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The Acute Abdomen – An Overview

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Acute abdominal conditions are not uncommon in veterinary medicine. The history may be very non-specific and can include signs of lethargy or depression, anorexia, retching, vomiting, diarrhea and abdominal distention. The definition of an acute abdomen is a sudden onset of a painful abdomen; however, although these patients are usually painful on abdominal palpation, pain may not be clinically evident if the patient is in severe shock or is severely depressed. As they are being resuscitated these patients can often become excruciatingly painful. The clinician should have a very high index of suspicion that these patients may require surgery and serial abdominal exams (physical, ultrasonographic and cytological) should be performed with this in mind. Some of these patients can, and should be managed medically, and some require emergency surgery (within minutes to hours of presentation); therefore, it is important to be able to determine rapidly whether or not surgery is indicated. If there is any doubt it may be better to perform an exploratory laparotomy rather than wait and have the patient deteriorate.

Physical Examination

Patients with an acute abdomen may be unstable from a respiratory and cardiovascular standpoint. On presentation a primary survey examination (evaluation of level of consciousness, airway, breathing, and circulation) should be completed within 30 to 60 seconds. Abnormalities should be treated as indicated. For instance the patient that presents obtunded with shallow respiration should be intubated and positive pressure ventilation should be instituted. Not only will this help respiration but it will also protect the airway against aspiration. Depending on the severity of the patient's condition resuscitation may need to be instituted prior to completing a physical exam. A very brief history is obtained at this time if possible; however, resuscitation should not be delayed in the critical patient while a complete history is obtained. Instead permission should be rapidly obtained from the owner to allow treatment to be started.

A secondary survey, or complete physical examination, is completed once the primary survey is completed and resuscitation is instituted as indicated. Vital signs are taken at this time. Rectal thermometers may induce a vagally-mediated arrest in the severely bradycardic or hypotensive patient and should be avoided in these patients. Toe web temperatures can be taken and compared with rectal temperatures. If the patient is perfusing normally the ΔT (or the difference between the two temperatures) should be less than 7 degrees Fahrenheit. The jugular vein should be clipped and evaluated for distention since this will provide a crude estimate of central venous pressure. Patients with abdominal diseases may have concurrent pneumothorax, secondary aspiration pneumonia, metastatic disease, etc., and close attention should be paid to the ventilatory pattern, presence of cough, and bilateral auscultation of the thorax. The abdomen should be palpated, ausculted, and percussed with the goal of localizing pain, and detecting the presence of fluid waves, gas-filled organs, or solid masses. Auscultation should precede palpation since palpation can cause gut sounds to diminish. A rectal exam should be performed and the following should be evaluated: consistency of stool, evidence of blood, presence of foreign material or masses, dilation or contraction of the rectum, etc. (Rectal dilation in puppies with hemorrhagic diarrhea is almost always parvovirus enteritis.) The ventral abdomen should be clipped. Petechiation or ecchymoses may indicate thrombocytopenia, a coagulopathy or disseminated intravascular coagulation. Periumbilical hemorrhage may be seen with a hemoabdomen and periumbilical masses may be seen with pancreatic carcinoma. Distended superficial abdominal veins are consistent with increased intraabdominal pressure, almost always secondary to ascites or abdominal masses, which can be associated with decreased preload and decreased cardiac output.

Blood pressure should be considered one of the 4 vital signs and should be assessed as part of the initial exam since fluid resuscitation will depend to a large extent on the patient's blood pressure. A Doppler ultrasonic blood flow detector or an oscillometric device can be used; however, the Doppler is preferred since it allows the clinician to evaluate perfusion or flow as well as blood pressure. In addition arrhythmias can be detected with a Doppler.

Diagnostic Tests
Diagnostic tests are required frequently in order to determine the extent of the disease and to confirm the diagnosis. Resuscitation of the critical patient should not be delayed while tests are being performed unless those tests are required to guide resuscitation. Blood tests including packed cell volume, total solids, and glucose should be part of a STAT database. Many septic patients are hypoglycemic and require an immediate intravenous bolus of dextrose and dextrose supplementation in the intravenous fluids. An extended STAT database would include electrolytes, a blood gas (venous or arterial) and a creatinine. Ideally a complete blood count with microscopic evaluation of a blood smear for the differential and platelet estimate, prothrombin time, activated partial thromboplastin time, blood chemistries (especially albumin), fecal (if diarrhea is present), and urinalysis should be performed. The choice of tests may vary to some degree based on the presenting complaint. The advent of point-of-care devices has made it easy to assess many of these parameters within a matter of a couple of minutes.

Survey abdominal radiographs are always indicated. Chest radiographs should be evaluated preoperatively in every trauma patient, and in any patient in which aspiration pneumonia or metastases are a potential concern. Contrast studies including barium series, intravenous urography, cystography (single and double contrast), and angiography may be indicated. Water-soluble contrast material should be used instead of barium if there is any concern for gastrointestinal perforation or aspiration. Abdominal ultrasound can be very useful for diagnosing many causes of acute abdomen unless there is a significant amount of air within the peritoneal cavity and an AFAST is always indicated to assess for free fluid. Abdominal centesis or paracentesis should be performed in 4 quadrants. Ultrasound-guided centesis is preferred if available. Abdominocentesis may provide false negative results, and diagnostic peritoneal lavage should be performed if further assessment is indicated.

An electrocardiogram should be assessed for the presence of arrhythmias and tall T waves which are consistent with myocardial hypoxia/ischemia. Ventricular premature contractions and ventricular tachycardia are the most common malignant arrhythmias seen and are often associated with splenic disease in acute abdomen patients.

Diagnostic Peritoneal Lavage
Diagnostic peritoneal lavage allows for accurate evaluation of acute abdominal conditions. Four quadrant abdominocentesis can yield a high percentage of false negative results unless there is a large amount of fluid present whereas diagnostic peritoneal lavage has an extremely low incidence of false negative results. Results of lavage fluid examination are extremely useful in not only diagnosing a condition but also in determining the need to exploratory surgery in cases where the diagnosis is uncertain.

The animal is placed in left lateral recumbency with the goal of keeping the spleen away from the midline. Ideally the urinary bladder is emptied. A clip and surgical prep is performed of a 4 cm square area 2 cm distal to the umbilicus on the midline. A local block is placed in the skin and peritoneum 2 cm caudal to the umbilicus either on the midline or just lateral to the midline. Sedation is used if necessary. Surgical gloves are worn and ideally a drape is placed. A stab incision is made in the skin and a multi-holed catheter is inserted into the abdomen. In cats and small dogs an 18g 2 inch (5 cm) catheter is ideal. In medium and larger sized dogs a 16g or 14g 5.25 inch (13 cm) catheter is inserted. Side-holes should be added using a #15 scalpel blade. Alternatively a commercial diagnostic peritoneal lavage catheter can be used. The catheter is inserted in a caudal direction. If fluid is retrieved a sample is collected aseptically for analysis. To complete the lavage 20 ml/kg of warm (body temperature) isotonic crystalloid fluid is infused. Since this will increase pressure on the diaphragm, the respiratory rate and effort should be watched closely and fluid infusion stopped if the animal starts to show signs of respiratory distress. Once the fluid has been infused the animal is gently rotated to mix the fluid around and then fluid samples are collected for analysis. A packed cell volume, protein level, white blood cell count, and microscopic examination of the fluid should be performed. Cultures are indicated if bacteria are present. Blood chemistries such as amylase, lipase, alkaline phosphatase and bilirubin can be analyzed. Levels that are higher than serum suggest pancreatitis, intestinal disease, and biliary disease respectively. High potassium levels are consistent with urinary tract rupture. Urea nitrogen levels will equilibrate rapidly between the serum and peritoneum but in an acute bladder rupture the peritoneal level will be higher than serum. An abdominal glucose concentration that is greater than 20 mg/dL less than the serum

glucose is consistent with a septic peritonitis as is a blood to fluid lactate difference of less than 2 mmol/L. The catheter is removed and a dressing is placed over the incision. A suture or staple can be placed if desired.

Resuscitation

The goal of resuscitation is to reverse the signs of shock and provide effective oxygen delivery to the cells. Resuscitative efforts should be aimed at maximizing hemoglobin levels (oxygen-carrying capacity), blood volume and cardiac function. Patients presenting with signs of shock should have oxygen administered via flow-by. This can be followed with nasal oxygen supplementation if longer-term support is indicated. Temporary positive pressure ventilation may be indicated in patients presenting in severe shock who show an inadequate response to supplemental oxygen (improvement of respiratory rate and effort, mucous membrane colour, pulse oximetry, blood gas analysis).

If there is sufficient distention of the abdomen to interfere with ventilation, measures should be taken to remedy this. Trocarization or insertion of an orogastric or nasogastric tube should be placed if there is severe gastric distention secondary to air. In the gastric dilatation and volvulus patient, the stomach should be decompressed once fluid resuscitation has been instituted since rapidly relieving pressure on the vena cava may cause acute hemodynamic collapse; however, if the patient cannot ventilate, the stomach should be trocarized immediately. Severe abdominal distention from fluid accumulations may need to be addressed by drainage of the fluid. Dorsal recumbency should be avoided in these patients since the additional pressure on the abdominal vena cava can significantly decrease preload.

One or two large bore peripheral intravenous catheters should be placed. Resuscitation of these patients will often require a combination of both crystalloids and colloids. Buffered isotonic solutions such as Normosol-R, or Plasmalyte-A should be administered. These patients are often acidotic and administration of saline, which has a pH of 5.4, should be avoided. Saline must be administered to the patient with a metabolic alkalosis from a gastric outflow obstruction. Electrolyte abnormalities should be corrected based on blood test results.

Crystalloids rapidly redistribute to the interstitial space and only approximately 20% is left in the vascular space within 20 to 60 minutes. Crystalloids should be considered interstitial rehydrators and not intravascular volume expanders. Infusion of excessive volumes of crystalloids may lead to tissue edema which creates a barrier to oxygen diffusion. Synthetic colloids such as hydroxyethyl starch should be administered to any patient showing signs of significant hypovolemia. Colloids are large molecular weight compounds that are not capable of diffusing across intact membranes and are effective intravascular volume expanders.

Fluids should be infused to achieve or maintain a systolic blood pressure of 100-120 mm Hg, a diastolic blood pressure of 60-80 mm Hg and a positive central venous pressure. Although ideally an arterial line for direct arterial pressure monitoring should be placed in every critically ill patient, this is not realistic. If blood pressure is being monitored indirectly a Doppler is recommended. If patients do not respond to infusion of fluids (i.e., blood pressure remains low) and volume is assessed to be adequate then a vasopressor or positive inotrope may be indicated. Norepinephrine is the first choice in septic patients. Urine output should be monitored in patients in shock or with renal dysfunction. An indwelling urinary catheter may be indicated to be able to quantify urine production.

Whole blood or packed red blood cells should be administered to maintain a packed cell volume as close to 30% as possible. Autotransfusion may need to be considered if the patient has a significant hemoabdomen and large quantities of blood products are not available. Fresh frozen plasma should be administered to help maintain an albumin close to 20 g/L and to provide clotting factors to any patient with a coagulopathy. In large dogs albumin may be indicated. Patients with a prolonged prothrombin time, activated partial thromboplastin time (or activated clotting time), a prolonged buccal mucosal bleeding time, or significantly decreased platelets (<75,000 or 5/oil immersion field) may have a clinically significant coagulopathy. If in doubt it is always better to err on the side of providing coagulation factors and red cells. Preventing a problem from occurring is always better than trying to treat a problem once it has occurred.

Ventricular premature contractions should be treated if they are multifocal, are affecting perfusion (significant pulse deficits or alteration in peripheral flow as assessed by Doppler), if the heart rate is elevated (greater than

160-180 beats per minute), or if there is evidence of R on T phenomenon. Treatment includes the use of supplemental oxygen, ensuring tissue perfusion is being maximized, analgesics, and a constant rate infusion of antiarrhythmic drugs (lidocaine, magnesium sulfate).

Patients with an acute abdomen may present with hypothermia. Or they may become hypothermic during resuscitation secondary to intravascular infusion of large volumes of room temperature fluids. Hypothermia interferes with normal metabolic functions leading to vasodilation, cardiac dysfunction, and interference with the coagulation cascade. Core rewarming should be instituted since peripheral rewarming may lead to worsening of the vasodilation and subsequent worsening of the hypothermia. Artificial warming devices should be insulated from the patient since they can cause burns. Means of rewarming patients includes the use of warm water bottles, warm water circulating blankets, oat bags, warm blankets, and hot air circulating devices. Fluids should be infused at 104F in the hypothermic patient.

If the patient is vomiting or regurgitating a nasogastric tube should be placed for gastric decompression and initiation of early enteral feeding. Antibiotics may not be indicated in all cases; however, in general the patient should be started on broad-spectrum antibiotics to cover both aerobic and anaerobic bacterial infections.

Analgesia is a key part of treatment for most patients presenting with an acute abdomen. Non-steroidal anti-inflammatory drugs should be avoided due to their negative effects on splanchnic organs, and in some cases coagulation. Opioids such as butorphanol, hydromorphone, methadone, morphine, and fentanyl are recommended. They should be given intravenously since absorption from subcutaneous or intramuscular sites may be unpredictable. In cases of severe pain constant rate infusions may be required. Alternatively epidural analgesia can be administered. This is a very effective means of controlling pain and if an epidural catheter is placed repeat doses can be given. In the critical patients doses of opioids may need to be reduced to 25-50% of normal since the patients often cannot tolerate usual doses. For those patients who are not responding as desired to systemic analgesics a peritoneal lavage with or without local anesthetic may provide significant pain relief, especially in patients with pancreatitis or serositis.

Overview of Surgical Treatment

Surgical treatment is indicated in many acute abdominal conditions. The sun should never rise or set on gastrointestinal obstructions, ischemic abdominal diseases (organ torsions, vascular accidents), or peritonitis. The patient should be closely monitored while it is being resuscitated and prepared for surgery. Vital signs, blood pressure, central venous pressure, and electrocardiography should be evaluated as frequently as continuously to as infrequently as every 30-60 minutes if the patient is stable. All numbers should be recorded since often the trend of change is more important than the absolute numbers.

A team of a minimum of 3 people - surgeon, assistant surgeon and anesthetist/circulating nurse - is very important in the management of these patients. Balanced anesthesia with close monitoring of blood pressure and ventilation is essential. Isoflurane has no analgesic properties and pain medication should be administered intraoperatively if the patient appears to be perceiving pain. A Doppler blood pressure monitor for indirect pressure monitoring is very useful for this purpose and is strongly recommended. Many of these patients do not ventilate well under anesthesia and may require hand ventilation or preferably the use of a mechanical ventilator.

Appropriate patient positioning is obviously key to getting good exposure to the surgical site; however, patient positioning can potentially adversely affect hemodynamics and ventilation. Patients with abdominal masses that are hemodynamically compromised may be even further compromised when placed in dorsal recumbency. Abdominal masses, a large spleen or a full uterus can effectively occlude the abdominal vena cava significantly decreasing preload. Patients placed in dorsal recumbency with limbs held in an extreme extended position cannot ventilate well. Patients placed in a tilted position with the head down may have difficulty moving their diaphragm normally.

Due to the fact that a hollow viscus may be incised or the gastrointestinal tract may be compromised at the time of surgery, broad-spectrum antibiotics must be started prior to beginning surgery. A complete exploratory always should be performed. The skin incision should extend from the xiphoid to the pubis.

Incisions heal from side to side, not end to end, and morbidity is likely to be higher due to lack of visualization or poor surgical exposure than a long incision. A headlight is strongly advised. Time, trash, and trauma must be minimized. This means the surgeon must have a thorough knowledge of anatomy since surgery for the critically ill or injured can take you anywhere.

Since many of these patients have altered coagulation capability accurate hemostasis is important in order to minimize blood loss. Several factors will influence the body's natural ability to clot including blood pressure and tissue perfusion, the absence of coagulation factors, hypothermia and acidosis (respiratory or metabolic). The presence of clots or hematomas can lead to delayed healing as well as an increased likelihood of infection. Intraoperatively hemorrhage can be controlled using ligatures or vascular clips, electrosurgery, hemostatic agents, or by removing whatever is bleeding.

A conscious decision should be made in regard to placement of a feeding tube in each patient. Ideally a nasogastric tube should be placed in all dogs for postoperative decompression and early enteral feeding as well as with in cats with evidence of gastroparesis. Gastric decompression helps decrease the chance for bloat, decrease interference with diaphragmatic excursions, and has been proven to significantly decrease the time it take for normal gastric motility to return. A gastrojejunostomy or jejunostomy feeding tube should be considered in all patients with upper gastrointestinal surgery (including hepatobiliary and pancreatic surgery) if there are any concerns that enteral nutrition will not be able to be started within 24-36 hours.

"Dilution is the solution to pollution." The abdominal cavity always should be lavaged with warm isotonic fluids. The number of litres of saline used will depend to some extent on the degree of contamination. It has been recommended that approximately 200 to 300 mL/kg minimum – or until the lavage effluent is clear - be used to lavage a contaminated or infected abdomen. Gloves and instruments should be changed after lavage if there was any contamination during the surgery or if the gastrointestinal tract was entered. Cultures should be taken after lavage is performed.

Closure of the linea alba is performed using a simple continuous pattern of polypropylene or polybutester in the external rectus sheath. The peritoneum should not be closed.

Peritoneal drainage is indicated in cases of peritonitis if the source of the contamination has not been completely controlled, if an anaerobic infection is likely, if relaparotomy is planned or if significant peritonitis is present. The two most common options for peritoneal drainage include open peritoneal drainage and closed suction drainage.

Postoperative Care

Postoperatively the patient should be monitored in a similar fashion as it was preoperatively. The patient should be aggressively rewarmed. Vital signs should be returned to normal as soon as possible. The endotracheal tube should remain in place with the cuff inflated until the patient is awake and has a strong swallow reflex and is ventilating appropriately based on end-tidal CO_2 measurements. Regurgitation and aspiration can occur at any time and not infrequently occurs during recovery. For this reason the cuff should remain inflated until the patient is ready to be extubated. A nurse or doctor should remain with the patient until extubation. Lab tests should be run in the immediate postoperative period to ensure that parameters such as packed cell volume, albumin, electrolytes, creatinine and glucose are in the normal range.

Pain should be managed aggressively. Patients should receive pain medication on a schedule but also on an as needed basis since every animal's condition is different. Some opioids such as hydromorphone/methadone may last as long as 4 hours if the patient does not have an extremely painful condition but may last less than an hour if the patient is very painful. Good intraoperative pain control will help with postoperative pain control. Constant rate infusions are the most effective means of keeping patients comfortable.

References available on request.

Acute Pancreatitis

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Acute pancreatitis is one of the most difficult diseases a clinician can manage. The systemic inflammatory response syndrome can be severe in these animals. Major organ failure – refractory hypotension, liver failure, gastrointestinal failure, ARDS (acute respiratory distress syndrome), and DIC (disseminated intravascular coagulation) may develop. Only through aggressive medical management and sometimes surgical management can the clinician hope to minimize morbidity and mortality. Commonly used diagnostic tests do not necessarily correlate with severity of disease or prognosis, which means that the clinician should treat all pancreatitis patients as having potentially life-threatening disease. The ultimate diagnosis of pancreatitis is a histopathologic one which is rarely achieved. Aggressive fluid therapy, analgesia and nutritional support form the cornerstone of therapy. If patients have necrotic, abscessed or neoplastic pancreatic tissue present, the inflammatory process may not subside until the affected tissue is debrided. Surgery is rarely indicated but may be important in the management of some patients.

Pathophysiology

Multiple causes of pancreatitis have been identified but in most dogs and cats it is considered to be idiopathic. Regardless of the cause the pathophysiology is similar and ultimately is a result of activation of the pancreatic enzymes within the pancreas leading to autodigestion as well as digestion of the peripancreatic tissues and subsequent activation of the inflammatory process. If the inflammatory cascades persist unabated the systemic inflammatory response syndrome (SIRS) can result.

The systemic uptake of all of the products that are liberated during the inflammatory process can then lead to systemic inflammation and multisystem involvement. The protective plasma protease inhibitors such as α–2-macroglobulin and α–1-protease inhibitor are consumed as the necrotizing process continues. Alpha macroglobulins change the configuration of the proteases when they bind to them which allows macrophages to clear the enzymes. As the plasma protease inhibitors are depleted death can occur from acute disseminated intravascular coagulation and shock as the circulating proteolysis and cytokines activate the complement, coagulation, and fibrinolytic cascades.

Grossly pancreatitis progresses from that of edema and mild saponification and a few one millimeter sized abscesses to that of severe edema, numerous areas of saponification and many small abscesses. Then it progresses to hemorrhagic pancreatitis, localized peritonitis and edema of the surrounding tissues and advances to necrosis, larger abscesses, and the formation of very firm sections of cellulitis and pancreatitis (a phlegmon). In some cases bacteria are thought to translocate from the duodenal lumen and generalized peritonitis, bacterial abscessation, secondary biliary blockage and necrosis of the ventral aspect of the duodenum may occur. In the most severe cases the entire pancreas becomes involved. In some cases necrosis of fat that normally accumulates in the retroperitoneal space and falciform ligament may be present. Gastric and duodenal ileus are common.

