decreased stress hormones. As well, cats may be housed within the sight of dogs, or at the least, within the smell and sound of dogs.

Veterinary hospitals should have procedures in place for monitoring of food intake, BW, and BCS of hospitalized cats, as well as guidelines for intervention. Cats should be weighed and body condition scored at admission; this should be repeated regularly during the hospital stay. More frequent evaluation is indicated for sick cats and those on medications (many drugs cause hyporexia/anorexia or vomiting in cats). Daily assessment should be performed before cage cleaning, and should include food and water intake, presence of vomitus, and fecal frequency and quality (using the Nestle Purina fecal scoring system). With ad libitum feeding plans, it can be difficult to detect hyporexia/anorexia, so daily weighing of food bowls is recommended. Cats prefer shallow bowls for food and water, such as dog-size water bowls and paper plates.

For older kittens and adults, nutritional intervention should be implemented if the cat is eating less than 85% of RER, the cat is anorexic for 3 or more days, or the cat has lost 10% BW or more in a short period of time. Young kittens and sick cats or kittens are more vulnerable to the detrimental effects of inadequate nutritional intake and need closer monitoring. Intervention should begin if a kitten has not eaten for a 24-hour period. Assessment of hyporexic/anorexic cats therefore must include at a minimum: complete physical examination, evaluation of available medical history, nutritional assessment, and environmental assessment. Whenever possible, underlying diseases should be identified and treated where feasible. Use of feline facial pheromone in hospitalized cats is associated with increased food intake and increased normal behaviors such as grooming. Basic supportive care may be required for hyporexic/anorexic cats and could include hydration, vitamin B12 supplementation, and treatment of fever, pain, or nausea if present.

Food aversion occurs readily in cats if they learn to associate eating or the sight or smell of food with feeling sick, nauseous, or painful. Once they are feeling better, they may avoid that food or similar foods for prolonged periods of time. It is important to recognize signs of nausea in cats (e.g., gulping, drooling, dropping food from the mouth, turning away from food) and institute treatment early. Avoid leaving food in the cage of a nauseous cat; instead, offer food intermittently and then remove it. Offering food that is chilled may help overcome aversion by reducing the odor. Whenever possible,
avoid administering medications in food (an exception would be a phosphate binder). Cats recovering from food aversion may be helped by offering a different diet, feeding in a new but quiet environment, and even being fed by a new caretaker.

Feeding strategies can be grouped into three levels based on level of intervention:

- **Level 1 (simple interventions):** The sense of smell is particularly important for cats to eat normally and may be impaired in cats with URTD or facial trauma. Enhancing smell and palatability can be accomplished by feeding fresh canned foods that are warmed no higher than body temperature, and adding water or chicken or tuna broth. Canned foods not only have higher water content than dry diets (>75% compared with <10%) but are more palatable due to their higher fat and protein content. For cats that do not accept canned diets, dry kibble can be soaked in water. Human baby foods are a popular choice for tempting cats to eat and are acceptable as long as they do not contain onion and are used for less than 2-3 weeks. In the short term, caloric intake is more important than nutritional balance. Offer small frequent meals as early satiety is common in illness. Hand-feeding, petting, and praise may also be helpful. Appetite stimulating drugs are not very reliable and many have undesirable side effects. Their effect on appetite is short-lived and they are best reserved for convalescent cats with hyporexia and cats overcoming food aversion. They are not likely to induce adequate nutritional intake in an anorexic sick cat.

- **Level 2 (syringe feeding):** Syringe feeding has limited usefulness and is best for cats that are not totally anorexic and will tolerate the procedure. It may be difficult to meet daily caloric needs with this method, and many cats will struggle and resist. Orogastric feeding with a mouth speculum and tube is not recommended by this author as it is too stressful. However, orogastric tube feeding is appropriate and effective for feeding neonatal kittens.

- **Level 3 (tube feeding):** Tube feeding is indicated when nutritional support will be needed for more than 1 or 2 days. The easiest method is nasogastric (NG) or nasoesophageal (NE) tube feeding. The tube is easy to place, does not require anesthesia, is relatively easy to maintain, and is inexpensive. The drawbacks are that NG/NE tubes are easy to dislodge, are not useful for long term feeding (up to about 7 days), and only liquid diets (e.g., CliniCare, Rebound; both 1 kcal/mL) can be fed. Feeding can be in intermittent boluses or trickle feeding. Contraindications to placement of NG/NE tubes include the inability to swallow or lack of gag reflex. Complications may include rhinitis, esophageal reflux, aspiration, inadvertent tube removal, or obstruction of the tube. For longer term feeding (weeks to months), an esophagostomy tube is ideal and can be used with a variety of diets.
Common antiemetic and appetite stimulating drugs for cats