Diagnosis

Animals with acute pancreatitis are usually presented because of depression, anorexia, vomiting, and in some cases, diarrhea. In severe cases shock and collapse may be present. In other cases the signs are very vague to almost nonexistent. Cats with mild pancreatitis are often presented with a vague history of being inappetent. Some animals with severe pancreatitis will exhibit signs of cranial abdominal pain and even a "praying" position. Pain may or may not be evident. Patients in shock may not show any signs of pain until perfusion is restored with fluid therapy. Occasionally the only clinical signs the patient exhibits are from systemic complications. Physical examination should include careful auscultation, palpation and visual inspection of the animal. Lack of gastrointestinal sounds is consistent with ileus, which may be localized or generalized. The right and left cranial

abdominal quadrants should be individually evaluated using palpation underneath the rib cage. Large dogs may need to have their front feet placed on a stool or chair to shift abdominal contents caudally. The umbilicus should be closely inspected since masses involving the umbilicus have been associated with pancreatic neoplasia. A rectal examination should be performed to evaluate for evidence of diarrhea as well as the presence of blood. Vomitus should also be evaluated for blood.

Although a leukocytosis with a left shift is commonly observed in more serious cases there may be no changes in the white cell number or types in milder cases. Red blood cell morphology should be closely examined, especially in cats, for signs of oxidant-induced damage (suggesting depleted glutathione levels). Assays of pancreatic enzymes (amylase, lipase) do not provide any useful information in dogs and cats. Species specific pancreatic lipase immunoreactivity (fPLI and cPLI) are sensitive (85-90%) for pancreatitis but some feel they are not very specific. Both SNAP and Spec tests have been validated. Spec tests are quantitative and repeat tests may allow for trending of the disease process. Liver enzymes and bilirubin may be elevated. If the inflammatory process has progressed then albumin levels may be decreased due to third-spacing. Blood gas abnormalities will reflect the degree of perfusion abnormalities as well as any possible secondary pulmonary involvement (aspiration pneumonia, ARDS). Electrolyte abnormalities typically reflect a combination of dehydration and losses through vomiting and diarrhea. Hypocalcemia may result from calcium soap formation, intracellular shifts due to alterations in membrane function, or altered levels of thyrocalcitonin and parathyroid hormone. Ideally ionized hypocalcemia should be assessed rather than total calcium. Coagulation profiles (PT, PTT, platelet counts or estimates) are indicated in sick pancreatitis patients in order.

Radiographs often reveal increased density, diminished contrast, and granularity in the right cranial quadrant of the abdomen, displacement of the stomach, widening of the "angle" between the antrum and the descending duodenum, and displacement of the descending duodenum to the right with gas patterns in the duodenum. The subjective loss of visceral detail in the cranial abdomen is probably the most common radiographic sign observed. In cats the loss of detail associated with pancreatitis is more commonly seen on the lateral view immediately caudal to the stomach and extreme lateral displacement of the duodenum does not occur.

Ultrasonic interrogation of the cranial abdomen will be helpful but is operator dependent. The appearance of mixed echogenicity or a mass effect within the pancreas as well as cystic areas, abscesses (complex cystic regions), edema, and free intraabdominal fluid are occasionally observed. Changes in the duodenum consistent with pancreatitis include a fluid and gas-filled descending duodenum, a thick-walled duodenum and atony. Caution should be exercised in ruling out pancreatitis on the basis of a normal ultrasound exam.

Medical Management

Supplemental oxygen should be provided to all patients showing signs of shock, typically using nasopharyngeal catheters. Aggressive fluid support is indicated. This requires a continuous rate intravenous infusion of a crystalloid and often colloids. Use a replacement formula to rehydrate the animal and replace fluids and electrolytes lost secondary to vomiting, diarrhea, and third spacing and plan to rehydrate over 6 to 8 hours. Colloids should be used immediately in more critical patients (hypotensive, evidence of hemorrhagic vomiting or diarrhea, systemically ill patient, hypoproteinemic, evidence of developing coagulopathy) to improve microcirculatory blood flow and help in the prevention of endothelial, interstitial and intracellular edema.

Albumin levels should be maintained above 2 mg/dL using plasma. Not only is plasma an important contributor to oncotic pressure but albumin is important also as a free radical scavenger. Plasma provides a source of α–macroglobulin, which binds the activated and liberated proteases. In the author's opinion fresh frozen plasma should be used during resuscitation if there is any concern that a coagulopathy is present or is developing.

To ensure adequate fluids are being administered adequate urine output (at least at 1/2 ml/kg/hr in cats, 1 ml/kg/hour in dogs), central venous pressure (3-7 cm H_20), and normal heart rate and arterial blood pressure should be maintained.

Pain kills. Analgesics should be provided immediately to patients in pain in adequate doses and at frequent enough time intervals to control the pain. Methadone and hydromorphone are effective intermediate acting pure mu agonists. Butorphanol may be indicated in very critical patients (0.05-0.2 mg/kg) and may be effective in cats, but it should be kept in mind that butorphanol may only last 20 to 60 minutes and is not very effective if pain is moderate to severe. A constant rate infusion of butorphanol may be helpful in more painful cats. Patients with severe pancreatitis may require continuous rate infusions of fentanyl. For those with intractable pain peritoneal lavage with lidocaine and bupivacaine is often very effective. Nonsteroidal antiinflammatory drugs (NSAIDs) should be avoided.

Antiemetics are usually indicated, maropitant being the most effective drug in most patients. Serotonin antagonists such as ondansetron hydrochloride or dolasetron can also be used. Metoclopramide may help improve gastrointestinal motility and clinically seems to be more effective given as a constant rate infusion (2 mg/kg/d) than when given as intermittent injections. Nasogastric (NG) tubes should be placed for gastric decompression in patients that have significant gastric distention with fluid or frequent large volume vomiting.

Nutritional support ideally should begin within 12 hours of admission. Partial parenteral formulas can be given by peripheral catheter. ProcalAmine (B. Braun Medical), which is a hyperosmolar solution containing 3% amino acids, 3% glycerol and maintenance concentrations of electrolytes, is an excellent partial parenteral nutritional support product. It is given at a rate of 0.5 mL/kg/hr as a constant rate infusion. Maintenance fluids to which 3% amino acids and 3-5% dextrose are added can be used instead of commercially prepared solutions.

Enteral feeding is always preferred over parenteral. Jejunal feeding is the ideal route since feeding in this location does not stimulate pancreatic enzyme secretion and is generally well tolerated. Patients that have surgery have an advantage since a jejunostomy or gastrojejunostomy tube can be placed. Evidence also suggests that gastric feeding may be possible in some patients. It is recommended that an NG tube be placed and used for gastric decompression as well as microenteral feeding. This trickle feeding (0.1 – 0.25 mL/kg/hr) of an electrolyte solution containing an isotonic mixture of electrolytes and 3 to 5% glucose is well tolerated. This will help prevent gastric stress ulceration, help prevent the down regulation of the gastrointestinal tract that occurs when the patient is not eating, and help improve the transition to full enteral feeding. This microenteral nutrition is only continued if hourly aspirations of the NG tube reveal no accumulation of this fluid in the stomach and/or no vomiting of the material is detected.

Close monitoring is essential in patients with severe pancreatitis. Monitoring should include regular (q 1 to 4 hr) measurement and documentation of level of consciousness, temperature, heart rate and rhythm, pulse rate and strength, respiratory rate and effort, blood pressure, central venous pressure (if a jugular catheter is in place), pain/analgesia, gastrointestinal sounds, amount and characteristics of vomitus and diarrhea, and volumes of fluid suctioned via the NG tube. Blood tests are indicated at least every 24 hours including packed cell volume, total solids, albumin, glucose, creatinine, electrolytes, blood gas, and blood smear evaluation. Additional tests (complete blood counts, other blood chemistries, radiographs, fluid analysis, etc.) may be indicated based on the status of the patient. All parameters should be kept in as normal a range as possible. More critical patients or those with clinically relevant abnormalities will require more frequent monitoring.

Indications for Surgery

A decision to perform surgery is made based on history, physical examination findings, laboratory parameters, and diagnostic imaging; however, many of these findings are nonspecific, especially in cats. One study showed that there was no definitive means of determining acute necrotizing pancreatitis from chronic nonsuppurative pancreatitis. The presence of septic peritonitis based on paracentesis or diagnostic peritoneal lavage, or a mass lesion found on ultrasound consistent with an abscess is an absolute indication for surgery. Other indications are more subjective.

Surgical exploration should be considered in patients with a waxing and waning history of recurrent pancreatitis in order to procure an exact diagnosis as well as determine if resolution of the disease is possible. Patients who have been diagnosed with pancreatitis that is not responding to medical management should be explored – again to diagnose the underlying cause, debride or resect necrotic, infected or neoplastic tissue, and place an enteral feeding tube.

References available on request.

Gizmos and Gadgets

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Crash Cart

A crash cart can be made from a handyman's cart with multiple drawers in it (available from any hardware store) or fishing tool box. Each drawer should be labeled. Foam padding can be used to line each drawer and holes can be cut out of the foam to hold tube and bottles in place. The first drawer should contain airway materials - endotracheal tubes, a long polypropylene 3.5 or 5 Fr catheter for instilling drugs intratracheally during CPR, forceps for removal of foreign material and a scalpel or Mayo scissors for surgical airways. Mechanic's helpers available from any automotive store make very useful grabbers for oral, airway and esophageal foreign bodies. Each endotracheal tube should have a partially inflated syringe attached to the cuff and gauze attached to the tube for securing the airway once it is in place. The second drawer should contain emergency drugs and syringes (1 cc and 12 cc) preloaded with 18ga needles. The third drawer should contain hypodermic needles, peripheral catheters of various sizes, butterfly catheters, and larger 13 cm 14g and 16g catheters for pericardiocentesis and diagnostic peritoneal lavage. Syringes, tape, number 15 scalpel blades for making side holes in catheters and a 35 to 60 cc syringe with an extension set and 3-way stopcock connected should be present. All equipment should be compartmentalized in order to visualize the retrieve the appropriate equipment rapidly. Instead of compartmentalization certain supplies can be placed in labeled zip lock bags. The fourth drawer should contain fluids and administration set, extension sets, t-ports and male catheter plugs. Buretrols are useful for making up smaller volumes of fluids with additives. Blood transfusion sets and filters ideally should be available.

AMBU Bag

AMBU bags are resuscitator bags with one-way valves. A section of corrugated tubing or a rebreathing bag is attached to the end of the AMBU bag to act as a reservoir for oxygen to be stored in while the AMBU bag is squeezed, delivering positive pressure ventilation to the patient. When using an AMBU bag, conventional or high frequency ventilation can be delivered easily without concern for the pop-off valve and worrying about matching flow rates to the rates needed during resuscitation. Because the hands of the ventilator are closer to the patient he/she can "feel" the pressure developing in the lungs much better than if using a rebreathing bag on an anesthetic machine. Also pure oxygen, not oxygen that is scented or containing any anesthetic gases can be delivered via an endotracheal tube or mask if assist ventilation is being attempted. In the former case this is important because even a small amount of anesthetic can have disastrous negative consequences in an animal that is arrested. In the latter case it is important in the conscious patient that frequently objects to the anesthetic.

"Y" Connector

Oxygen is given by tubing connected to the anesthesia unit by a "Y" connection. The oxygen hosing from the source to the anesthetic machines is removed at the insertion to the anesthetic machine. A "Y" connector is inserted at the tubing. If a "Y" connector is not available then a "T" connector from the plumbing section of a hardware store is used. One end of the "Y" is connected back into the anesthetic machine via a piece of suction or oxygen hosing. The other arm of the "Y" is connected to suction or oxygen hosing and coiled up for use in emergency situations as oxygen tubing. The "Y" has 2 clamps on it- one going to the anesthetic machine and one going to the oxygen tubing. If oxygen is required the clamp is closed going to the anesthetic leading to the anesthetic circle to prevent oxygen going anywhere than to the oxygen hood, mask, nasal cannula or AMBU bag. The tubing and connectors are all available through medical supply companies but can also be purchased in home hardware stores. A commercially available mare uterine flush system can also be used in place of "Y" or "T" connectors.

Oxygen Hood (Collar)
These can be made from Elizabethan collars and plastic food wrap or it can be commercially purchased. Homemade collars should have the top ¼ of the collar open to the air. The oxygen tube is placed into the collar from the neck side and taped in place to the inside of the collar and to the outside of the collar to prevent accidental dislodgement. A roll of 1" or 2" tape taped to the outside of the underside of the collar will create a pendulum effect and help prevent the collar from rotating. Oxygen flow rates vary from 1-10l/min depending on the size of the patient. The oxygen should not be humidified to prevent moisture build-up. The patient must be monitored closely for signs of overheating – especially if the patient is panting.

Foerster Sponge Forceps
These 10" slightly curved sponge forceps should be always available for the retrieval of oral, pharyngeal and upper airway foreign bodies. A gauze sponge can be placed in the jaws and the oropharynx can be swabbed effectively to help clear an airway obstruction of mucus, blood or vomitus without having to insert fingers into the mouth of the animal. They can also be helpful when used across the hilus of the lung or spleen when these are badly traumatized and hemorrhaging badly.

Velsellum Forceps
These straight forceps have jaws with 2 sharp prongs on each side. They are very useful for grabbing smooth objects such as rubber balls that become lodged in the oropharynx.

Brake Line Suction Unit
This is a hand-held suction unit used to clear air from brake lines. It is a very effective device for suctioning airways and will generate pressures of up to 760 mm Hg. A fluid trap can be placed between the suction tubing and the suction tip to avoid having fluid accumulate in the suction unit. It can be purchased from hardware and automotive stores.

Clear Endotracheal Tube
Endotracheal Tube - The clear low pressure, high volume cuffed tube is the preferred to opaque tubes. This is because of the ability to monitor the inside of these tubes for a vapour trail or the lack of it, blood, vomitus, etc. The cuff is much safer than those in many other types since it is lower pressure than the red tubes. The cuff inflating mechanism has a one-way valve on it, making it easier to inflate. Red tubes tend to become more brittle with continued use and may create more trauma to the tracheal mucosa.

Tracheotomy Tube - The connector is removed from the end of the tube. Two incisions 180 degrees apart are made in the tube, peeling it down like a banana. Care is taken to keep the cuff inflation mechanism intact. The incisions are made so that the intact section of the endotracheal tube is the right length for the patient (i.e. from the tracheotomy incision to the thoracic inlet). The plastic connector is reattached to the tube and the split pieces are connected to gauze or sections of umbilical tape.

Chest Tube - This can be made out of a clear disposable endotracheal tube and the use of a bone rongeur to make side holes. The cuff inflation tubing needs to be tied off. The chest tubes can be sterilized by ethylene oxide or glutaraldehyde.

Mouth Gag – Sections of 3-4 mm endotracheal tube can be used to make mouth gags.

Copper Wire
Copper wire that is sanded on the tip makes a malleable stylet for endotracheal tubes. The size of the cooper wire can be adjusted based on the size of the endotracheal tube.

Fluid Bags
Closed Collection Systems - Partially or completely empty fluid bags should be kept sterile and saved for use as urine collection bags for closed systems. The drip set can be left attached to the bag and tied off so it won't be used further, or the bag can be emptied, a new drip set is attached and the entire unit is sterilized as a closed collection system.

Irrigation Fluids - Intravenous fluid bags are sterile inside the outer wrap. If the outer wrap is properly opened the bag can be placed on the surgical table and used by the surgeon as sterile lavage fluids.

Dressings - Fluid bags can be emptied and opened to be used as sterile waterproof dressings for open abdominal drainage. This is ideal if there is tension due to abdominal packing, bowel edema, bowel distention, or any other situation when closure may create abdominal compartment syndrome (excessive intraabdominal pressure). The bag can be sutured in place to provide a complete seal. If only a temporary, non-waterproof closure is indicated it can be secured to the wound edges using safety pins.

Fluid bags make strong waterproof coverings to protect foot bandages from getting wet.

Autotransfusion Sets – Empty fluid bags can be sterilized with a blood administration set and kept ready for use as autotransfusion sets. The blood is collected into syringes or sterile suction bottles and then placed into the fluid bag and delivered to the patient.

Enteral Feeding Bags – Empty fluid bags can be filled with liquid enteral feeding formulas and dripped through a regular fluid administration set. The bag should be washed out with very hot water every 24 hours to prevent residue build-up and avoid bacterial contamination.

Fluid Administration Set Drip Chamber
Tracheostomy - The drip chamber is cut in half. The spiked end can be inserted in an emergency into the trachea as a transtracheal cannula. The open end will fit exactly onto an AMBU bag so that the patient can be ventilated. Since the spike is made of hard plastic that can damage the trachea, this device should not be used except in a dire emergency. As packaged these drip sets are sterile. A feeding tube can be placed into the trachea via the drip chamber and the chamber can then be removed. This provides transtracheal access for delivery of oxygen.

Tracheal Prosthesis – The drip chamber is cut into thin sections and sutured in place as a tracheal prosthesis for surgical repair of tracheal collapse.

Fluid Administration Set Line
Used fluid lines can be recycled and used as ties for endotracheal and tracheostomy tubes. The line is cut into sections of a suitable length and kept in a bag beside the anesthetic machine. The line should be stretched prior to use which will help the knot stability.

Syringe Case
Oropharyngeal Airway - A syringe case with the end cut off makes an effective oropharyngeal airway. This can be used in times of emergency when there is significant oral trauma but the larynx and trachea are functional.

Mouth Gag – The end of the syringe case is cut off and both ends are padded with gauze or tape. The case can then be inserted between the upper and lower canines as a mouth gag.

Tail Protector – Sutured tail wounds tend to rebleed when the dog knocks its tail. The plastic case is placed over the lightly padded bandage on the tip of the tail. When the tail wags the sutures are protected and repeat

hemorrhage is minimized.

Mask – The end of a large syringe case is cut off and a hole is made in the tip of the case. This can be attached to oxygen or to a gas anesthetic circuit for birds, pocket pets and other small patients.

Syringes
Mouth Gag – The ends of the syringes are cut off and both ends are padded with gauze or tape. The syringe tubing can then be inserted between the upper and lower canines as a mouth gag.

Tubing Connector – The plunger of a 1 cc syringe is withdrawn and discarded. The base of the barrel is cut off. The tip will fit all narrow gauge tubes and the barrel end will fit almost all suction hosing and oxygen hosing.

Suction Drain – The plunger of the syringe is withdrawn approximately two-thirds of the length of the barrel and an 18 ga needle is placed across the base of the barrel to stop the plunger from depressing. The tip of the needle is cut off to prevent injury. The needle is withdrawn and the plunger is depressed fully. The syringe is then attached to the suction drain and the plunger is withdrawn. The needle is reinserted creating steady negative pressure.

Slam Bags
Fluid Infusor - Fluids often need to be given rapidly to patients in hypovolemic shock. This requires that the fluids be delivered under pressure. A pressure infusor bag is an effective way of delivering pressurized fluids. The fluid bag is inserted into the pressure infusor bag and the pressure then can be inflated up to 300 mm Hg.

Pressure Cuff – The bag can be placed proximal to or over the site of a large bleeding wound (with or without padding). The bag can be inflated to a sufficient pressure to control active hemorrhage. In small animals this can be used as an abdominal counterpressure wrap (see below).

Blood Pressure Cuff
Hemorrhage Control - A Doppler blood pressure cuff can be placed proximal to a bleeding wound and inflated to 20-40 mm Hg above systolic pressure. This will control arterial hemorrhage to the region. This is especially useful for distal limb hemorrhage. Adult human thigh cuffs can be used as abdominal counterpressure wraps in small patients (see below).

Feeding Tubes
Three and a half, 5 and 8 French feeding tubes can serve multiple purposes - especially if they are made of minimally reactive material such as medical grade silicone.

Nasal Tubes – Feeding tubes can be placed with the tip in the nasopharynx or in the trachea to deliver oxygen into the respective sites. They can be placed into the esophagus or stomach and used as nasoesophageal or nasogastric tubes for decompression and feeding.

Intravenous Catheters - They make effective long central lines in dogs in which the commercial lines are too short. A 14 ga or 16 ga over the needle 2 inch catheter is inserted into the vein. A 5 Fr or 3.5 Fr feeding tube, respectively, is inserted through the catheter to the desired length. A few drops of 50% dextrose placed on the outside of the feeding tube will help the tube slide easier through the catheter. The catheter is withdrawn from the vein and the feeding tube is sutured in place and a sterile dressing is placed.

Vascular Loops - When using as a vascular loop the tube is passed around the vessel or vascular pedicle and the loop is tightened by sliding hemostats down the tubing and tightening on the vessel. This is a modified Rumel tourniquet.

Bubble Wrap
Splints - Bubble wrap makes effective lightweight splints for distal limb fractures. Radiographs can be taken through bubble wrap.

Blanket - It also can be heated in a microwave in a bowl of water to create a warm "blanket". This can be particularly useful in the operating room.

Oxygen Tent - When placed over the front of a cage it creates an effective "oxygen tent".

Towels
Abdominal Counterpressure - Towels can be wrapped around the pelvic limbs and abdomen of a patient and anchored with duct tape to serve as external counterpressure wraps. When doing this a towel first should be placed as padding between the pelvic limbs. A second towel is placed around the pelvic limbs wrapping from the toes to the hips in a barber pole fashion. The wrap is continued then around the abdomen to the level of the diaphragm if needed. It is anchored in place with duct tape. Care should be taken not to wrap the towels too tightly. Two fingers should easily be able to be placed under the abdominal counterpressure wrap once it is in place.

Surgical Paper Drape
Surgical drape material makes an effective water repellant outer layer for bandages. It can be sutured in place or tied in place using umbilical tape to provide a water repellant outer layer for open abdominal drainage bandages. It can be safety-pinned or taped in place to cover larger wounds.

EMMA®
The EMMA (Masimo, Irvine, CA) is a portable battery run capnograph. Within as short a period of time as 15 seconds the device will provide a respiratory rate and continuous capnogram and an end-tidal carbon dioxide measurement ($ETCO_2$). It is waterproof and has been designed to withstand being dropped. Capnography provides a continuous noninvasive assessment of ventilation and the $ETCO_2$ provides an estimation of the $PaCO_2$. The $ETCO_2$ provides information about pulmonary blood flow in the face of severe hypotension. During anesthesia if the $ETCO_2$ drops below 18 mm Hg the arrest is imminent. During CPR if the $ETCO_2$ rises to 15 mm Hg or higher return of spontaneous circulation is very likely.

Radical 7®
The Radical 7 (Masimo, Irvine, CA) is a portable pulse oximeter that continuously calculates a plethysomographic variability index or pleth variability index (PVI). The PVI is an assessment of changes in the amplitude of the pulse oximetry waveforms during different phases of respiration. Patients do need to be mechanically ventilated to maintain consistency in changes in intrathoracic pressure. In the face of hypotension the PVI will indicate whether a patient is likely to be fluid responsive or not.

Kitty Kollar®
The Kitty Kollar® (Orange, CA) is a collar designed to replace a standard bandage for an esophagostomy tube. It is made of a soft padded washable fabric. The tube exits the collar through a buttonhole and a Velcro hook and loop fastener secures the tube to the collar. The collar is secured around the patient's neck with a Velcro tab.

References available on request.

Metabolic Nightmares:
Tricks for Managing Acute Renal Failure and Diabetic Emergencies

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Appropriate management of acute renal failure and diabetic emergencies requires that appropriate attention be paid to the patient's metabolic abnormalities. This lecture will discuss treatment of these two diseases with a focus on how understanding the electrolyte and acid-base abnormalities can lead to decreased morbidity and mortality.

Chloride

Chloride values must be corrected to take into account any changes in plasma free water before assessing whether or not the chloride concentration is low, normal or elevated. This is calculated by the following formula:

$$[Cl^-]_{corrected} = [Cl^-]_{measured} \times 156/[Na^+]_{measured}$$

The number of 156 is used in cats under the assumption that 156 mEq/L is the mean sodium concentration in cats. The number 146 should be used in dogs. This corrected value can have a significant impact on the choice of fluid therapy in certain conditions. For instance a ketoacidotic diabetic cat with a sodium of 140 mEq/L and a chloride of 118 mEq/L may become even more acidotic if 0.9% saline is infused. The corrected chloride in this situation is 131 mEq/L which is already a contributing factor to this cat's metabolic acidosis. There is a potential that this will only be worsen if 0.9% saline is infused.

Renal Failure

The primary goals of therapy are the following:
Normalize renal blood flow
Establish urine output
Normalize electrolytes and acid-base status
Diagnose the cause of the real failure and provide specific treatment
Provide nutritional support

Mean arterial blood pressure must be maintained at greater than 65 mm Hg to ensure renal perfusion. This means that both systolic and diastolic pressure must be measured. If diastolic pressure is not being measured it is essential that systolic pressures be maintained as close to normal as possible. Systolic pressures less than 110 mm Hg can be associated with mean arterial pressures less than 60 mm Hg.

Blood pressure can be normalized in most patients using fluid therapy. A combination of crystalloids and colloids should be used. In order to ensure blood volume (preload) is optimized a jugular catheter should be placed so that central venous pressure can be measured. If a jugular catheter is not an option then the jugular veins should be clipped and carefully assessed.

Fluid therapy must be closely tailored to the animals needs and should be based on cardiac status, volume status (central venous pressure), dehydration, sodium concentration, potassium concentration, albumin, and type of renal failure (polyuric, oliguric or anuric).

Dehydration should be restored using crystalloids. Generally buffered electrolyte solutions are indicated. Fluids containing potassium must be avoided in the hyperkalemic patient until urine output is restored and the potassium level is starting to decrease. Patients who are hypernatremic may require fluid with low sodium concentration. Patients who are hyponatremic are often volume overloaded and both sodium concentration and fluid rates need

to be monitored carefully. Patients who developed the dehydration rapidly should be rehydrated over 4-8 hours. Those with chronic dehydration should be hydrated over 12-24 hours. Hourly maintenance requirements should be added to this amount along with ongoing losses. Ongoing losses in patients with polyuria can be significant and urine output in these patients must be measured to ensure fluid requirements are not underestimated. Anuric patients may not even tolerate the amount of fluids required to restore dehydration until urine output is restored. If diuresis is the end goal then fluid will need to be adjusted to ensure urine output is greater than 2 ml/kg/hr.

Urine output in hypovolemic or hypotensive patients hopefully will be restored once perfusion to the kidneys is improved. If the patient is not responding several options are available. Mannitol is a hyperosmotic agent that causes an osmotic diuresis, which flushes the tubules. It also has benefits as a free radical scavenger. It is dosed at 0.25 g/kg over 15-20 minutes. This dose can be repeated if it is effective and it can be followed with a constant rate infusion at 1 mg/kg/min until it is no longer effective. It should be used with extreme caution, (and preferably not used) in patients that are hypervolemic since volume overload will result if diuresis does not result. Dextrose at 5% -20% concentrations can be used as an osmotic diuretic if mannitol is not available. The dextrose will be metabolized ultimately making this perhaps a safer choice than mannitol.

Furosemide is a loop diuretic that is most effective when given as a constant rate infusion. A bolus dose of 1-2 mg/kg can be given intravenously followed by a constant rate infusion of 1 mg/kg/hr. If there is no response after 4 hours it is less likely to be effective.

Dopamine at dopaminergic doses (0.5-3 mcg/kg/min) is designed to impact dopaminergic receptors in the kidneys and improve renal perfusion and thus renal function. There is no clear evidence this occurs. The cat lacks the appropriate dopaminergic receptors in the kidneys and one study showed no improvement in urine output, sodium excretion or glomerular filtration in cats given dopamine.

Patients in renal failure may have significant acid-base abnormalities. Acidemia related to perfusion abnormalities should correct once perfusion is restored. Dogs and cats with chronic renal failure often lose large amounts of bicarbonate in their urine due to kidney dysfunction. This is more common in the cat than the dog. These cats must be supplemented with bicarbonate or their values will never return to normal. In the author's experience these cats often require much higher doses of bicarbonate than is typically recommended. In addition the anorexia and nausea seen in cats often improves once the acidemia is improved. These cats often will require oral supplementation to maintain normal acid-base status. Bicarbonate is typically supplemented at 0.3 x kg body weight x deficit (18- measured bicarbonate level) with ¼ of this dose given over 1 hour and the remainder over the next 12 hours. If blood gas assessment is readily available this dose can be given more quickly. If blood gases are not available but total carbon dioxide levels are the bicarbonate can be estimated by the total carbon dioxide minus 1. Bicarbonate supplementation should not be provided if measured levels are not available since the side effects can seriously outweigh the benefits.

Patients in anuric renal failure will develop hyperkalemia. Hyperkalemia should be treated if it is lifethreatening as determined by evidence of significant electrocardiographic abnormalities in combination with clinical signs. Ultimately unless the animal is able to urinate the hyperkalemia will persist. If anuria persists dialysis is indicated.

Vomiting can be a substantial problem in patients with renal failure. If large volumes of fluid are being vomited a nasogastric tube should be placed for gastric decompression. This tube can then be used for delivering microenteral nutrition. Uremia triggers vomiting centrally and central acting antiemetics are likely to be the most effective at controlling vomiting. Uremia can be associated with gastric erosions and ulcerations. Administration of H-2 blockers or omeprazole and sucralfate may be indicated and are definitely indicated if there is evidence of hematemesis. Enteral nutrition has been shown to be as effective as, if not more effective than, antacids at preventing gastric ulceration. Oral ulcers are not uncommon in patients with renal failure. Oral rinses using 0.005% chlorhexidine can help prevent infection. Rinses with topical anesthetic agents have also been used anecdotally by the author to try and minimize the pain associated with the ulcers.

Nephrotoxic drugs should be discontinued and specific treatment aimed at the cause of the renal failure should be instituted as soon as possible. Hyperphosphatemia may resolve with fluid therapy; however if the hyperphosphatemia persists then phosphate binders should be administered orally once the patient is eating.

Patients with chronic renal failure may be hypertensive. Amlodipine, a calcium channel blocker, has been found to be the most effective in treating hypertension caused by renal disease. Blood pressures greater than 200 mm Hg systolic can lead to retinal detachment and should be aggressively managed.

Diltiazem has been recommended as an agent to help with renal failure associated with ischemia. It appears to decrease the intracellular calcium levels following ischemia thus decreasing the production of reactive oxygen species. It also prevents apoptosis. The dose recommended is 0.3-0.5 mg/kg over 10 minutes followed by 1-5 mcg/kg/min for 48-96 hours or as long as it takes to decrease the serum creatinine concentration to normal. The dose should be decreased if bradycardia or hypotension develops.

Angiotensin-converting enzyme (ACE) inhibitors (enalapril) are used to treat protein-losing glomerulonephropathy. The drug appears to attenuate glomerular hypertrophy and preserve glomerular function. In addition it may help control hypertension. Angiotensin-converting enzyme inhibitors should be used with caution in the acute stages of renal failure since the drug can decrease glomerular filtration rate and worsen azotemia. It can also cause hypotension and should be avoided in hypotensive patents.

Antibiotics should be administered based on culture and sensitivity results; however, occasionally, antibiotics may need to be administered without confirmation. Prophylactic antibiotics should be avoided in patients with indwelling urinary catheters since these patients are predisposed to infection and the use of antibiotics will lead to microbial resistance. Doses or dosing intervals may need to be adjusted based on creatinine levels.

Analgesics should be provide to all patients showing signs of pain. Nonsteroidal antiinflammatory agents should be avoided. Opioids should be given intravenously to effect and constant rate infusions may be required.

Diabetic Ketoacidosis

Diabetic ketoacidosis is a life-threatening complication of diabetes mellitus characterized by metabolic acidosis, hyperosmolality, and electrolyte disorders. These patients have diabetes mellitus compounded by another significant illness such as a urinary tract infection, pancreatitis, cholangiohepatitis, hyperadrenocorticism, pneumonia or an abscess leading to an increase in diabetogenic hormones such as cortisol, epinephrine, glucagon and growth hormone. The absolute insulin deficiency and insulin resistance from the secondary infection or inflammatory disorders leads to a significant cellular energy deficit. In an attempt to keep up with energy requirements the ensuing lipolysis leads to excessive hepatic production of ketoacids. The metabolic acidosis is primarily related to the ketoacids but can be complicated by a lactic acidosis that develops secondary to perfusion abnormalities. Ultimately the body's normal buffer systems are overwhelmed.

Electrolyte disorders include hyponatremia, hypokalemia, and occasionally hypomagnesemia. Hyponatremia may be due in part to the hyperglycemia but is usually compounded by urinary losses as well as the possibility of third spacing into the gastrointestinal tract or peritoneal cavity. Hypokalemia can occur secondary to loss in the urine from the osmotic diuresis as well as vomiting. The presence of hypokalemia in the face of a significant acidosis should alert the clinician to a severe total body potassium depletion which will worsen substantially when insulin therapy is instituted. The electrolyte disorders are compounded by the ketoacids which worsen the osmotic diuresis of a normal diabetic as well as the aggressive fluid therapy that is provided during treatment. In addition hypomagnesemia may develop secondary to increased free fatty acids which bind the magnesium as well as insulin which can shift magnesium intracellularly. Because measurement of serum levels (total magnesium or ionized) may not reflect total body stores, hypomagnesemia should be considered in patients with refractory hypokalemia or hypocalcemia or unexplained weakness or gastrointestinal motility abnormalities. Mild hypomagnesemia rarely causes clinical signs.

The diagnosis of diabetic ketoacidosis is made based on the history as well as laboratory findings of hyperglycemia, ketonuria and a metabolic acidosis. Patients that are known diabetics or are ketotic with normal or only mildly elevated blood glucose levels are usually in severe decompensatory shock and mortality rates are high. There are three ketoacids – acetoacetic acid, β–hydroxybutyric acid and acetone. The urine test strips only confirm the presence of acetoacetic acid and acetone as do the routine serum tests. The β–hydroxybutyrate is the most common ketoacid formed in shock states and not until insulin treatment is instituted, which converts the β–hydroxybutyric acid to acetoacetic acid, will the tests show a positive result. Blood gas results showing a metabolic acidosis with a severe base deficit but evidence of only a mild or moderate decrease in the bicarbonate concentration are consistent with unmeasured acids such as ketoacids.

The goals of treatment are to restore normal perfusion, provide insulin to ensure the cells are no longer energy deficient and the ketoacids become metabolized, correct electrolyte abnormalities, and treat any underlying additional illness.

Oxygen should be provided to patients in shock. Intravenous fluids (balanced electrolyte solution) should be provided and dehydration should be corrected over 4 to 12 hours unless the patient is at risk for fluid overload in which case hydration may need to be corrected over 24 hours. Normal saline may not be the ideal choice since the hyponatremia will correct as the glucose concentrations normalize which can lead to a hypernatremia and the chloride load can lead to a worsening of the metabolic acidosis. Synthetic colloids may be required if the patient is hypoalbuminemic secondary to concurrent disease process. Insulin therapy is generally begun several hours following initiation of fluid therapy although it may be more appropriate to start it as soon as possible. Constant rate infusions are easier to regulate than intermittent injections but require closer monitoring. Giving insulin into the intramuscular and subcutaneous tissues can lead to unpredictable uptake due to altered perfusion. This can lead to a depot effect followed by a rapid uptake of insulin at some later stage leading to significant rapid decreases in glucose levels. It would be ideal to maintain tight glycemic control with glucose levels ideally maintained between 100 and 200 mg/dl but this usually is not possible. Glucose levels should be maintained below 300 mg/dl and rapid shifts in glucose levels should be avoided in order to minimize the likelihood of causing cerebral edema. Hypokalemia secondary to intracellular fluid shifts secondary to correction of the metabolic acidosis as well as insulin therapy which drives both potassium and glucose intracellularly, is not uncommon. Hypophosphatemia can develop secondary to dilution, diuresis, and the increased production of ATP as glucose is driven intracellularly and can be a life threatening complication. Requirements for phosphorus supplementation are often much higher than what is recommended. Ultimately nutritional support will be required, preferably via the enteral route. Long acting insulin is not recommended until the patient is well hydrated and eating and the ketoacids have been metabolized. Close monitoring of these patients is essential if patient morbidity – and mortality – is to be minimized.

Hyperglycemic Hyperosmolar Syndrome

Hypoglycemic hyperosmolar syndrome or hyperosmolar hyperglycemia nonketotic syndrome is an uncommon condition that can be diagnosed in preexisting diabetics and in those who have been never been diagnosed with diabetes. It is characterized by a hyperglycemia of greater than 600 mg/dL and an osmolality of greater than 350 mOsm/L. Ketonuria is not present. Common clinical findings include severe dehydration, renal dysfunction and brain dysfunction. The disease has a very poor prognosis in large part because congestive heart failure and renal failure are frequently found in association with the syndrome.

The goal of treatment is to reduce the glucose levels slowly to avoid rapid shifts in cerebral osmolality. Idiogenic osmoles have developed over time in the brain to counteract the effects of the hyperglycemia; therefore, if the plasma osmolality is decreased too rapidly cerebral edema will develop. Hyponatremia is commonly found in association with hyperglycemia. This is a normal physiologic response by the body to the hyperosmolality although other causes for hyponatremia must be ruled out. Changes of greater than 1 mEq/hr in the plasma sodium concentration should be avoided so close monitoring of electrolytes (hourly initially) is essential. Fluid therapy should be tailored according to the response of the patient to treatment. The cornerstone of therapy is to

increase the glomerular filtration rate to allow the kidneys to filter the glucose. Due to the fact that heart disease and renal disease are often present in these patients, high fluid rates are often not tolerated making management of this condition complicated. If the patient is not tolerant of high rate intravenous fluid therapy, enteral fluid therapy may also need to be initiated. Insulin therapy should be instituted once the patient is rehydrated. The recommended starting dose is 50% of that used for treatment of diabetic ketoacidosis.

Hypoglycemic Crisis

Severe hypoglycemia can occur in diabetics that have been overdosed with insulin. The overdose may be an acute problem where the patient is double-dosed inadvertently. It is also associated with an inadequate decrease in the face of decreased food intake or a Somogyi effect. The latter is very common when glucose curves are not being performed and insulin doses are increased based solely on the finding of a single elevated blood glucose level or when changes in insulin dosing are based on laboratory results as opposed to clinical status (i.e., resolution of polyuria, polydipsia and weight loss. In cats it can occur when the animal reverts back spontaneously to being a non-diabetic or a non-insulin-dependent diabetic.

The brain is an obligate user of glucose and has a very poor ability to use other energy sources, nor does it have a significant store of glycogen. This means that neural tissue can be severely and sometime permanently damaged by neuroglycopenia. The degree of damage will depend on the severity of the hypoglycemia as well the duration of the hypoglycemia. Abnormal mentation, seizures and blindness can persist even after resolution of the hypoglycemia.

Hypoglycemic patients should receive an intravenous bolus of 1-2 ml/kg of 25% dextrose. This should be followed immediately with a constant rate infusion of 2.5% to 5% depending on the severity of the hypoglycemia. If seizure activity does not resolve a blood glucose level should be checked immediately since hypoglycemia may not be the sole cause of the seizure activity. A blood glucose level should be checked within 15 minutes to ensure the patient's glucose has normalized. If it is still low another bolus should be given and the infusion should be increased by 2.5%. This process should be repeated until the blood glucose has normalized. Some patients may require 10% dextrose infusions. Infusions of greater than 5% dextrose ideally should be administered via central lines due to the hyperosmolality. If placement of a central line is not an option then the smallest gauge catheter possible should be inserted. This should improve the blood flow around the catheter relative to one of a larger diameter which should help decrease the likelihood that phlebitis will develop.

References available on request.

Nutritional Support: Tubes, Tubes, Tubes

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Why is nutrition support important in the critically ill or injured patient?
Adequate nutrient intake is necessary to provide energy for cellular function, substrates for protein synthesis and, vitamins and minerals for daily metabolic processes and maintenance of homeostasis. Hypermetabolism is characteristic of the acute illness or injury and a catabolic state rapidly develops. Anorexia associated with severe injury or sepsis has been shown to lead to: glycogen depletion within 8 to 12 hours leading to muscle weakness, substantially decreased fibronectin levels within 48 hours of anorexia contributing to immune dysfunction, and decreased protein synthesis. The deleterious effects of malnutrition are more pronounced in the acutely ill or injured patient due to the higher metabolic rate necessary to increase liver and immune function as well as provide substrates for wound healing. Experimental and clinical research has emphasized the importance of beginning enteral nutritional support as early as possible to prevent immune system depression, serum albumin decreases, muscle weakness, bacterial translocation, infection, major organ failure, and death.

How do I decide to feed enterally or parenterally?
Enteral feeding is preferred over parenteral feeding whenever possible as it is more physiologic. It is also less expensive than total parenteral nutrition and it avoids the risk of catheter-related sepsis. When compared with total parenteral nutrition, enteral feeding has been shown to maintain gut mucosal integrity thus decreasing bacterial translocation, improve lymphocyte function, improve wound healing and improve survival from peritonitis. The adage of "if the gut works use it" should be followed as much as possible. During severe injury or infection gut perfusion may be inadequate and the gut mucosal barrier may become compromised leading to bacterial translocation. Lack of luminal nutrients leads to mucosal atrophy and destruction of the gut barrier. Early enteral feeding has been found to blunt the release of stress hormones thus reducing the elevation in metabolic rate. Parenteral nutrition should only be used if the gut is not accessible or is not functioning adequately. This includes patients with GI obstruction, peritonitis, intractable vomiting, acute pancreatitis, short bowel syndrome and ileus. Parenteral therapy has no beneficial effects on the course of inflammatory bowel disease or pancreatitis and enteral feeding should be considered as a first line of therapy.

What is meant by parenteral nutrition and how is it administered?
Parenteral nutrition is comprised of total parenteral nutrition (TPN) and partial parenteral nutrition (PPN). PPN provides a 3% amino acid solution and is usually supplemented with carbohydrate source (glycerol, dextrose) to prevent all the amino acids from being used as a glucose source. It may also contain lipid.It should be kept in mind that amino acids and glycerol are bacteriostatic, but lipid and dextrose are not. TPN provides amino acids, glucose and fat. Both solutions can be given by peripheral intravenous lines; however, central lines are preferred for TPN and in both cases lines should be kept dedicated.