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<th>Drug</th>
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| Metoclopramide              | 0.2 – 0.4 mg/kg SC, PO q 8hr 1 – 2 mg/kg/day CRI | Also prokinetic  
Centrally acting? |
| Maropitant                  | 1 mg/kg IV, SC, PO q 24 hrs (up to 5 days)  | Inhibits substance P binding to NK-1 receptors                           |
| Phenothiazines: prochlorperazine chlorpromazine | 0.1 – 0.5 mg/kg SC q 8hr | Centrally acting via multiple mechanisms  
May cause sedation |
| Mirtazapine                 | 1.9 – 3.75 mg/cat PO q 48 hrs Often given as ¼ of 15 mg tablet | 5-HT3 receptor antagonist  
Appetite stimulant |
| Cyproheptadine              | 1.0 – 2.0 mg/cat PO q 12-24 hrs | Do not give with mirtazapine (can be used as antidote for serotonin syndrome) |

References

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage (International Association for the Study of Pain).

Pain is a component of many diseases and procedures in the cat and is an important welfare issue, but it has only been commonly discussed in recent years. Unfortunately, pain is still underappreciated and undertreated in cats. Studies in Canada and other countries show that cats receive analgesics less often than dogs and analgesia is often withheld for fear of adverse consequences. An important barrier is that recognizing the signs of pain and its impact on quality of life is challenging in cats. However, the effects of pain are detrimental to the animal’s wellbeing in the short term, and pain interferes with healing and causes disease in the long term. Fortunately, therapeutic options have expanded as more pharmacological agents and adjunctive approaches are available.

Situations that require a pain management plan include:
- Peri-operative analgesia (before, during, and after surgery)
- Painful inflammatory or infectious conditions
- Non-surgical trauma
- Chronic painful conditions such as arthritis

Signs of pain are subtler in cats than in dogs and humans because cats may hide pain as a natural protective behavior. Cats should be considered similar to human infants, where pain evaluation is performed by assessing facial expression and body position. Physiologic parameters, such as heart rate, respiratory rate, blood pressure, and rectal temperature are poor indicators of pain in cats. The best way to assess pain in cats is to observe the patient before and during interaction and to evaluate body posture, facial expression, and response to handling, including palpation of surgical sites. Evaluations should be carried out repeatedly to monitor efficacy of analgesia and to determine if a change in the treatment plan is required. Ideally the same observer, which may be a trained veterinary technician, would score the patient during the entire hospitalization period.

Adult cats and seriously ill or obtunded patients are the most difficult to assess. Seriously ill cats may not be able to show behaviors associated with pain and yet may require management for severe pain. Adult cats are more stoic than kittens and their behavioral changes associated with pain may be subtle. As well, pain perception is an individual experience and behaviors vary among cats. Fear and stress may cause behaviors that are difficult to differentiate from pain. These factors make a standardized
assessment of pain difficult in cats. Return to normal behaviors is a sign of good pain control. Veterinary support staff can provide information on a patient’s normal behavior before surgery and owners can provide valuable insight into what constitutes normal behavior for their cat at home.

Some indicators of pain in hospitalized cats include:

- Inability to sleep or rest
- Hiding in the back of the cage, reluctant to interact
- Change in attitude – anxious, irritable, aggressive or dull and quiet
- Reaction on palpation of a surgical site or affected organ (e.g., ‘splinting’, tensing, withdrawal, vocalizing)
- Change in facial expression – staring, dilated pupils, squinting
- Lack of food and water intake
- Lack of grooming
- Change in resting posture – hunched or lying flat out

In the last few years, two acute pain scoring systems for cats have been developed and are undergoing validation. The UNESP-Botucatu multidimensional composite pain scale (www.animalpain.com.br) was developed with healthy cats undergoing ovariohysterectomy. It is relatively long (about 2.5 pages) and requires the ability to measure blood pressure. The Glasgow composite measure pain scale for acute pain in cats is shorter (1 page, 6 questions) and is based only on behavior assessment. The Glasgow researchers are working on the addition of a facial expression component.

Regardless of which scoring system is used, or even if a visual analog scale is used, veterinary hospitals should have a clear policy regarding assessment of pain in their feline patients, including when assessments are performed, who performs the assessments, what action should be taken if inadequate pain control is determined, and when the assessments should be repeated.

Recommended reading