What are the disadvantages to TPN?
Complications of TPN include catheter-related sepsis, metabolic abnormalities and gut atrophy. Hepatic cholestasis also occurs as does pancreatic atrophy. Parenteral feeding is associated with higher rates of mortality in infected animals, and higher rates of sepsis in human trauma patients than those fed enterally.

Why should a feeding tube be placed?
Many ill or injured patients are unwilling or unable to eat; yet the gastrointestinal tract is still able to digest and absorb nutrients. By providing a more palatable diet, the anorectic animal may be encouraged to eat. By utilizing tube feeding the problems associated with anorexia can be avoided.

What types of tubes exist?
Tube enteral nutrition in the ICU is provided primarily via nasoesophageal, nasogastric, esophagostomy, and gastrostomy tubes. Nasal tubes can be placed under local anesthesia. Occasionally mild sedation will be required. All other tubes require general anesthesia.

What are these feeding tubes used for?
In general the tubes are used for enteral feeding but they can be used to deliver electrolyte infusions and water. Radiographs should always be taken of nasal and esophageal tubes to confirm their location prior to use. All tubes can be used for suctioning, which is important in the immediate postoperative period to remove gas and fluid from the esophagus and stomach to help prevent ileus. Decompression is also essential in conditions such as acute megaesophagus and post gastric dilatation-volvulus surgery. Suction can be done intermittently with a syringe or continuously with a thermotic pump. Radiographs are also recommended if the animal vomits, if the tube appears obstructed, or if suctioning is producing much lower volumes of gas or air than expected.

How do I decide what kind of tube to place?
Often the type of tube placed is determined by the patient's underlying disease, whether or not anesthesia is an option and whether or not abdominal surgery is being performed. Nasal tubes are typically used for short term feeding. Esophagostomy tubes are used for long term feeding. In the author's opinion gastrostomy tubes have no benefit over esophagostomy tubes except in rare situations and they have the potential to lead to lifethreatening complications.

How do I take care of these tubes?
All ostomy and incision sites must be examined on a daily basis while the patient is in hospital. Any dressing must be changed as soon as it gets wet and a minimum of every 72 hours. If the bandage is still clean and dry this can be done through a window cut in the bandage - creating a 'trap door' that can be replaced when the old dressing is removed. When removing the bandage it is extremely easy to cut the tube, therefore the bandage should be removed slowly and layer by layer. An indelible marker can be used on the bandage to denote the approximate location of the tube to facilitate removal of the dressing. In general the tube should be looped up over the back of the patient, taking care not to kink the tube at the ostomy site. If a small bore tube is cut it can often be salvaged by placing a hypodermic needle into the cut end after using hemostats or needle holders to break off the needle tip with a bending motion. The needle is taped carefully into the tube and an extension set attached to the hub.

The ostomy site should be cleaned with an antibacterial solution and examined closely for signs of discharge or inflammation. The area around the tube should be thoroughly palpated to check for any signs of swelling or crepitus. Antibacterial ointment should be placed over the ostomy site and the bandage replaced.

When do feedings start?
Early enteral feeding has been shown to be very beneficial in the trauma patient and should start as soon as the patient is resuscitated. The patient should have full control of its airway before feeding is started. Feeding into the stomach should be done cautiously postoperatively as gastric motility often does not return to normal for at least 1-2 days.

What should I feed?
Only liquid diets can be fed through small bore tubes (less than approximately 10 French). Blenderized canned foods can be fed through larger bore tubes; however, it is recommended that liquid be used initially until it has been determined that the patient is tolerating the food. The choice of diet may depend on the patient's underlying disease but in most cases feeding the patient is more important than what is being fed.

How fast should the liquid be delivered?
Initially the delivery rate should be 0.1-0.25 ml/kg/hr. This can be used in all patients including those who have had gastrointestinal surgery. These rates may even be too fast for those patients who have had massive bowel resection, pancreatitis or prolonged anorexia. If the patient is tolerating the rate of delivery the rate can be increased as frequently as every 12 hours by increments of 30% until 100% of the required volume is being delivered. Rates should be increased no faster than every 24 hours in patients with a history of prolonged anorexia or severe bowel disease. The volume of feeding required is calculated using the basal energy requirement (BER) in kcal for the weight of the animal and knowledge of the caloric density of the food. A commonly used linear formula for BER for adult dogs is 30 x kg + 70. BER does not need to be multiplied by stress factors as this is more likely to lead to overfeeding in animals in a cage. Overfeeding has been shown to have more negative consequences than permissive underfeeding. Intravenous fluid rates should be decreased in proportion to the amount being delivered enterally. Cats often will not tolerate greater than 20 ml/kg per feeding when being fed intragastrically.

What are the exceptions to the above delivery rates?
If a patient has been anorectic for longer than a few days the lower rate of 0.1 ml/kg/hr may be better tolerated as the stomach, duodenal and pancreatic atrophy that may have occurred during this time can be significant. The atrophy is associated with down regulation of the digestive enzyme systems and decreased absorptive surface area in the small intestine. The length of time the bowel takes to return to normal will vary depending on how long the patient has been anorectic. If a large percentage of the small bowel (generally greater than 80% of the small intestine) was removed at surgery the animal may suffer from "short bowel syndrome" and increases in rates may need to be adjusted even further as the absorptive surface area will have been significantly reduced.

What about microenteral nutrition?
Microenteral nutrition is the delivery of small amounts of 0.1 to 0.25 ml/kg/hr of a glucose and electrolyte solution into the gut. This is provided for the patient who is fairly intolerant of oral nutrition e.g. the vomiting patient who is continuing to vomit intermittently, pancreatitis patients who are no longer vomiting, the patient with severe esophageal injury and patients with short bowel syndrome. This form of nutritional support will hopefully help 'feed the gut", and "wake it up" functionally and help prevent further down regulation of the enzyme systems.

What do I feed?
Both monomeric and polymeric diets are used. Monomeric diets are elemental diets that require no digestion prior to absorption. These include amino acid diets and peptide based diets. Amino acid-based diets require active absorptive processes whereas di- and tri-peptide-based diets can be passively absorbed and are preferred. In general monomeric diets are reserved for patients who have had large amounts of their bowel removed, have malabsorptive or maldigestive problems or have pancreatitis. In all other patients polymeric diets should be able to be used. These are also less expensive and generally have a much better taste if forced oral feedings are used.

What concentration of diet should be delivered?
If the gastrointestinal tract is functioning then full strength polymeric diets should be tolerated right from the start. In the case of GI dysfunction, short bowel syndrome or pancreatitis, polymeric diets at 30-50% concentration or elemental diets should be used. In these cases the osmolality should not be greater than 300 mOsm. If there is serious concern regarding GI function, enteral administration of water, glucose and electrolyte-based oral rehydrating solutions or intravenous fluid solutions can be used. If there are problems maintaining an intravenous catheter an enteral feeding tube can be used to deliver replacement or maintenance crystalloid solutions. If a diluted diet is being used the concentration of the diet should not be increased until full volumes (see under delivery rate) are being delivered.

Note: In some cases the patient may be volume restricted and more concentrated diets may be required i.e. cardiac cachexia, chronic starvation. In these patients administration of full volumes may either never be possible or may

take more than a few days to achieve. Special attention should be paid to fluid balance in these patients.

What should I use to dilute the diet?
Water should be used to dilute the diet unless there is a specific reason for using another fluid.

How do I deliver the feedings?
All diets should be fed at room temperature. Most patients tolerate a constant rate infusion much better than bolus feedings. Constant rate infusions may alter homeostasis and fuel use as it does not allow for the normal cascade and feedback mechanisms to occur. Enteral feeding pumps are available although some of the diets can also be given via the regular fluid infusion pumps. If a diet is being delivered as a constant rate infusion no more than eight hours of diet is hung at any one time. All patients should have their tubes flushed with 2 to 5 ml of warm water (depending on the size of the tube) every 6 hours. If the patient is going to be tube fed at home a gradual switch to bolus feedings must be done, ideally over a period of 2 to 3 days. The first day the hourly feedings are delivered over 5 minutes. If this is being tolerated then the amount of the feeding can be doubled in 12 hours and the feeding given every 2 hours. The second day the amount is increased and the frequency decreased to every 3 to 4 hours. (Due to volume restrictions it is rare to be able to deliver the required number of calories in fewer than 6 to 8 feedings per day if total caloric requirements are being met by tubes requiring liquid diets.) Bolus feedings should always be given over at least 5 minutes. After a bolus feeding an attempt should be made to hold a column of water in the tube. This is done by flushing the tube and clamping the tube by kinking it prior to removing the syringe. The syringe is removed and the cap placed prior to unkinking the tube. Hypodermic needle caps make excellent caps for most larger bore feeding tubes.

How do I tell if the diet is not being tolerated?
If the patient starts coughing discontinue feeding, administer oxygen if required and take a chest radiograph. The patient may show signs of abdominal discomfort, nausea, hypersalivation, vomiting or diarrhea. On occasion gastric feedings will reflux into the esophagus and jejunal feedings will reflux into the stomach and be subsequently vomited. Gastrointestinal motility modifying drugs may be required (i.e., metoclopramide). If none of these signs discussed is observed then the patient is believed to be tolerating the administration well.

What about enteral feeding in the face of pancreatitis?
Traditionally TPN was used for feeding patients with pancreatitis. A number of studies have looked at enteral feeding in the face of pancreatitis and have shown that outcome is improved as long as the feeding is tolerated. The presence or absence of ileus is a good predictor of tolerance for enteral nutrition.

What are the complications and how do I prevent them?
1. Kinking: This usually only happens with small diameter tubes and is the first thing that should be checked if the feeding solution is not flowing. Careful looping of the tube when bandaging usually prevents this problem. On occasion suture material is tightened too much around the tube creating an obstruction.

2. Clogging: When blenderizing diets the consistency should flush easily through a tube of similar diameter. All tubes being used for continuous rate infusions should be flushed every 6 hours with warm water to prevent buildup of the diet on the sides of the tube. If clogging does occur tubes can be usually be unclogged using water, Diet Coke, or meat tenderizer. A tube declogger is available commercially. Flushing with small syringes (tuberculin) builds up higher pressure than larger syringes and is usually more successful. On rare occasions the passage of an angiographic wire down the lumen is needed to unclog the tube. If infusion of the diet is still not possible radiographs should be taken to check for internal kinking of the tube.

3. Infection: Signs of inflammation with or without discharge or fever may indicate an early wound infection. This must be differentiated from fasciitis since a simple wound infection can usually be treated locally with gentle cleaning with an antibacterial solution, use of topical antibacterial ointments and more frequent dressing changes. The application of warm compresses three times daily may also be recommended. The systemic administration of

antibiotics should be reserved for patients with systemic signs of infection.

4. Necrotizing fasciitis: This potentially fatal complication, where the bacterial infection travels along fascial planes, is possible with any of the surgically placed gastric or jejunal tubes. Early warning signs include swelling and inflammation around the tube and in dependent areas near the tube, fluid or crepitus under the skin, and fever with no identifiable source. Fasciitis requires immediate aggressive surgical debridement. The condition should be considered to be similar to gas gangrene and treated appropriately.

5. Tube dislodgement: This is most common with nasal tubes. An Elizabethan collar may be required. Nasal or esophageal tubes that pass through the lower esophageal sphincter in cats are more likely to trigger vomiting and should be backed out to just caudal to the base of the heart (about the ninth intercostal space.) Surgically placed tubes should be covered with a light bandage to prevent the animal from scratching or chewing at the tube. Gastric tubes that are dislodged prior to a seal forming at the ostomy site can cause peritonitis. If this occurs the possibility of peritonitis should be aggressively investigated.

6. Metabolic complications: Disorders of electrolytes and glucose are possible - these parameters should be monitored daily while the patient is stabilizing.

7. Aspiration: This is the most common complication in humans being fed into the stomach; the incidence in animals is unknown. The aspiration is often silent, in other words, the event cannot be detected by simple observation. Signs of possible aspiration include moist lung sounds, areas of dullness on auscultation or percussion of the lungs, coughing or fever. Feeding should be discontinued, oxygen given as required and chest radiographs taken.

8. Vomiting: This can occur with any of the tubes and can be related to the placement of the tube, the feeding process, or the underlying disease. Nasal and esophageal tubes should not pass into the stomach unless specifically indicate. Diets should be fed at room temperature and should not be given too rapidly. If the underlying disease if the problem antiemetics may be required.

9. Diarrhea: Studies in human medicine have shown diarrhea to be a major complication often necessitating discontinuing enteral feedings. Diarrhea is usually defined as the presence of 3 or more liquid bowel movements per day. The incidence of diarrhea in human patients is decreased if the diet fed is isotonic, lactose free and is delivered by a constant infusion rather than bolus feedings. Feeding through acute diarrhea in people has shown better maintenance of mucosal barrier. Rice based oral rehydration solutions decrease stool volume relative to glucose based oral rehydration solutions as the glucose and peptides in rice provide the substrates for electrolyte pumps thus improving water absorption. The true incidence of diarrhea in veterinary patients is unknown.

10. Refeeding syndrome: The refeeding syndrome is usually thought of as the severe hypophosphatemia and its associated complications that occurs in malnourished patients receiving aggressive nutritional support. It is characterized by acute cardiopulmonary decompensation leading to death. Refeeding leads to fluid retention, increases in heart rate and blood pressure and oxygen consumption that may cause the demands on the heart to exceed supply, increased carbon dioxide production leading to respiratory distress, Central nervous system dysfunction including seizures, diarrhea, red blood cell dysfunction and leukocyte dysfunction. The rapid hypophosphatemia is in response to a rapid intracellular shift due to the demands for phosphorylated compounds and increased insulin activity, which promotes uptake of phosphorus.

Remember no critical animal has ever benefited from acute malnutrition - only the opposite - therefore, feed early, and increase gradually, and most nutritionally related complications will be avoided.

References available on request.

Electrolyte Disorders: Which Fluid and Does It Really Matter?

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Important electrolytes in the body include sodium, chloride, potassium, magnesium, calcium and phosphorus. The list of diseases that can be associated with abnormalities of these electrolytes is lengthy and the reader is referred to other sources to discuss diagnosis and management of specific diseases. Electrolyte concentrations are reported on many blood tests that are routinely run in most veterinary practices; however, it is rare that these values fall into extremes. Normally these numbers, which are often taken at face value, in absolute terms, instead of being interpreted in light of the underlying disease, are only just out of the normal range. If the underlying reason for the electrolyte disturbance is known then the ideal choice of fluid should become apparent. If the fluid type is not available or not indicated for other reasons related to the patient's underlying disease then an understanding of electrolyte physiology will allow the clinician to monitor the patient for potential complications that might develop. Based on an understanding of electrolyte physiology and case examples, this lecture will discuss how to deal with electrolyte disorders that are life-threatening but more importantly to make the most appropriate fluid choices for a patient with only slightly abnormal sodium or chloride values.

Sodium

Sodium is primarily an extracellular anion with less than 10% being found intracellularly. An increase or decrease in the serum sodium concentration is almost always a reflection of an alteration in the water balance of the patient rather than an absolute increase or decrease in the amount of the total body sodium. This makes it extremely important to evaluate the patient's blood volume and hydration status whenever the serum sodium concentration is being assessed. It is essential to try and determine if the patient's blood volume is low, normal or high and whether or not the patient is dehydrated, normally hydrated or overhydrated. There are no specific measurements that can be made but physical exam parameters in particular, can provide a good estimation.

Water makes up approximately 60% of the weight of an adult animal of which two-thirds is intracellular and one third is extracellular. Three quarters of the extracellular water is in the interstitium and one quarter is in the intravascular space. The interstitial space is assessed by physical exam parameters such as mucous membranes and skin elasticity. Dehydration can be suspected based on the presence of dry mucous membranes, prolonged skin tenting, hyperalbuminemia and concentrated urine. Overhydration can be suspected based on parameters such as serous ocular or nasal discharge, gelatinous subcutaneous tissues and hyposthenuric urine.

Approximately 10% of the blood volume lives in the arteries, 20% in the capillaries and 70% in the veins. For this reason it is essential to evaluate the venous side of the circulation when evaluating the patient's volume status. Central venous pressure provides an estimation of central venous volume. If a central line is not present a subjective assessment can be made of central venous volume based on jugular venous distention. If the vein remains collapsed when the vein is occluded at the thoracic inlet then the patient is hypovolemic. A distended jugular vein may indicate hypervolemia but, similar to an increased central venous pressure, it may also indicate an obstruction to venous return to the heart such as occurs with pericardial tamponade, right-sided heart failure, pneumothorax or advanced liver disease. Delayed capillary refill and hypotension are often associated with hypovolemia. Blood pressure is a function of cardiac output as well as systemic vascular resistance so, although hypotension is usually associated with hypovolemia in small animals, it is not always the case. Hypervolemia is also associated with ascites, pleural effusion and pulmonary edema.

Normally when the plasma concentration of sodium decreases or increases it alters the osmolality of the blood, Hypernatremia triggers the thirst mechanism (adding free water) and antidiuretic hormone (vasopressin) release (decreasing water excretion in the kidney). The same osmoreceptors are triggered when other effective osmoles are added to the serum such as occurs with diabetes mellitus. Alterations in renal excretion of sodium in the

kidney are under the influence of aldosterone, atrial natriuretic factor as well as renal factors. These hormones become very important in diseases such as hypoadrenocorticism, dilated cardiomyopathy and acute hemorrhage.

It is important to attempt to classify the type of water disorder that exists when considering treatment. Hyponatremia can be classified based on hydration status or plasma osmolality and volume status. Hypoosmolar hyponatremia is the most commonly seen clinical entity. Hypoosmolar hyponatremia can be associated with gain of free water (hypervolemic hyponatremia), gain of hypotonic fluid (normovolemic hyponatremia) and salt loss (hypovolemic hyponatremia). Free water gain occurs with congestive heart failure, advanced liver disease and advanced renal disease. Hyponatremia in the sick diabetic patient is a combination of the osmolar effects of the hyperglycemia, and osmotic diuresis as well as third space losses. Normovolemic hyponatremia is rare but can occur with syndrome of inappropriate antidiuretic hormone secretion. Salt loss can occur with vomiting, diarrhea and third-spacing of fluids. Clinical signs related to the hyponatremia primarily relate to the central nervous system and are not normally evident until the sodium concentration is less than 125 mEq/L in the dog and 130 mEq/L in the cat. Signs include weakness, vomiting, diarrhea altered levels of consciousness and seizures. The presence of clinical signs depends on the severity of the hyponatremia and how rapidly the hyponatremia develops. Rapid onset hyponatremia leads to cerebral edema.

Hypernatremia can be present secondary to a free water deficit (normovolemic hypernatremia), hypotonic fluid loss (hypovolemic hypernatremia) or solute gain (hypervolemic hypernatremia). A free water deficit is caused by decreased water intake or diabetes insipidus. Hypotonic fluid occurs with vomiting and diarrhea, third-spacing of fluids, and renal loss from chronic renal failure, osmotic diuresis, drugs such as furosemide or postobstructive diuresis. Solute gain occurs with salt poisoning or infusion of hypertonic fluids. Clinical signs related to the hypernatremia primarily relate to the central nervous system and are not normally evident until the sodium concentration exceeds 170 mEq/L in the dog and 175 mEq/L in the cat. Signs vary depending on the severity of the hypernatremia and the rate of onset of the hypernatremia. Acutely the hyperosmolality causes movement of water out of the brain cells which can lead to hemorrhage from rupture of cerebral vessels if the rise is rapid and severe enough. With more chronic elevations idiogenic osmoles develop to maintain a normal water balance and clinical abnormalities may not be evident. Development of these idiogenic osmoles starts within a few hours but takes as long as 24 hours to fully compensate for elevation in the sodium. Clinically signs such as anorexia, lethargy, weakness, disorientation may be evident. If severe enough hypernatremia can cause seizures and death.

Care should be taken to assess the disease condition carefully prior to making an attempt to alter the sodium concentration. Minor alterations in sodium concentration will usually return to normal with treatment of the underlying condition. If the patient has a disease such as congestive heart failure it may be inappropriate to attempt to manipulate the sodium concentration other than through treating the congestive heart failure since this may lead to worse patient morbidity. When a decision is made to treat the sodium the concentration ideally should not change by more than 0.5 mEq/L/hr. Whenever sodium levels are being corrected blood or serum concentrations should be assessed very 2 to 4 hours depending on the patient's condition.

If the hyponatremia is mild then water restriction or hypertonic fluid may be the appropriate treatment. If the hyponatremia is more severe and the patient is hypovolemic an isotonic fluid may be indicated. If the patient is suspected to be chronically severely hyponatremic (sodium less than 135 mEq/l) then fluids should be adjusted to ensure the sodium levels do not rise faster than 0.5 mEq/l/hr to avoid central pontine myelinolysis. If the patient is normovolemic then furosemide will help prevent the sodium concentration from rising too rapidly if this becomes a concern.

If the patient is suspected to be chronically severely hypernatremic then hypotonic fluids may be indicated. Care should be taken to ensure the sodium levels do not drop faster than 0.5 mEq/L/hr to avoid causing cerebral edema. If the patient is comatose or seizing the sodium levels initially may need to increase at a rate of 1 to 2 mEq/L/hr until the patient's neurologic status stabilizes.

The free water deficit should be calculated by the following equation.

Na deficit (L) = TBW x serum Na^+/146 –1 (dogs)
Na deficit (L) = TBW x serum Na^+/156 –1 (cats)

Total body water (TBW) is calculated as 0.6 x the body weight in kg.

The volume of fluid to be administered is calculated as the sodium deficit in litres divided by the sodium concentration of the fluid being administered. Usually 5% dextrose in water is used to replace free water deficits but depending on the degree of hypernatremia a different fluid may be chosen. The number of hours the fluid should be administered over is calculated by subtracting 140 (150 in the cat) from the patient's sodium concentration and dividing by 0.5. The fluid rate is calculated by dividing the volume of fluid by the number of hours the fluid is to be administered over.

Chloride
Chloride is one of the most important anions in the body, representing approximately two-thirds of the anions in the blood. It is primarily extracellular. It is filtered by the glomerulus and reabsorbed in the renal tubules.

Fluids and drugs containing chloride such as 0.9% saline, hypertonic saline and potassium chloride can increase the chloride levels as can total parenteral nutrition. Chloride retention in the kidneys can occur secondary to renal failure, renal tubular acidosis, diabetes mellitus and chronic respiratory alkalosis. Loop diuretics and thiazide diuretics can cause an increased loss of chloride relative to sodium. Hypochloremia can occur with gastric vomiting and as an adaptive mechanism with chronic respiratory acidosis. Pseudohyperchloremia occurs when patients are being treated with potassium bromide. Most abnormalities of chloride are associated with acid-base abnormalities and clinical signs relate primarily to the acid-base disturbance rather than the alteration in the chloride. Hyperchloremia is typically associated with an acidosis and hypochloremia with an alkalosis. Because of this, it is essential to evaluate abnormal chloride levels in light of the acid-base status of the patient.

Chloride values must be corrected to take into account any changes in plasma free water before assessing whether or not the chloride concentration is low, normal or elevated. This is calculated by the following formula:

$$[Cl^-]_{corrected} = [Cl^-]_{measured} \times 146/[Na^+]_{measured}$$

The number of 146 is used in dogs under the assumption that 146 mEq/L is the mean sodium concentration in cats. The number 156 should be used in cats. This corrected value can have a significant impact on the choice of fluid therapy in certain conditions. For instance a ketoacidotic diabetic cat with a sodium of 140 mEq/L and a chloride of 118 mEq/L may become even more acidotic if 0.9% saline is infused. The corrected chloride in this situation is 131 mEq/L which is already a contributing factor to this cat's metabolic acidosis. There is a potential that this will only be worsen if 0.9% saline is infused.

Normal saline at 0.9% has a sodium concentration of 154 mmol/L which makes it hypertonic for most patients. The chloride is also 154 mmol/L which can lead to the development of a hyperchloremic metabolic acidosis. Due to its acidifying nature (pH of 5.4) it should generally be reserved for patients with gastric outflow obstructions, hypercalcemia and hypoadrenocorticism. It is important to note that electrolyte abnormalities are difficult to correct in patients with the first 2 conditions without administration of saline – usually in large volumes.

Potassium
Potassium is the major intracellular cation and 95% of the body's stores of potassium are maintained intracellularly. Potassium levels, along with sodium, play a key role in maintaining the resting membrane potential. If the patient is hyperkalemic then the membrane will be hyperpolarized making it impossible to develop an action potential. Hypokalemia also alters membrane excitability. The clinical manifestations of altered

potassium concentrations are similar, whether the potassium is low or high. Ultimately muscle weakness, especially involving the cardiac and skeletal muscles, will become apparent.

Potassium excretion is regulated primarily in the kidney, but to some extent in the colon, under the influence of aldosterone. Transcellular levels are primarily regulated by insulin, catecholamines, acid-base balance and the sodium-potassium-ATPase pump. Insulin drives potassium intracellularly along with glucose, and insulin also stimulates the sodium-potassium-ATPase pump directly, which also helps drive potassium intracellularly. When a patient becomes acidemic the body will shift hydrogen ions intracellularly in an attempt to maintain a more normal pH. For every 0.1 change in pH the potassium changes by 0.6 mEq/L. The hydrogen ions will be exchanged for potassium ions; therefore, hyperkalemia is expected with an acidosis and hypokalemia with an alkalosis. The finding of hypokalemia in the face of a significant metabolic acidosis should alert the clinician to the possibility of significant total body potassium depletion. If the patient has a metabolic alkalosis and a hypokalemia, the hypokalemia will actually tend to perpetuate the alkalosis via stimulation of increased bicarbonate resorption in the kidney.

In general terms hypokalemia can be caused by dilution, movement of potassium intracellularly, loss through the gastrointestinal tract and loss in the urine. Iatrogenic causes include fluid therapy, infusion of glucose or other hyperosmolar solutions, and the administration of loop and thiazide diuretics. Clinical signs rarely become apparent until the concentration decreases below 2.5 mEq/L. Clinical signs relate to weakness of the skeletal, cardiac and gastrointestinal muscles. Cervical ventroflexion occurs with significant hypokalemia, forelimb hypermetria and a broad-based stance have also been reported in cats. Hypokalemic polymyopathy has been reported in cats with chronic renal disease and poorly regulated diabetes mellitus. If the hypokalemia becomes severe enough respiratory paralysis and death will result.

Unfortunately there are no exact formulas for calculating the total body potassium depletion, nor the requirement for supplementation. Guidelines exist (see below) but the guidelines should always be modified based on how the patient is responding to therapy. A patient with hypokalemia and an osmotic diuresis will have a much higher requirement for potassium than one with normal urine output. It is recommended that the infusion rate not exceed 0.5 mEq/kg/hr; however, higher rates may be required in some patients. Rates as high as 1.5 mEq/Kg/hr can be used as long as the patient's heart rate and electrocardiogram are monitored continuously. Hypomagnesemia should be ruled out in patients with refractory hypokalemia.

Potassium (K^+) Supplementation Chart

Serum K^+	K^+/1000 ml
< 2 mEq/l	60 mEq
2.0-2.5	40
2.5-3.0	30
3.0-3.5	20

In general terms hyperkalemia can be caused by increased intake, movement of potassium extracellularly, and inadequate excretion in the kidneys secondary to renal or postrenal causes. Massive tissue damage such as occurs with severe crush injury as well as abrupt reperfusion such as can occur following a saddle thrombus can also cause severe hyperkalemia. Additional less common causes include severe thrombocytosis and severe leukocytosis (greater than 100,000 WBC). Iatrogenic causes include fluid therapy, the administration of spironolactone and angiotensin-converting enzyme inhibitors loop and thiazide diuretics. As with hypokalemia clinical signs relate to weakness of the skeletal, cardiac and gastrointestinal muscles. Cardiotoxic effects can become evident when the potassium concentration exceeds 7.5 mEq/L.

There are distinct electrocardiographic findings associated with hyperkalemia, although, the order with which they appear in the cat seems to be less consistent than with the dog. Also the electrocardiographic abnormalities

are less likely to be apparent in the acute hyperkalemia that exists in cats with lower urinary tract obstructions. The abnormalities (in the order they typically appear) include tall or peaked T waves, a prolonged PR interval, an absent P wave, a prolonged QRS complex, bradycardia, atrial standstill, sine wave complexes, ventricular fibrillation and complete standstill. By the time a sine wave is evident the patient is in imminent danger of dying.

Although dialysis can be used to decrease potassium concentration, it is not commonly used. The three primary treatments for a hyperkalemia that is significant enough to cause cardiotoxicity include infusion of insulin and dextrose, sodium bicarbonate and calcium gluconate. It is important to note that concurrent definitive treatment of the underlying condition is essential. Infusion of 0.5 to 1.5 ml/kg of 10% calcium gluconate has an immediate effect on the muscle because it decreases the membrane potential. Sodium bicarbonate given at a dose of 1 to 2 mEq/kg will cause an immediate transcellular shift of potassium, which once again decreases the resting membrane potential. Regular insulin can be injected at a dose of 0.5 U/kg IV which will drive the potassium intracellularly. The insulin injection should be followed by an injection of 2 g of 25% dextrose for every unit of insulin that was given to avoid iatrogenic hypoglycemia. It is likely that the infusion of dextrose alone should be sufficient to stimulate the release of endogenous insulin, which would cause the same effect. The insulin/dextrose treatment is an effective one but may require up to 20 minutes to achieve a peak effect.

References available on request.

Pediatric Emergencies

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The term pediatric usually refers to the first 12 weeks of life in dogs and cats. The neonatal stage is from birth to 2 weeks of age, infant from 2 to 6 weeks of age, and juvenile from 6 to 12 weeks of age.

Healthy neonates are active and have good muscle tone. Crying is normal in response to pain, cold, hunger, or loss of contact with the mother; however, crying should not continue longer than 20 minutes. Hyperemic mucous membranes are normal until day 4 to 7. Renal function does not mature until about 8 weeks of age although by 4 weeks of age they are able to excrete drugs at the same rate as adults. By 6 weeks of age hepatic metabolizing enzyme systems are functioning at nearly adult levels.

Environment

Neonates lack the ability to regulate their temperature well and easily become hypothermic. If they are separated from the mother they should be placed in an incubator that is kept at 29-32C (84-90F). Humidity should be kept between 55-65%. External warming devices such as hot water bottles and heating pads can be used but the neonate should be able to get away from the heat and the source should be covered in a towel or blanket to prevent burns.

Oxygen

Neonates may require oxygen supplementation. This can be provided by placing the neonate in an oxygen-rich environment or by placing a small nasal catheter (intravenous catheter in very small patients).

Fluid Therapy

Intravenous or intraosseous fluids are preferred over subcutaneous or intraperitoneal fluids. Intraosseous access is performed using hypodermic needles or commercial intraosseous needles. Commonly used access points include the greater tubercle of the humerus and trochanteric fossa of the femur. The tibia can also be used. If only rehydration and maintenance fluids are indicated then fluids can be given into the gastrointestinal tract if it is functional. A long intravenous catheter can be used as a nasogastric tube to deliver fluids. If the patient is not eating the fluid will need to be supplemented with dextrose at concentrations between 2.5% to 10% to maintain euglycemia. Maintenance fluid requirements are between 2-4 ml/kg/hour for pediatric patients.

Blood Transfusions

Blood transfusions may be required to treat parasitic infestations, trauma, or rodenticide coagulopathies. They should be given intravenously or intraosseously. The same rules apply to transfusion medicine in pediatric patients as in adult patients. As a last resort intraperitoneal transfusion can be given; however, only about 70% of the blood will be absorbed over 72 hours.

Nutrition

Nutrition is key in the treatment of neonates since they lack sufficient glycogen stores to maintain glucose levels for extended periods of time. Hypothermic neonates should not be fed until they are warm since hypothermia leads to ileus and poor digestion, often causing curdling of milk in the stomach. The patient should be weighed on a daily basis and should gain approximately 10% of its body weight daily. A goal of 2.5-4 g/kg of anticipated adult weight also is an acceptable estimation.

Hypoglycemic neonates should be treated with intravenous or intraosseous dextrose (1-2 ml/kg of 25% dextrose). Dextrose given orally is rarely effective at reversing a crisis.

Milk replacers should be used until weaning (which can be done as early as 2.5-3 weeks of age). Patients can be fed with nursing bottles or eye droppers. Some nursing bottles have nipples that require the neonate to generate a lot of negative suction. Expanding the hole a little using a hypodermic needle will help the weaker patient nurse more effectively. If the patient does not have bowel sounds oral feeding should proceed very slowly. If the patient is too weak to nurse tube feeding may be required.

Tube feeding can be accomplished with an orogastric tube (short term) or with nasogastric tubes (longer term). For orogastric feeding a red rubber or other infant feeding tube approximately 5-10 Fr in size is premeasured from the tip of the nose to the last rib. The tube can be cut short if necessary. A small amount of water soluble gel is used to lubricate the tube and the tube is passed with the neck held in a flexed position. The gag reflex does not develop until approximately day 10 so the tube always should be checked for proper placement prior to infusing liquids or food. This can be done by aspirating to check for air or gastric contents or taking a radiograph. Caution should be exercised in interpreting results of injecting a small amount of air and listening over the stomach with a stethoscope, or injecting a small amount of sterile saline or water and observing for a cough a this may not confirm the tube is in the right location. Once the feeding has been completed the tube should be kinked and then withdrawn. This will help prevent liquid from being aspirated during tube removal.

The stomach capacity is approximately 50 ml/kg. Initially feedings may need to start at 1-2 ml/kg every 1-2 hours. This can progress to larger volume feedings every 4 hours. Gastric overdistention should be avoided since this will lead to delayed emptying, nausea, and sometimes compromised ventilation. Feedings should always be done at body temperature.

If diarrhea is present in the neonate milk replacer may need to be diluted 1:1 with an oral electrolyte solution.

Analgesia
Pain kills. No matter how small the patient analgesics should be provided. Opioids can be used safely in pediatric patients. However, it should be kept in mind that the effects of the drugs may be much more magnified in the pediatric patient especially if the animal is sick or injured. Doses should be reduced significantly (20-25% of normal) and titrated upwards.

Antibiotics
Due to an increase in body water neonates and infants may need a higher dose and a longer dosing interval of dugs such as penicillins, cephalosporins, and aminoglycosides. Because they have lower albumin levels, drugs that are protein bound may be more active in pediatric patients. Tetracycline and trimethoprim-sulfonamide antibiotics should be avoided. Fluoroquinolone antibiotics also should be avoided since they can cause a developmental arthropathy.

Miscellaneous Medications
Vitamin K1 may be indicated in any sick neonate less than 48 hours old or any neonate showing signs of bleeding since they have decreased thrombin levels.

Diagnostics
A drop of blood retrieved from an intravenous or intraosseous catheter or from a jugular stick can be placed on a portable glucometer reagent stick. Larger blood samples should be taken from the jugular; however, the total blood volume of a 300g patient may be less than 30 ml and, in very small animals iatrogenic anemia is a possible complication of blood sampling, especially if the patient is anemic to begin with.

Radiographs of pediatric patients are indicated as for adult patients. Abdominal radiographs may be difficult to interpret due to the lack of body fat.

Specific Conditions
Sick neonates often cry incessantly until they become too weak. Mucous membranes may be pale or cyanotic. Dehydration is not uncommon secondary to lack of intake or disease causing increased losses and can be difficult to assess due to the lack of body fat. Mucous membranes should be moist. Due to their increased maintenance fluid requirements it is often easy to underestimate their fluid needs.

Diarrhea is common in pediatric patients. This can be due to dietary changes, maternal disease, and infections (virus, bacteria, parasites). Bowel sounds may be absent in these patients which often is consistent with generalized gastrointestinal dysfunction. If severe enough this can lead to problems such as prolapsed rectum and intussusception.

Whelping and Cesarean Section
Hypoxia and trauma can develop during whelping secondary to early placental separation, entrapment in the birth canal, and difficulty in passage through the birth canal. Fortunately these complications are not common. More commonly problems occur during delivery of puppies or kittens during a cesarean section. In order to minimize problems the hospital should be ready to deal with the arrival of the neonates. An incubator or box lined with a heating pad or hot water bottles should be made ready. Plenty of sterile (ideally) towels should be available to dry off the neonates. Oxygen should be available as well as small masks and an AMBU bag. Over-the-needle catheters (14-20 ga) can be used as tracheotomy tubes to provide oxygen and assist ventilate the newborns. The adaptor from 2.0-3.5 mm endotracheal tubes fits onto the end of the catheter so that an AMBU bag can be attached to aid in resuscitation. Suction may be necessary in order to be able to remove meconium and other secretions from the oropharynx and sometimes from the trachea. An ear bulb syringe can be used if mechanical or electric suction is not available. Extra hemostats and suture should be available to tie off the umbilicus which should be tied about 0.5 cm from the body wall.

If an animal is delivered by cesarean section the surgeon can administer naloxone to reverse any of the opioid effects present from the maternal circulation. Naloxone also appears to have other stimulatory effects in the brain. Naloxone can be given sublingually but uptake is unpredictable and ideally injections should be given into the umbilical vein. Doxapram is only useful if the animal is breathing and can lead to a worse outcome if the patient is not breathing. The neonate should not be swung back and forth between the legs since this can cause traumatic brain injury.

Neonates should be encouraged to nurse as soon as the bitch or queen is alert.

Congenital Abnormalities
A variety of congenital abnormalities can lead to dysfunction of multiple organ systems and the reader is encouraged to consult other texts for detailed information. Serious abnormalities often lead to mortality in the early hours or days of life. Some abnormalities may not show up immediately. These include problems such as atresia ani and megaesophagus secondary to a persistent right aortic arch (which may not be evident until the animal is weaned). Cleft palate can lead to nursing problems, swallowing disorders, and aspiration pneumonia. Isolated swallowing abnormalities can lead to aspiration pneumonia and an unthrifty neonate. Other neurologic abnormalities can lead to abnormal ambulation.

Fading Puppy/Kitten Syndrome
Fading puppy or kitten syndrome can be caused by malnutrition, hypoglycemia, and septicemia (see below). Common signs associated with hypoglycemia include weakness, collapse, stupor, and hypothermia. Tremors and seizures can be seen but often are absent. Intravenous or intraosseous access should be established immediately and 1-2 ml/kg of 25% dextrose infused. Vitamin B should be supplemented whenever glucose is used to control seizures since vitamin B is required for aerobic metabolism of glucose. If a drop of blood is retrieved it can be used for blood glucose determination. If the puppy or kitten responds or if hypoglycemia is diagnosed the animal should be placed on a constant rate infusion of 5-10% dextrose until it is eating normally.

Infection
Many neonatal infections caused by viruses or bacteria can be rapidly fatal. As the healthy puppy or kitten becomes older their ability to fight off infection improves; however, aggressive supportive care may be needed to improve the chance of survival. Particularly susceptible times for viral infections include the neonatal period and the juvenile period when the maternal antibody protection has worn off but the protection from vaccination is not yet effective.

Neonatal Conjunctivitis
Neonatal conjunctivitis results from accumulation of purulent exudate behind the eyelids before they open. The eyelids should be separated to encourage drainage. A scalpel blade is rarely necessary and should be used with extreme caution due to the possibility for damaging the eyelids. If the eyelids are very stuck warm compresses will often cause them to separate. Gentle cleansing should be performed using warm compresses, saline lavage and a broad spectrum topic antibiotic drop or ointment should be instilled.

Umbilical Infection
Umbilical infections can develop in the first 4 days of life. They are often associated with the neonate's environment. A streptococcal infection is most likely. Any abscess should be lanced and drained and the umbilicus should be treated with warm compresses and systemic antibiotics. Fluid therapy and other supportive care may be indicated.

Neonatal Septicemia
Neonatal septicemia can be associated with staphylococcal, streptococcal, E. coli and Pseudomonas infections. Lack of colostrum intake and maternal infections (mastitis, metritis) can lead to the development of septicemia. The neonate should be separated from the mother and the bitch or queen should be treated for any infection. Intravenous fluids, antibiotics, nutritional support, and supportive care are key if the neonate is to survive.

Toxic Milk Syndrome
Mastitis and metritis in the bitch or queen can lead to toxic milk syndrome which is characterized by signs of bloating and green diarrhea. The neonate should be treated with fluids and a milk replacer until the infection in the bitch or queen has resolved.

Parasites
Intestinal parasites can start to become a problem as early as 2-4 weeks of age. Some parasites can be transmitted transplacentally and some can be transmitted in the milk. Most parasites will cause vomiting, diarrhea, and lack of appetite. Hookworms can cause significant anemia as can fleas. Pyrantel pamoate can be used as early as 2-3 weeks of age. Giardia is treated with metronidazole or fenbendazole. Coccidiosis is common in infant and juvenile patients and is often found in addition to other infections. It is treated with sulfadimethoxine. External parasites can be treated with pyrethrin once the animal is old enough. Label directions should be followed closely. Flea combs can be used in patients too young for insecticides. Cleaning the environment is essential in the control of parasitic infections.

Juvenile Cellulitis
This is an idiopathic disease that occurs between 3-16 weeks of age. Facial swelling, lymphadenopathy, fever, and anorexia are hallmarks of the disease. Deep pyoderma may be present. Immunosuppressive doses of prednisone are required until clinical signs resolve. Antibiotics are recommended and are essential if a deep pyoderma is present. Topical antibacterial shampoos also may be needed.

Trauma
Trauma in early life can be caused by the bitch or queen lying on or stepping on the neonate. This can lead to head trauma, pulmonary contusions, and fractures. Later in life trauma can lead to lacerations, head injury, and fractures most commonly. Treatment should be directed to the specific injury. Fortunately most young patients

have an incredible ability to heal.

Electric Cord Injury
Electric cord injuries can be seen in juveniles as their natural curiosity leads them to chew on objects. The electrical injury causes oral burns, which are usually seen on the tongue and commissures of the lips, as well as neurogenic pulmonary edema. Supplemental oxygen should be provided until the patient is breathing normally and eating well. A dose of furosemide may help relieve the pulmonary edema. Bronchodilators also may be useful. An esophagostomy tube may be needed if several oral burns are present. Cage rest is indicated until the pulmonary edema has cleared which generally takes 48-96 hours.

Foreign Body Ingestion
Juvenile patients often ingest foreign materials. Inducing vomiting may be helpful in removing objects still in the stomach although this should be done with care if the object is sharp or large since it may cause lacerations or obstruction respectively during emesis. Other material will require endoscopic or surgical removal.

Intussusception
Chronic diarrhea (viral, bacterial, parasitic, dietary indiscretion-related) can lead to intussusception. Patients with chronic diarrhea should be palpated 3-4 times daily for the presence of a tubular structure that may indicated an intussusception. This is a surgical emergency. The intussusception is reduced if possible, nonviable intestine should be resected and, enteroplication of the intestine should be performed to prevent recurrence. Even with enteroplication recurrence is possible – especially if the cause of the diarrhea is not diagnosed and treated appropriately.

Prolapsed Rectum
A prolapsed rectum is not uncommon with severe diarrhea. A fecal exam is always warranted to help determine the underlying etiology. If the rectum is prolapsed it should be manual reduced. The blunt end of a pencil should be placed about 1 cm into the rectum and a pursestring should be placed and tied tightly round the pencil. Once the suture is tied the pencil is removed. This ensures the pursestring is tight enough to prevent a recurrence of the prolapse while ensuring the animal can still defecate.

References available on request.

Toxocologic Emergencies

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Toxicological emergencies are a common part of veterinary practice. Both dogs and cats have an amazing ability to ingest all sorts of foreign substances. Some of these substances can cause life-threatening problems while some just cause minor problems. In many situations the amount of the toxin ingested will dictate how serious the problem is. Often veterinarians work on assumptions since it is not uncommon that the actual identity of the toxin is never known. Thorough history taking and physical examinations are key in order to avoid missing a diagnosis of a toxin that requires a specific antidote. Aggressive supportive care is indicated for all those patients who ingested an unknown toxin to avoid morbidity and mortality.

Overview

History and Clinical Signs:

History from an owner is essential in the accurate diagnosis and treatment of most toxicities since clinical signs can be extremely variable. If the toxin is suspected or identified it is essential to get accurate and detailed information on the chemical or chemicals involved in order that a poison control center can be contacted for information on expected effects, treatment and prognosis. The type of toxin, the amount ingested, the time since ingestion, the clinical signs the patient is showing, and the previous medical history of the patient are all key. In the case of unknown exposure the owner should be questioned closely as to the type of chemicals, and especially medications that are available in the house that the pet might have access to. Although owners will not uncommonly try to indicate the 'neighbour has poisoned their pet' this is uncommon in the author's experience. It is much more likely that the animal ingested a natural or man-made toxin in the house or on the owner's property.

Diagnosis:

The identification of a specific toxin often requires a high index of suspicion. The clinician should work closely with poison control centers - both local human centers and any veterinary centres that are available. The National Animal Poison Control Center at the University of Illinois has a vast bank of information and is staffed 24 hours a day by veterinarians. Blood, urine and gavage samples may be required for assay to identify suspected toxins and samples of whole blood, serum, urine, and gastric contents or vomitus should be taken on admission whenever possible. If the owner has had the animal vomit at home instructions should be given to have them save the contents in a plastic bag and bring it in with the animal.

Treatment Overview

Treatment will in many cases be symptomatic unless a specific antidote is known. Fluid diuresis may be indicated. Seizure activity, ventilation and oxygenation, blood pressure and perfusion, cardiac rhythms and rates, renal function and coagulation are just some of the parameters that should be assessed and maintained as normal as possible.

Inducing Vomiting

Vomiting should be induced as soon as possible in the patient ingesting a suspected or an unknown toxin, unless vomiting is known to be specifically contraindicated (strong acids or alkalis, petroleum distillates, etc.). Apomorphine should be used intravenously for induction of vomiting. Hydrogen peroxide and salt can be given by the owner at home and are generally very effective in inducing vomiting. The dose of hydrogen peroxide is 1 to 2 teaspoons of 3% hydrogen peroxide per 10 kg body weight. This can be repeated 3 times at 5 minute intervals. Salt should be avoided whenever possible but can be given at a dose of 1/8 teaspoon per 10 kg. The sooner the toxin is out of the system the less likely toxic effects will be seen... even making the animal vomit in the car on the way to the clinic is a good idea.

Dexmedetomidine or xylazine can be used to induce vomiting in cats; however, in the author's experience neither work very well Both drugs can have serious cardiovascular side effects and the patient should be carefully assessed prior to administration of the drug and monitored for undesirable side effects.

Gastric Lavage and Activated Charcoal

Gastric lavage is widely used in small animals poisoned by ingestion of toxins. Experts are beginning to question the value of gastric lavage and it is currently not recommended in human medicine in most situations since studies have failed to confirm its value. Even when gastric lavage can be performed within minutes of ingestion, recovery of the toxin is limited. If the procedure is not completed within an hour of ingestion, recovery of many toxins is less than 15%. In small animal veterinary medicine, it is rare that gastric lavage would be completed within this period. In addition, administration of activated charcoal without lavage has shown very similar outcomes in people with many different types of toxin ingestion.

Activated charcoal should be administered via a gavage or nasogastric tube if it is indicated. Ideally a cathartic should be administered with the charcoal to hasten removal of the toxin. Many activated charcoal compounds are manufactured with cathartic (sorbitol magnesium sulfate) already present. The charcoal may need to be repeated over an extended period (sometimes 3 days) since some toxins undergo enterohepatic cycling. The decision to do this should be on a case-by-case basis. Activated charcoal often seems to stimulate vomiting which should be kept in mind when a decision is being made to administer the compound.

Skin Contamination

Skin contaminants should be rinsed thoroughly. Because these compounds also may be toxic to humans gloves should be worn. Sedation may be required with cats and aggressive animals. Make sure if sedatives are used that there is no interaction between the sedative and the toxin that might preclude its use. In many cases large volumes of warm water will suffice. In some situations washing with a mild dish soap or pet shampoo may be indicated. Make certain all soaps are rinsed from the fur and the animal should be actively dried to prevent hypothermia and avoid having the animal lick any residual chemicals from the skin during grooming.

Airway and Breathing

On presentation the patient should be checked for the presence of a patent airway and adequate ventilation. If the patient has an obstructed airway an emergency tracheotomy may be required. Patients who do not have a gag reflex should be intubated. Patients who are not ventilating adequately should have positive pressure ventilation instituted immediately. Patients with evidence of anemia, cyanosis, increased respiratory effort, or shock should have supplemental oxygen provided immediately.

If the patient has signs consistent with pulmonary edema then furosemide should be administered intravenously in addition to supplemental oxygen. If the patient will not tolerate an intravenous injection the drug should be given intramuscularly into the epaxial muscles. If the patient is extremely stressed mild sedation with an opioid or acepromazine (if the patient is hemodynamically stable) may be indicated.

If the patient has evidence of bronchospasm then supplemental oxygen should be provided and bronchodilators should be administered. Aminophylline and β–2 agonists can be given parenterally; however, in the author's experience nebulized β–2 agonists tend to be superior to parenterally administered agents. Aminophylline can cause anxiety and tachycardia whereas side effects of β–2 agonists are rare.

Circulation

Patients that are hypotensive may require crystalloids and colloids for resuscitation. Animals that are significantly anemic should receive red cells. Patients with coagulopathies should received fresh whole blood (if also anemic) or fresh frozen plasma. Patients that are hypoalbuminemic may require a combination of synthetic colloid and albumin replacement depending on the serum albumin concentration. Blood pressure and perfusion status should be returned to normal. Some toxins may cause hypotension by depressing cardiac function or by causing

excessive vasodilation. In this case positive inotropic drugs, β–blockers, antiarrhythmics, or vasopressors may be indicated depending on the toxin. Patients that are dehydrated should have their fluid deficit calculated and administered over an 8-12 hour period.

Certain toxins can cause hypertension. Systolic blood pressure greater than 200 mm Hg can lead to significant patient morbidity. The underlying cause should be identified if possible in order to treat with the appropriate drug. Nitroprusside at 0.5-10 mcg/kg/min constant rate infusion will lower blood pressure in many patients and can be titrated to effect. Acepromazine will cause hypotension through vasodilation but can be difficult to titrate. If hypertension is associated with tachycardia then a β–blocker (propranolol at 0.02-0.06 mg/kg IV over 5 minutes) should be given. Hydralazine, angiotensin-converting enzyme inhibitors and calcium channel blockers may also be helpful in controlling hypertension depending on the underlying cause. Unfortunately many of these medications are in an oral form only which may limit their usefulness in the acute stages.

Severe bradycardia (heart rates less than 50-60 beats per minute) with concurrent heart blocks, or bradycardia associated with hypotension should be treated with atropine or glycopyrrolate. Bradycardia associated with normal to high blood pressure should not be treated with anticholinergic drugs.

A urinary catheter should be placed and urine output monitored if the animal was exposed to a nephrotoxin. Alkalinizing the urine by systemic administration of sodium bicarbonate may aid in excretion of certain toxins. The urine pH will need to be monitored in these patients to ensure the goal is being achieved.

Seizure Management

Seizures should be controlled using intravenous or intranasal diazepam. If this is unsuccessful intravenous phenobarbital should be given. Both diazepam constant rate infusions and phenobarbital constant rate infusions can be given to help maintain control of seizures. The two drugs are synergistic when given together. Phenobarbital loading may be required to achieve therapeutic phenobarbital levels. If the animal has never received phenobarbital before this generally can be achieved by giving 16 mg/kg divided into 4 doses given every 20 minutes. (A dose of 3 mg/kg will raise the blood level by approximately 5 mcg/ml.) If the patient becomes excessively sedate or loses a gag reflex the clinician may prefer not to give further doses of phenobarbital until the patient is more alert. Muscle activity during recovery from pentobarbital can be easily confused with seizure activity. Levetiracetam is often used instead of phenobarbital due to the high cost of the latter drug.

Management of Stupor and Coma

Patients who do not have a gag reflex should be intubated and positive pressure ventilation should be instituted if the animal is not ventilating adequately. The patient should be placed in a 30 degree body tilt to help minimize the risk for aspiration. Pressure on the jugular veins should be avoided. Patients should be rotated every 2-4 hours to prevent atelectasis and reduce the risk for pneumonia. Pressure points should be padded to minimize the risk of pressure sores developing. The eyes should be kept lubricated with ocular ointments and the tongue may need to be kept moistened. Chlorhexidine rinses may help minimize the colonization of the mouth with potentially pathogenic bacteria.

Mannitol may be useful in helping treat cerebral edema.

A nasogastric tube may be indicated for helping with gastric decompression if regurgitation or vomiting and aspiration. The tube also can be used to provide enteral nutrition. Sneezing can raise intracranial pressure. This is not an issue for comatose patients but if sneezing is not desirable in more aware patients then placement of a nasal tube may not be appropriate.

Management of Tremors

Tremors are best controlled by use of intravenous methocarbamol, diazepam or midazolam. Constant rate infusions may be required to control the tremors. Dosing should be adjusted to ensure the patient does not become

anesthetized. If general anesthesia is necessary to control the motor movement the patient should be intubated to help protect the airway.

Management of Temperature Abnormalities
Hyperthermia may result from excessive seizure activity, muscle rigidity, malignant hyperthermia, or a hypothalamic disorder. The patient should be actively cooled if the temperature is above 104F. While the patient is being cooled appropriate measures to secure the airway, provide oxygen, fluids and control seizures or muscle activity should be taken. Cooling can be done by running the fluids through an ice bath, and placing icepacks around the head and over superficial major vessels such as the femoral and brachial arteries. Spraying the patient with water and then placing a fan on the patient will cause evaporative heat loss. Application of topical alcohol should be avoided since it can be absorbed systemically leading potentially to alcohol intoxication. Cooling should be stopped once the patient's temperature reaches 103F. If the patient's temperature is in an extreme danger zone (greater than 105F) active core cooling may be indicated. This can be done by administering cold water enemas and cold water gastric lavage. These patients frequently develop the systemic inflammatory response syndrome with all of its accompanying complications (hypotension, vasculitis with secondary albumin loss and third-spacing of fluids, coagulopathy, and multiple organ failure).

Hypothermia can be caused by certain toxins that depress the patient's level of consciousness or reset the hypothalamus. Certain medications used to treat toxicities that depress the metabolic rate (opioids, anesthetic agents, etc.) can also lead to hypothermia. Any patient that has a depressed level of consciousness should be kept warm with warm intravenous fluids, blankets, warm water circulating blankets, etc. Patients that require long term ventilation can be cooled significantly from the cold oxygen in the circuit and ideally an air warmer should be placed in the circuit. Spontaneous ventricular fibrillation can occur if the temperature drops to 28C.

Anticoagulant Rodenticide
Mechanism of Toxicity: Interferes with production of vitamin K dependent clotting factors (II, VII, IX, X) leading to active hemorrhage.

History and Clinical Signs: Signs relate to hemorrhage which can be external or internally into any body cavity, tissue space, or organ. Clinical signs generally take a minimum of 48 hours to develop and more serious signs usually indicate exposure 4-5 days prior to presentation. Hemorrhage around the larynx can cause an acute upper airway obstruction. Life-threatening hemorrhage can occur into the lungs and mediastinal tissues.

Specific Diagnostic Tests: Prothrombin time, activate partial thromboplastin time, activated clotting time, PIVKA (proteins induced by vitamin K absence or antagonism) test. Prothrombin time will prolong first and return to normal first.

Treatment: Animals who have ingested the toxin should have vomiting induced.

Animals with clinical signs should have supportive care provided (see above). Vitamin K1 should be given subcutaneously at a loading dose of 5 mg/kg followed by 5 mg/kg divided every 12 hours for 2-3 weeks for first generation coumarins and 4-6 weeks for second and third generation coumarins. Once the patient is able to take oral medications the vitamin K1 can be given orally.

If the owner is uncertain whether or not the pet actually ingested the toxin or ingested sufficient to induce hemorrhage the prothrombin time can be monitored on a daily basis for 3 days. If at 72 hours there is no evidence of a prolonged prothrombin time treatment is not necessary.

Pyrethrin
Source: Insecticides especially flea products

Mechanism of Toxicity: Neurotoxin (prolongs sodium conductance and antagonizes GABA)

History and Clinical Signs: Pets have usually been exposed to topical or premise spray products. Clinical signs include depression, muscle fasciculations, salivation, vomiting, bronchospasm and ataxia.
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Treatment: Skin decontamination should be performed if this was the route of exposure. Vomiting can be induced if the patient ingested the toxin within the previous 1-2 hours and the animal is neurologically stable and able to protect its airway against possible aspiration and the product did not contain petroleum distillates. Atropine can be used to control salivation as long as the patient is not tachycardic. Most patients recover within 24-48 hours with supportive care.

Metaldehyde
Source: Slug or snail bait

Mechanism of Toxicity: Unknown

History and Clinical Signs: Signs usually appear within 15 minutes to 3 hours of ingestion. Early signs include anxiety, salivation, panting, ataxia and possibly mydriasis and nystagmus. Later signs include muscle fasciculations, hyperthermia, and possible seizures.

Diagnostic Tests: Stomach contents, urine, plasma or tissue can be analyzed for metaldehyde.

Treatment: Emergency treatment to secure an airway, establish intravenous access and control seizures may be required. Gastric lavage should be performed followed by administration of a single dose of activated charcoal. Patients should be placed on a constant rate infusion of methocarbamol or diazepam to control the muscle tremors.

Garbage
Mechanism of Toxicity: Bacteria can release endotoxins and exotoxins. Molds can cause gastrointestinal irritation, hepatotoxicity or neurotoxicity.

History and Clinical Signs: Signs usually include vomiting and/or diarrhea. Endotoxemia can lead to the systemic inflammatory response syndrome (SIRS) and multiple organ failure. Certain toxins such as botulism can cause muscle tremors, ascending flaccid paralysis and coma.

Diagnostic Tests: Because garbage intoxication can mimic many other disease processes a full diagnostic workup is indicated.

Treatment: There is no antidote. Appropriate supportive and symptomatic care should be provided. This may need to be very aggressive care if there is evidence of endotoxemia. Supportive care may be indicated for several weeks if flaccid paralysis develops. Broad spectrum antibiotics such as penicillin, ampicillin and/or metronidazole are indicated in all cases of suspected garbage intoxication.

Chocolate
Mechanism of Toxicity: Theobromine is a phosphodiesterase inhibitor that causes an increase in cyclic AMP and a subsequent increase in catecholamines. Unsweetened baking chocolate and cocoa contain very high levels of theobromine. Dark chocolate also contains very high levels. Milk chocolate contains approximately one-tenth the amount found in unsweetened chocolate.

History and Clinical Signs: Vomiting and diarrhea may be present that are not direct causes of the theobromine but are related to the dietary indiscretion. Pancreatitis may be seen depending on the type of chocolate that was

eaten. Clinical signs include cardiac abnormalities (tachycardia, arrhythmias), central nervous system excitement (hyperactivity, tremors, seizures), panting, and urinary incontinence.

Treatment: Appropriate symptomatic and supportive care should be provided. Activated charcoal should be administered. Electrocardiographic monitoring is indicated in severe intoxications and arrhythmias should be treated appropriately.

Ethylene Glycol
Source: Antifreeze, windshield de-icing fluid, solvent in many chemical solutions

Mechanism of Toxicity: Ethylene glycol is oxidized to glycoaldehyde by alcohol dehydrogenase. Glycoaldehyde is oxidized to glycolic acid and then to glycoxylic acid. Glycoxylic acid is metabolized primarily to oxalic acid, which combines with calcium to form calcium oxalate crystals. Other end products include glycine, hippuric acid, formic acid, oxalomalic acid and benzoic acid. Ethylene glycol is an alcohol that can cause central nervous system depression and gastrointestinal irritation. It also inhibits the cytochrome P450 system which leads to increased production of oxygen radicals. The accumulation of acids can lead to a severe metabolic acidosis. The acid metabolites also interfere with oxidative phosphorylation glucose metabolism and protein synthesis and are toxic to renal epithelium. Calcium oxalate crystal deposition occurs in all organs including the brain. The minimum lethal dose is 1.5 mL/kg in cats and 6.6 mL/kg in dogs. Many solutions containing ethylene glycol also contain other toxins.

History and Clinical Signs: An environmental toxin, exposure typically occurs secondary to the animal drinking fluid that has leaked from vehicles and drinking from toilets that have been treated to prevent freezing. Early signs, which can be seen within 30 minutes of exposure and may last 12 hours may include nausea, vomiting, central nervous system depression and signs of “being drunk”. Polyuria and polydipsia may be seen secondary to the osmotic diuresis. Signs consistent with renal failure typically develop within 12-24 hours in cats and within 36-72 hours in dogs.

Diagnostic Tests: Serum ethylene glycol levels can be measured or estimated using a colourimetric test. The colourimetric test is not sensitive enough for cats although if the test is positive the cat definitely ingested a toxic dose.

Treatment: Vomiting should be induced within 30 minutes; after that time it is not likely to be effective due to the raid absorption rate. Activate charcoal is not effective. Treatment includes treatment and monitoring as for any renal failure patient. A central line and a urinary catheter are advised in order to be able to monitor central venous pressure and urine output respectively. Primary treatment involves administration of an antidote, either ethanol, which acts as a competitive substrate for alcohol dehydrogenase, or 4-methylpyrazole, which is an alcohol dehydrogenase inhibitor. Ethanol has many side effects; therefore; 4-methylpyrazole is preferred. The prognosis is excellent if dogs are treated with 4-methylpyrazole within 5 hours and cats within 3 hours. Dialysis is always advised but is probably unnecessary if 4-methylpyrazole is being administered early. Dialysis is continued until the ethylene glycol test is negative which usually requires 24-32 hours of continuous dialysis.

<u>Ethanol</u>
Administer 0.6 g/kg 7% ethanol intravenously or 0.6 g/kg 20% ethanol orally as a loading dose. Then begin 100 mg/kg/hr constant rate infusion of 7% ethanol. If intravenous therapy is not an option ethanol can be administered via a nasogastric tube; however, vomiting can be a problem when given by this route. Supplement fluids with multiple B vitamins. Treatment should be continued until the ethylene glycol test is negative (minimum 36 hours).

Acetaminophen
Source: Prescription and over-the-counter drugs

Mechanism of Toxicity: Acetaminophen is metabolized to non toxic and toxic metabolites. Glucuronidation and sulfation as well as combination of toxic metabolites with glutathione are key to minimizing the toxic effects of acetaminophen. The toxic metabolites cause direct cellular death and methemoglobinemia.

History and Clinical Signs: Dogs will present with signs consistent with liver failure. Cats will present with signs consistent with methemoglobinemia (cyanosis, respiratory distress, brown mucous membranes, brown blood) as well as facial edema. Cats are extremely susceptible to the drug since they cannot efficiently metabolize it.

Treatment: Appropriate supportive care should be provided. Gastric decontamination and activated charcoal administration are warranted. N-acetylcysteine is given at 240 mg/kg loading dose followed by 140 mg/kg every 4 hours for 3 days in dogs or 70 mg/kg every 6 hours for 3 days in cats. This can be given orally or intravenously. Vitamin C at 30 mg/kg orally or subcutaneously or 20 mg/kg intravenously may help convert the methemoglobin to oxyhemoglobin. Because cimetidine interferes with the metabolism of the acetaminophen its administration may be warranted.

Strychnine
Source: Pesticide

Mechanism of Toxicity: Strychnine antagonizes glycine which is an inhibitory neurotransmitter. Most signs relate to inhibition of glycine released by Renshaw cells which are neurons that mediate the activity of antagonistic muscle groups. Inhibition of these neurons leads to uncontrolled muscle contraction. Persistent muscle activity can lead to muscle injury, hyperthermia and rhabdomyolysis.

History and Clinical Signs: Early signs included anxiety and restlessness. Tonic muscle contractions of the extensor muscle groups become evident. A risus sardonicus is evident from facial muscle contraction. Muscle contractions are worsened by external stimuli. Tetanic contractions of the respiratory muscles can lead to apnea.

Diagnostic Tests: Vomitus, stomach contents, serum, or urine can be analyzed.

Treatment: Appropriate symptomatic and supportive care should be provided. Activated charcoal is indicated. Because of the mechanism of action of the toxin gastric lavage with a protected airway is preferred if clinical signs are evident. Muscle relaxation can be achieved using methocarbamol. Diazepam may be effective. More severe muscle contractions may need to be controlled with pentobarbital. Positive pressure ventilation may be required in serious cases. The patient should be kept sedated in a darkened, quiet room to avoid exacerbation of muscle activity.

Zinc
Source: Hardware, sun-block preparations, ointments, American pennies minted after 1982

Mechanism of Toxicity: Mechanism generally unknown – thought to interfere with enzyme function. Gastric irritant.

History and Clinical Signs: Gastrointestinal signs include vomiting, diarrhea and anorexia. Mores serious toxicity causes hemolytic anemia. Acute renal failure is possible.

Diagnostic Tests: Radiographs may reveal metallic foreign material. Laboratory tests abnormalities may be consistent with hemolytic anemia or renal failure. Serum, urine and tissue can be analyzed. Special tubes may be required to handle samples appropriately.

Treatment: Appropriate symptomatic and supportive care should be provided. Activated charcoal is indicated in acute toxicities. Metallic foreign bodies should be removed. Red blood cell transfusions, treatment for

disseminated intravascular coagulation, and treatment for acute renal failure may be required. Chelation with calcium EDTA may be indicated.

Mushrooms
Mechanism of Toxicity: Varies with type of mushroom. General toxic effects include central nervous system abnormalities (hallucinations), cellular damage (organ death), and autonomic nervous signs. Gastrointestinal irritation is common.

History and Clinical Signs: Clinical signs will depend on the mechanism of the toxin.

Treatment: Appropriate symptomatic and supportive care should be provided. Gastric decontamination and administration of activated charcoal are indicated. Close monitoring of liver and renal function is indicated. Dextrose supplementation may be required to maintain euglycemia along with plasma to treat coagulopathies.

References available on request.

Use and Misuse of Crystalloids, Colloids and Blood Products

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Many fluids are available to the clinician including maintenance and replacement crystalloids, colloids such as tetrastarch, and blood products. This session will discuss the properties as well as the pros and cons of the different fluids and how to ensure your patients are getting what they need.

Crystalloids

Crystalloids are fluids containing sodium chloride and other solutes that are capable of distributing to all body fluid compartments. Since approximately 80% of extracellular fluid is in the interstitial space crystalloids will rapidly redistribute and after as short a period of time as 20 minutes there will be only 20% to 30% of the administered volume remaining in the circulation. On a short-term basis crystalloids certainly will expand the intravascular space, but this effect will be short-lived. Thus, crystalloids should be thought of as interstitial dehydrators, not intravascular volume expanders. This increase in interstitial fluid can lead to tissue edema (thus decreasing the ability of oxygen to diffuse to the cells). Interstitial edema may be extremely detrimental in cases of cerebral edema and pulmonary edema.

Replacement fluids have electrolyte concentrations that resemble extracellular fluid whereas maintenance fluids contain much less sodium (40-60 mEq/l) and more potassium (15-30 mEq/l). Maintenance fluids should be used in patients who have ongoing losses other than normal losses through urine and feces, and in those who will not tolerate a sodium load. The latter typically includes patients with heart failure or severe liver or kidney disease.

The most commonly used replacement fluids are 0.9% saline, lactated Ringer's solution and Normosol-R, Plasmalyte 148 or Plasmalyte-A. Normal saline has a pH of approximately 5 so it can be very acidifying. It is primarily indicated in patients with gastric outflow obstructions, hypoadrenocorticism and hypercalcemia. Buffered solutions are usually indicated for resuscitating patients in shock since administration of a highly acidotic solution may worsen a preexisting metabolic acidosis. Buffered solutions are also an ideal choice for all patients requiring a replacement-type fluid. Buffered solutions usually contain lactate, gluconate or acetate. The liver must metabolize lactate whereas many cells in the body metabolize acetate and gluconate; however, end-stage liver disease must be present before the patient will have problems metabolizing the lactate. Plasmalyte-A is the only prebuffered solution; the pH is 7.4. All other buffered solutions have a pH of about 6.8; the metabolism of the buffer leads to increase in the pH to normal. Lactated Ringer's solution is no longer recommended by many due to the adverse effects of the lactate. These include neutrophil priming and worsening of cellular apoptosis. Calcium-containing fluids (i.e., lactated Ringer's solution) should not be administered concurrently through the same line as blood products anticoagulated with citrate since the resultant precipitate may be detrimental to the patient. Crystalloids are generally isoosmolar; however, they become hyperosmolar once other medications or supplements are added to the fluids. This may be important to patient therapy.

Hypertonic saline is a hyperosmolar crystalloid fluid used for resuscitation of hypovolemia. It is usually given as a 7.5% solution (2600 mOsm/L). The hyperosmolarity leads to rapid intravascular volume expansion by drawing fluids from the interstitial and intracellular space into the intravascular space. Its major benefit is that it can produce an equivalent intravascular volume expansion to colloids but at one-fourth the volume. Caution should be exercised when infusing this fluid in patients with uncontrolled internal hemorrhage since the rapid rise in volume, and; therefore, blood pressure, can worsen the hemorrhage. Because it is a crystalloid it will rapidly redistribute similar to all other sodium chloride-based solutions; however, its effects can be prolonged by concurrent administration of a colloid. It also appears to have an immunomodulatory effect including decreasing mesenteric lymph production and eliminating neutrophil priming, which decreases susceptibility to sepsis following hemorrhagic shock.

Colloids
Colloids are fluids containing large molecular weight substances that generally are not able to pass through capillary membranes and as such they can be considered intravascular volume expanders. Examples include synthetic colloids such as the, dextrans, hydroxyethyl starch (tetrastarch), and biologic colloids such as whole blood, plasma, and albumin. Colloids are usually isoosmolar. All synthetic colloids have the potential to cause a dilutional coagulopathy.

Since most patients in shock require sustained intravascular volume expansion, colloids are indicated frequently during fluid resuscitation. Patients with SIRS (systemic inflammatory response syndrome) or sepsis frequently have increased vascular permeability which leads to leakage of albumin and other small proteins out of the intravascular space ('third-spacing'). Synthetic colloids that have a larger molecular weight than albumin (69,000 Daltons) usually remain in the intravascular space.

Boluses typically are given to improve the blood volume and blood pressure to the desired end point. A constant rate infusion of 20 ml/kg/day can be given in patients with hypoalbuminemia less than 20 mg/dL or in those with ongoing albumin losses in an attempt to maintain oncotic pressure.

The use of colloids in the face of increased pulmonary vascular permeability seems to still be a matter of individual clinical decision. It has been proposed that larger molecules might block the open pores in the capillary membranes thus decreasing pulmonary edema; however, there is a concern that smaller molecules will pass through the open pores and lead to a worsening of the edema. Most synthetic colloidal fluids contain molecules that vary dramatically in size with some small enough to easily pass through pores along with particles far too large to pass through the pores. Once small colloid particles are in the pulmonary interstitium clearance has been shown in research situations to be very slow.

Hydroxyethyl starch is a molecule made from maize or sorghum and is primarily an amylopectin. Hetastarch expands the volume by about 1.4 times the volume infused. It has an average molecular weight of 450,000 Daltons. Doses greater than 20 ml/kg/day have been associated with an increased incidence of bleeding problems. Pentastarch has an average molecular weight of 260,000 Daltons. Tetrastarch has an average molecular weight of 130,000 Daltons. Much higher doses – up to 50 ml/kg - can be given on a daily basis. In cats the dose of hydroxyethyl starch should be infused slowly – over 15 to 20 minutes - as hypotension (related to histamine release??) may result with boluses. Due to the negative impact on renal function as well as an increase in mortality seen with hydroxyethyl starches they have been removed from the human market in Europe. Similar effects have not been documented in dogs or cats.

Human Albumin
Human albumin made from pooled human plasma is a concentrated source of albumin. At a 25% concentration the COP is 100 mm Hg, making it a very potent colloid that is able to expand the intravascular volume by 5 times the volume infused. It is also hyperosmolar at 1500 mOsm/L. For both of these reasons the patient must be monitored closely for signs of fluid overload when it is being infused. It provides all the beneficial effects of albumin (see below). The half life is approximately 16 hours. Doses of 2.5-5.0 mL/kg have been recommended with a maximum dose of 2 g/kg. Because it is human albumin allergic reactions are possible. This may manifest as facial swelling, vomiting or fever. Delayed reactions several weeks after administration have been documented.

Transfusion Medicine
Transfusion medicine involves the infusion of blood products. Ideally blood should be used when patients have lost whole blood. The lower the hematocrit becomes the more important hemoglobin replacement is to ensure adequate oxygen delivery to the cells. Packed red blood cells, which contain up to 80% packed red cells, should be used for patients with hemolytic anemia (loss of red cells but normal plasma components). Some packed red blood cells come with an extender making the packed cell volume only 45%. It is important to know what the packed cell volume of the blood product is in order to calculate the desired volume to be administered and to gain

an understanding of how fast the red cells are being destroyed in the case of a hemolytic anemia. Platelets are only found in fresh whole blood (administered within 6-8 hours) and in platelet-rich plasma.

If the patient has lost clotting factors then clotting factors should be replaced. This means administering fresh whole blood or fresh frozen plasma. Fresh frozen plasma is considered fresh frozen for 1 year and then frozen for another 4 years although there is some published information suggesting the clotting factors maintain their integrity for much longer than 1 year. Fresh frozen plasma contains coagulation factors, albumin and immunoglobulins. Frozen plasma contains Factors II, VII, IX, X, albumin and immunoglobulins. Cryoprecipitate contains 50% Factor VIII/vWf from the original unit, 20-40% fibrinogen and some Factor XIII. Cryopoor plasma contains the remaining clotting factors, albumin and immunoglobulins.

If the patient has a low albumin but normal clotting factors then fresh frozen plasma is not necessary and frozen plasma or human albumin can be given. Two-thirds of the albumin is in the interstitial space so replenishing albumin levels often requires significant volumes of plasma, especially in large dogs. For this reason plasma usually is used to replenish clotting factors and not restore albumin levels (except in small patients) and synthetic colloids are used to ensure adequate oncotic pressure is maintained.

Plasma not only is an important contributor to oncotic pressure but albumin also is important as a free radical scavenger. Albumin may improve microcirculatory flow and is important as a carrier of drugs. Plasma also provides a source of α–macroglobulin, which binds the activated and liberated proteases in patients with pancreatitis.

Unless the blood type of the recipient and donor are known all transfusion recipients should have a major and minor crossmatch. Dogs who are in danger of dying and have never received a transfusion usually can be transfused without a crossmatch but the clinician should watch carefully for any reaction including delayed reactions that may not show up for several weeks. Since cats have naturally occurring alloantibodies they must be crossmatched prior to transfusing since even a few drops of type A blood given to a type B cat can cause death.

References available on request.

Respiratory Emergencies - The Blue Patient

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Respiratory distress most frequently is associated with a condition that is causing hypoxia although these patients may also be hypercarbic. Respiratory distress is a more appropriate term to use in veterinary medicine than dyspnea which is defined as the subjective awareness of altered or uncomfortable respiratory functioning. Patients may be experiencing problems with getting oxygen into the alveoli which can be a result of upper airway obstructive or disruptive abnormalities or chest wall integrity problems such as fractured ribs, sucking chest wounds or a diaphragmatic hernia. It can be caused by difficulties with lung expansion caused by pleural space disease (pneumothorax, pyothorax, chylothorax) or lower airway problems such as pulmonary edema and pneumonia.

Physical Examination
Increased respiratory rate can indicate respiratory distress. This obviously needs to be differentiated from unrelated conditions such as pain or anxiety. Increased respiratory effort should always be taken as a sign of respiratory distress. Open mouth breathing and simply being able to easily observe chest wall movement and auscult lung sounds (unless an electronic stethoscope is being used) should be considered abnormal until proven otherwise.

The patient's posture should be noted. Dogs and cats with increased respiratory effort secondary to injury or disease often are unwilling to lie down although the cat may sit in sternal but refuse to curl up or lay in lateral recumbency. Any cat lying in lateral recumbency with signs of respiratory distress should be assumed to be close to arrest until proven otherwise. Nostril flaring indicates increased respiratory effort but does not necessarily indicate pathology.

Wheezing, crackles, and stridor all indicate abnormalities. The presence of stridor should alert the clinician to the fact that there may be an almost 80% airway occlusion. The trachea should be evaluated in all patients. Once the trachea has been ausculted the neck should be palpated noting tracheal position and tracheal/peritracheal integrity. The presence of subcutaneous emphysema in the cervical or thoracic region in a cat that has a history of a recent anesthetic or trauma to this region often is associated with a ruptured trachea. This can be associated with a pneumomediastinum and pneumopericardium, which can become a tension situation if there is no escape valve to the exterior of the animal. Auscultation of the trachea is often a more direct window into lower airway pathology than transthoracic auscultation.

The breathing pattern should be closely observed. Symmetry of chest movement and the presence of any abdominal component to the breathing pattern should be noted. Rapid shallow respiration typically is associated with pain (especially related to chest wall trauma) or pleural space disease where the patient is unable to expand its lungs. Pneumothorax, hemothorax, chylothorax, and pyothorax all can be associated with a restrictive breathing pattern. If paradoxical chest wall movement is observed a flail chest should be suspected. Increased chest wall expansion often is associated with lower airway disease although can indicate a collapsing trachea. Prolonged or forced expiration is associated with trapping of air in the lower airways such as occurs with allergic bronchitis or other diseases causing bronchospasm. Respiratory muscle abnormalities are associated with a significantly increased effort on inhalation with decreased chest wall expansion. This is most commonly seen with neuromuscular diseases and diaphragmatic hernia. Patients with paradoxical abdominal movement have severe respiratory compromise. These patients also should be assumed to be close to collapse due to exhaustion and ventilatory failure until proven otherwise.

The chest should be ausculted for the presence of breath sounds, areas of dullness, crackles or wheezes in at least 4 quadrants (upper and lower right and left sides). Crackles indicate alveolar exudate – typically pulmonary edema or pneumonia. Crackles may be very difficult to auscult in cats. Wheezes are consistent with obstructive lower airway disease. Foreign bodies in the lower airways also can cause similar sounds. Areas of dullness may indicate severe pulmonary infiltrate, pleural fluid, intrathoracic masses, or the presence of abdominal contents in the thorax. The heart should always be ausculted after ausculting the lungs since once the ear has accustomed itself to louder sounds quieter sounds can be more difficult to hear. Because of the narrow chest wall of the cat, lung sounds can be referred easily across both hemithoraces making it difficult to pick up unilateral abnormalities in this species.

Gastric distention secondary to aerophagia can lead to significant respiratory compromise or even cardiovascular collapse and the abdomen should be examined with this in mind.

Cyanosis is an indication of hypoxemia or a PaO_2 of less than 60 mm Hg. Cyanosis can be difficult to detect if the patient has a hemoglobin less than 5 g/dl or with certain fluorescent overhead lights.

Radiographs
Radiographs are an essential component of the evaluation process for the patient with respiratory compromise; however, they should not be a priority in the unstable patient. Stabilizing the patient is always the first priority. Care should be taken to ensure positioning does not compromise the patient's ability to breathe. The radiograph should be evaluated systematically to ensure abnormalities are not missed. The bones, soft tissues surrounding the thorax, pleural space, trachea and large airways, lungs, mediastinum, heart, great vessels and diaphragm all require assessment. In patients with upper airways diseases the cervical trachea and pharynx may require radiographic evaluation. Sedation may be required for diagnostic radiographs but this should be done with extreme caution in the compromised patient. Dynamic studies often provide valuable information.

Ultrasound
Point of care thoracic ultrasound can provide a rapid, efficient means of diagnosing pathology and has been shown to be more sensitive than a stethoscope. Five anatomic locations are interrogated. Pleural and pericardial effusion can easily be diagnosed. Lack of a glide sign indicates a pneumothorax and the presence of hyperechoic lines ("lung rockets") is consistent with pulmonary disease including contusions, pulmonary edema, pneumonia, and neoplasia.

Respiratory Support
Respiratory support of the critically ill or injured patient can be divided into oxygen support and ventilatory support. The end goal of respiratory support is to ensure adequate oxygen reaches the blood and carbon dioxide is removed from the blood. Oxygen should be considered a first line drug and should be provided to any patient that presents with an increased respiratory rate or effort or evidence of cyanosis.

Oxygen
Oxygen can be provided in a variety of forms. An oxygen source, baggie, plastic wrap, Elizabethan collar, and red rubber tubes are all that are necessary to provide oxygen to almost any patient. It is recommended that a direct oxygen source be available; however, if an anesthetic machine is used then a "Y"- shaped adapter should be used to bypass the anesthetic circuit. A "Y" connector is placed in the tubing before it enters the circle. A piece of tubing connects the "Y" to the circle and the second arm of the "Y" is connected to the oxygen tubing to the patient. A hemostat or C clamp is used to clamp off the oxygen to the patient or to the circle system depending on what is required. Nasal and tracheal oxygen should always should be humidified, although nasal oxygen may be able to be delivered for up to 24 hours not humidified. Hood, mask and flow-by oxygen should not be humidified.

Oxygen is most easily provided by using oxygen tubing that is connected directly to the oxygen source. The end of the tube is placed in front of the patient's nose or mouth. The flow rate is 1-10 L/min, depending on the size of

the patient, but it may need to be decreased based on patient tolerance. A mask also can be used but is often much less well tolerated and may cause increased stress unless the patient is recumbent. If a mask is used the rubber fitting should be removed. Many animals will tolerate having their heads or even most of their bodies placed inside a plastic bag. The oxygen tubing is placed through a small hole in the front of the bag and the back of the bag is left open to allow gas to escape. This is particularly useful in the obtunded patient because high concentrations of oxygen can be provided (75-95%) while allowing other procedures to be performed (blood drawing, placement of catheters, x-rays etc.) An oxygen hood can be made by covering the ventral 75% of an Elizabethan collar with plastic wrap. The Elizabethan collar should be 1 size larger than would normally be used for that size of patient. The oxygen tubing is placed along the inside of the collar and taped in place ventrally. Oxygen concentrations of up to 80% generally can be achieved. Flow rates of approximately 1 L usually provide an adequate FiO_2. Flow rates should be adjusted based on patient comfort, clinical status, pulse oximetry, and blood gases. Oxygen hoods generally are not tolerated by the panting dog as the hood rapidly becomes overheated and over-humidified.

Nasal oxygen is the most effective way to provide oxygen to the patient. For small patients 3.5 to 5 Fr tubes are used. For medium-sized dogs 5-8 Fr tubes are used and for larger dogs 8 to 10 Fr tubes are placed. Cats will usually tolerate 5-8 Fr tubes. The nasal catheter is typically measured from the tip of the nose to the lateral canthus of the eye so that the tip will be in the nasopharynx (nasopharyngeal catheter). Clinically animals tolerate the oxygen better if the tip is at this location as opposed to being in the nostril. A narrow bore red rubber or other pediatric feeding tube is placed in the ventral nasal meatus and sutured or stapled to the patient's nose and on the side of the face or on the bridge of the nose between the eyes. At flow rates of 100 ml/kg/min the FiO_2 will be a minimum of 0.4 and may reach as high as 0.65. Nasal oxygen should be avoided in the patient with severe nasal or pharyngeal disease and in the patient with severe thrombocytopenia. Sneezing will elevate intracranial pressure and nasal tubes should be avoided if this is a concern.

Oxygen cages also can be used to provide oxygen to patients but have several drawbacks and should be used only if other forms of providing supplemental oxygen are contraindicated. The biggest problem is the inability to evaluate the patient except through observation. Each time the door to the cage is opened the oxygen level drops substantially. This can lead to significant patient anxiety and respiratory compromise. The oxygen flow rates required to operate the units effectively makes this a costly alternative. On occasion, due to the stressed nature of cats with respiratory problems an oxygen care is essential. It would be ideal in these circumstances to use a small volume 'cage' such as a pediatric incubator.

Gastric Decompression

Patients with significant gastric distention that appears to be causing significant respiratory compromise or hemodynamic instability may require immediate gastric decompression. This can be accomplished either by transabdominal trocarization or orogastric intubation. Immediate decompression of a severely distended stomach can lead to cardiovascular collapse and ideally should be avoided until fluid resuscitation has been initiated.

Ventilatory Support

If the patient does not respond to supplemental oxygen rapid sequence induction, intubation, and ventilation should be considered. Suction should be readily available. Response to therapy usually can be gauged by monitoring respiratory rate and effort, presence of cyanosis, pulse oximetry readings, and blood gases.

Tracheostomy

A tracheostomy is indicated in the patient with an upper airway obstructive disorder that cannot be relieved, when airway control is indicated but an endotracheal tube is not possible or not desirable, in patients with severe bronchopneumonia, and in the patient who requires prolonged ventilatory support. If the thought occurs to you that a tracheostomy is indicated then one probably should be placed! Other indications include situations when an endotracheal tube cannot be inserted in a patient with an obstructed or near obstructed airway, when the obstruction is rostral to where the proximal portion of the tracheotomy tube ends, when it is necessary to assess

and treat the bronchoalveolar (pulmonary) tree such as delivery of medications and aspiration of exudate, and when it is necessary to decrease the dead space and airway resistance, in order to decrease the work of breathing.

There are no absolute contraindications but there are several relative contraindications. If the tracheostomy is the only breathing route for the patient then the patient must be monitored around the clock since coughing mucus into the tube will cause a complete airway obstruction and suffocation. Appropriate humidification and suction equipment as well as replacement tubes must be pleasant. A tracheostomy may not be ideal when the patient has a coagulopathy, when suction equipment does not exist, and in situations when an endotracheal tube may suffice.

A tracheotomy can be performed most easily on an anesthetized patient. The patient is placed in dorsal recumbency and a towel or IV fluid bag is placed under the neck which pushes the trachea ventrally. An incision (approximately 5-8 cm or 2-3 inches long) is made on the ventral cervical midline about midway between the cricoid cartilage and the thoracic inlet. The “strap” muscles (sternohyoideus) are separated using blunt or sharp dissection and the trachea is exposed. The trachea is elevated into the incision using thumb and fingers. An incision is made between 2 tracheal rings at the level of rings 3 to 6 extending about 40% of the circumference of the trachea and a tube is placed in the incision. Traction sutures are then placed through the 1 ring cranial and 1 ring caudal to the tracheotomy and tied with the knot approximately 8-10 cm or 3-4 inches from the trachea. These sutures are used for opening the trachea when the tube needs to be exchanged. A tube approximately 1-1.5 sizes smaller than what would be used for orotracheal intubation is placed.

Commercial tracheostomy tubes can be used or a clear endotracheal tube can be modified. To modify an endotracheal tube the plastic connector is removed from the end of the tube. Two cuts are then made in the tube 180 degrees apart. The cuts are made long enough so that the tube that remains intact is the right length for the patient (i.e., reaches from the tracheotomy to the thoracic inlet region). Do not cut the cuff inflating mechanism. The 2 wings that are created can be cut short if needed. The tube connector is placed back into the tube. Two holes are created the end of each wing and umbilical tape or IV tubing is placed through the holes and tied around the back of the neck of the patient. The tube is not secured in any other form to the patient. Two or 3 sterile 4x4 squares are placed between the tube and the tracheotomy incision.

Choosing an inappropriately-sized endotracheal tube can lead to a significant problems for a patient if they are breathing spontaneously. One study showed an increase in the work of breathing of 34% and increase in airway resistance of 25% if the diameter of the endotracheal tube was decreased by only 1 mm. When picking an appropriately-sized tube estimation by digital palpation of the trachea was shown to be the most accurate method.

Sterile saline (2-10 ml depending on the size of the patient) should be instilled or the patient should be nebulized (preferred) q2-4 hours to help lubricate respiratory secretions. The tube should be suctioned q6-8 hours after instilling saline and hyperoxygenating, and should be aseptically changed q6-12 hours or as needed. When suctioning larger patients the operator should inhale a normal breath and hold the breath. When the operator comfortably feels the need to breathe suction should be discontinued. For small patients the breath should be exhaled then held. When the operator comfortably feels the need to breathe the suction should be discontinued. Oxygen can be provided via the tracheostomy by placing a sterile red rubber catheter through the tracheostomy tube. Care should be taken to ensure the oxygen tube is not too large and does not obstruct exhalation. When the tube is no longer needed the tracheotomy incision is left to heal by second intention. It should not be bandaged until the tracheotomy incision is healed to avoid developing subcutaneous emphysema.

Thoracentesis

Pleural space disease (pneumothorax, hemothorax, pyothorax, chylothorax) often can be diagnosed based on the presence of a rapid shallow respiratory pattern, loss of airway sounds, or hollow sounds on percussion of the thorax. Any patient who is suspected of having pleural space disease should have a thoracentesis performed prior to taking radiographs. The stress of the radiographic procedure in a patient with severe pleural space disease may lead to respiratory arrest. Thoracentesis is performed between the 7^{th} and 9^{th} intercostal spaces. The thoracentesis

is performed in whatever position the patient is the most comfortable (sternal, sitting, lateral recumbency). Thoracentesis should always be performed bilaterally unless the patient is known to have unilateral disease. The area is clipped and prepped and if the patient is painful local anesthesia should be instilled in the skin and down to the pleura. The needle is introduced slowly until the pleura is penetrated at which point the needle is angled parallel to the chest wall with the bevel pointed medially. This will prevent injury to the lung as the pleural space is evacuated. If negative suction is not achieved a chest tube will need to be placed.

Chest Tubes
Chest tubes can be placed under sedation and local anesthesia or under general anesthetic. In most dogs chest tubes can be placed under sedation and local anesthetic. General anesthesia is required in most cats. If general anesthesia is required the patient should be intubated and ventilated. The size of the chest tube should be the approximate diameter of the mainstem bronchus in a patient with a pneumothorax since this is conceivably the largest hole that could exist. It also helps prevent having the tube clog with viscous fluids or blood clots. Smaller diameter tubes may be chosen for patients with a chylothorax or pyothorax.

In the case of a pneumothorax a 3-way stopcock can be placed in the tube and the tube can be aspirated on an intermittent basis; however, this is only advised if it is anticipated that the patient will only accumulate small volumes of air. Ideally continuous underwater suction should be used on chest tubes until it is established that the air leak is resolving.

Analgesia must be provided to every patient with a chest tube. This can be effectively provided using local or regional blocks a mixture of lidocaine and bupivacaine. Intercostal nerve blocks for 1-2 rib spaces either side of the tube can be performed or intrapleural analgesia can be provided by administering the local anesthetics via the chest tube into the pleural space. Local anesthetics should always be either warmed to body temperature or mixed (1:9) with sodium bicarbonate to decrease the sting. Parenteral narcotics should be provided if local anesthetics are not providing sufficient analgesia.

Continuous Positive Pressure Airway Support
Continuous positive airway pressure helps to decrease the work of breathing and improve gas exchange. It is defined as maintaining the pressure above atmospheric pressure throughout the respiratory cycle. This can be used as a bridge in patients that do not fully respond to oxygen support but positive pressure ventilation is not an option or if it is felt that some assisted ventilation may help avoid the need to positive pressure ventilation. A modified form of CPAP can be fairly easily provided to most awake dogs. A fairly tight fitting mask attached to an anesthetic circuit is placed on the patient. The pop-off valve is tightened down and the oxygen flow rate is increased until the pressure on the circuit registers at 5 cm H_2O. The patient breathes this oxygen under high pressure.

Nebulization
Nebulization therapy should be used for treating patients with pneumonia and bronchoconstrictive disease (i.e., feline allergic bronchitis). It is provided using a commercial unit or oxygen delivered at high flow rates through a nebulizer. The nebulized fluid can be delivered via face mask, into a baggie placed over the patient's head, or into an enclosed chamber if the patient will not tolerate the flow directed at the face. Saline (0.9%) is an excellent mucolytic if nebulization is being used to loosen secretions. Bronchodilators such as albuterol and terbutaline as well as corticosteroids such as fluticasone can be given by nebulization to asthmatics.

References available on request.

Anesthesia & Analgesia Mythbusters

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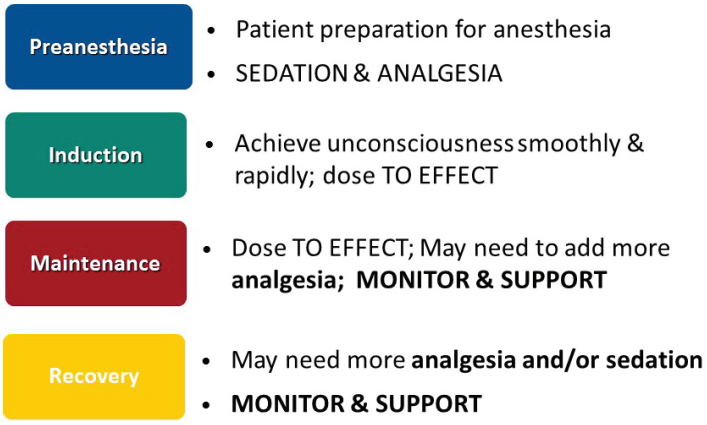
What we were taught, or what we remember, regarding anesthetic and analgesic drugs and techniques may no longer be true. Let's bust some myths!

Myths exist for anesthesia as a whole and also exist in all of the four phases of anesthesia:



Anesthesia Overview

The number one myth in all of anesthesia: *"My breeder said that my dog (or cat) is 'sensitive' to anesthesia"*. The only true breed association that we currently know is the inability of Greyhounds to efficiently metabolize drugs – primarily barbiturates. It may also be true that herding breed dogs like Collies will have an exaggerated response to some sedative/anesthetic drugs like acepromazine due to an alteration in the P-glycoprotein transport system caused by an alteration in the MDR1 gene (test for mutation available at http://vcpl.vetmed.wsu.edu/). There are, of course, breeds that have breed-related disease or anatomical abnormalities that make them more dangerous to anesthetize (eg, brachycephalics, Dobermans with VonWillebrand's disease, etc…) but this does not make them 'sensitive' to anesthesia. There are also size-related concerns (small dogs and cats are at higher risk for anesthesia-related death) but, again, not 'sensitivity'. Of course, some day all medicine will be determined by our unique DNA-makeup – and then we might discover more true anesthetic sensitivities.

For analgesia, an unfortunate persistent myth is that animals don't feel pain. Scientifically we can debunk this since mammals (and many other animal classes). If something is painful to a human, it will incite pain in other mammals. Another common myth is, 'pain is beneficial' in limiting a recovering animal's activity'. Protective pain, the pain that limits movement to protect tissue injury, is necessary – and is not eliminated by most of our analgesic drugs. Pathologic or maladaptive pain, the pain that exists beyond that needed for protection, leads to pain-related adverse effects and should be treated. In reality, animals are more restless when they are in pain (think about how you feel when you are painful) and, again, the pain can cause adverse effects. Furthermore, most animals will move if they want to, whether protective pain is present or not. We have to be good caregivers and limit movement using sedatives, cages, stalls, leashes, cross-ties, etc…. Pain won't limit movement – but we can!

Preanesthesia

Myth: Old or sick patients don't need a premedicant. WRONG. And dangerous. Old and sick patients definitely need a premedicant so that the dose of induction and maintenance drugs can be decreased. They just don't need the same premedicant – or the same dose – as a young, healthy patient.

Sedatives / tranquilizers / analgesic drugs

1. Opioids

- Morphine, hydromorphone, methadone, oxymorphone, fentanyl, butorphanol, buprenorphine
- **Advantages**: provide moderate to profound analgesia; reversible
- **Disadvantages**: may not provide enough sedation when used alone in young, healthy or excited patients; DEA controlled drugs (not really a disadvantage, just something to remember)
- **Myths:**
  1) *Opioids cause profound respiratory depression*. This is actually true in humans but not in veterinary patients.
  2) *Opioids should not be used because they cause vomiting*. Unless the patient has a reason that vomiting is contraindicated (eg, esophageal foreign body or increased intracranial pressure), vomiting empties the stomach prior to anesthesia – which is generally a good thing.
  3) *Butorphanol provides adequate duration analgesia for surgical pain*. Butorphanol is an agonist-antagonist with moderate potency and a very short duration of action (approximately 60 mins in a dog and 90 mins in a cat). Most surgeries last longer than butorphanol-mediated analgesia lasts.
  4) *Tramadol is a potent opioid that is an excellent choice for treating pain*. Tramadol is actually a weak opioid that has a highly variable bioavailability and rapid clearance rate in dogs. It is a decent add-on drug as part of multimodal therapy but is not generally appropriate for pain management when used alone.

2. Acepromazine

- **Advantages**: Inexpensive; mild to moderate sedation; long-lasting (good if you want a slow recovery)
- **Disadvantages**: No analgesia; mild to moderate sedation (ie, may need more sedation in some patients); long-lasting (bad if you don't want a slow recovery).
- **Myths**:
  1) *Acepromazine causes seizures*. This myth has been proven wrong by several very good clinical research projects. Acepromazine does not cause seizures and may even be protective against seizures.
  2) *Acepromazine causes hypotension*. Acepromazine causes vasodilation and can cause hypotension if used at high dosages or used in patients that are already prone to hypotension (eg, septic or dehydrated patients) but it does not cause hypotension when used at clinically appropriate dosages in clinically appropriate patients.
  3) *Acepromazine should never be used in patients with heart disease*. Actually, low-dose acepromazine can decrease afterload through vasodilation, which decreases the amount of cardiac work needed to eject blood. So a light dose of ace might be a good choice – unless the patient is hypotensive.

3. Alpha-2 adrenergic agonists (Domitor®, Dexdomitor®)

- **Advantages**: provide analgesia; effects are reversible; can provide anything from light to deep sedation.
- **Disadvantages**: cause cardiovascular changes that are well-tolerated in patients with healthy hearts but are not appropriate for patients with cardiovascular disease.
- **Myths**:
  1) *Alpha-2 agonists are very dangerous and are not appropriate for most patients*. Alpha-2 agonists actually have a very wide safety margin and are appropriate for many patients. Plus they are reversible, which provides a 'safety net' if adverse events do occur. Of course, alpha-2 agonists are not appropriate for patients with cardiovascular disease.
  2) *Alpha-2 agonists cause bradycardia, which causes **hypo**tension*. The bradycardia caused by alpha-2 agonists is actually a normal physiologic reflex that occurs in response to alpha-2 receptor mediated vasoconstriction and **hyper**tension. The decreased heart rate decreases cardiac work, which is a good thing!
  3) *The effects of alpha-2 agonists must always be reversed*. Not true! Reversal is an excellent safety net or convenience factor but many patients (think barking dogs!) benefit from alpha-2 mediated sedation. If

they are recovering well and are in a location where they can be observed, it might be a good idea just to let them sleep. And remember that reversal also eliminates any alpha-2 mediated analgesia.
4) *Alpha-2 agonists should not be administered to patients over 7 years of age*. There is no magic at 7. If the patient could benefit from a potent sedative that is reversible and provides analgesia then the patient should have that sedative no matter what age it is. Only cardiovascular disease – not age – precludes the use of alpha-2 agonists.

4. Benzodiazepines *- Diazepam (Valium®) and Midazolam (Versed®)*

- **Advantages**: minimal to no side effects, reversible
- **Disadvantages**: generally don't provide adequate sedation when used alone in young, healthy or excited patients; no analgesia; DEA Class IV drugs (not really a disadvantage, just something to remember).
- **Myths**:
  Benzodiazepines are great sedatives. Benzodiazepines are actually fairly poor sedatives in animals but can add to sedation – and muscle relaxation – provided by other sedatives. They can cause paradoxical excitement by 'relieving inhibitions' in patients that are 'inhibited' to misbehave.

Induction

1. Propofol

- **Advantages**: rapid induction and recovery; multiple routes of clearance from the body; good muscle relaxation.
- **Disadvantages**: must be administered IV; causes mild to moderate respiratory and cardiovascular depression.
- **Myths**:
  1) *Propofol does not cause any adverse effects, which is what makes it the best choice for critical patients.* Propofol actually causes moderate respiratory and cardiovascular depression but this is dose dependent so be sure to premedicate so that the dose is as low as possible. Propofol is a good choice for critical patients because it can easily be titrated 'to effect' (meaning that we can give the patient exactly the dose it needs for induction – unlikely to overdose when titrating 'to effect') and is cleared by multiple routes, so that organ dysfunction does not cause delayed recovery from the drug.
  2) *Propofol must be discarded after within hours after opening*. That is the recommendation for the propofol without preservatives. There is a new product available that does not require discard for 28 days☺.
  3) *Propofol is dangerous to cats*. The **dose** of propofol (and any other drug) is dangerous to cats – just like it is to dogs – but it is easy to administer propofol to cats without a premedicant because the volume is small so many people administer this way. However, this causes an overdose and it is the overdose – not the propofol – that is dangerous. Neither preservative-free nor preservative-containing propofol is labeled for cats but there is a great deal of data to prove that propofol is both safe and effective in cats.
  4) *The new propofol (Propoflo28) cannot be administered to cats because the preservative in the product kills cats.* The preservative (benzyl alcohol) in Propoflo28® is not at all dangerous to cats when the propofol is administered at clinically relevant dosages (Taylor et al., Evaluation of propofol containing 2% benzyl alcohol preservative in cats. J Feline Med Surg. 2012;14(8):516-26). An overdose could cause toxicity – but an overdose of the propofol is probably more dangerous than an overdose of the preservative.

2. Ketamine

- **Advantages**: inexpensive; can be administered IM; mild respiratory depression; no cardiovascular depression in heart-healthy patients.
- **Disadvantages**: very poor anesthesia and no muscle relaxation when use alone - must be combined with a sedative such as valium, medetomidine or dexmedetomidine; DEA Class III drug (not really a disadvantage, just something to remember).

- **Myths**:
  1) *Ketamine is an old drug that has no place in modern veterinary medicine*. Ketamine is an excellent induction drug (see advantages above) and can be used in an infusion to help provide analgesia.
  2) *Ketamine cannot be used in certain dog or cat breeds*. Absolutely wrong. There is way too much inappropriate and incorrect information on the internet!

3. Telazol®

- **Advantages**: potent; rapid induction; can be administered IM
- **Disadvantages**: recoveries can be prolonged and rough (especially in dogs); fixed ratio of tiletamine:zolazepam; DEA Class III drug (not really a disadvantage, just something to remember).
- **Myths**:
  Maybe none, but the combination is similar to ketamine/diazepam so myths might be similar.

4. Alfaxalone

- **Advantages**: rapid induction and recovery; can be administered IM.
- **Disadvantages**: causes mild to moderate respiratory and cardiovascular depression; can cause hyper-reactivity in recovery; must be discarded 6 hours after opening vial; DEA Class IV drug (not really a disadvantage, just something to remember)
- **Myths**:
  1) *Alfaxalone is safer than propofol.* Actually, the physiologic effects caused by alfaxalone are very similar to those caused by propofol. Both drugs excellent choices when the drugs are titrated 'to effect' to patients that have been premedicated with drugs that lower the necessary induction dose.
  2) *Alfaxalone is a great choice for IM administration in cats.* It is an okay choice if used at low dosages in combination with other sedatives. The volume is too large if the IM label dose is used (10 mg/kg outside US – not on US label). Best IM use is for small mammals ('pocket pets') and small 'exotic' pets, not cats.

***5.* Etomidate**

- **Advantages**: no cardiovascular changes
- **Disadvantages**: expensive; poor muscle relaxation; vocalization
- **Myth**:
  Etomidate is the only drug that can safely be used to induce patients with cardiovascular disease. This is the drug preferred for patients with very severe heart disease but most patients with mild to moderate disease can be safely induced with an opioid/benzodiazepine/low-dose propofol or alfaxalone combination.

***6.* Mask Induction or box induction**

- **Drugs**: Isoflurane, sevoflurane or desflurane
- **Myth**:
  Induction to anesthesia with an inhalant alone is the safest way to induce patients to anesthesia.
  WRONG. In fact, using an inhalant for both induction and maintenance with no other drug on board is a risk factor for anesthesia related **death** (Brodbelt 2009). Induction to anesthesia with inhalant anesthetic drugs alone ('masking' or 'boxing') should be avoided in all but the direst circumstances. Here are the reasons that induction to anesthesia with inhalant anesthetic drugs alone is not recommended for most patients:
- Masking / boxing down is **dangerous to the patient**
  - The dose of the drug is extremely high and adverse effects are dose-dependent; excitement causes increased need for drugs so the induction dose has to increase even more; excitement causes adverse physiologic effects
- Masking/boxing down is **dangerous to the staff**
  - Chronic exposure to anesthetic gases can cause health problems

Maintenance

Anesthetic Drugs:

1. Isoflurane - moderate cardiovascular and respiratory depression, small % metabolized
2. Sevoflurane – physiologic effects similar to isoflurane but faster induction, recovery and change of anesthetic depth
3. Desflurane – physiologic effects similar to isoflurane but even faster changes in anesthetic depth than sevoflurane, very expensive vaporizer

- **Advantages of inhalants in general**: easy to administer; relatively inexpensive; are eliminated with minimal metabolism; require oxygen for delivery; generally require intubation for delivery.
- **Disadvantages of inhalants in general**: contribute significantly to hypoventilation, hypotension and hypothermia. MONITOR, MONITOR, MONITOR.
- **Myth (inhalants in general)**:
  Inhalant anesthetics are very safe, no matter what dose is delivered by the vaporizer. Inhalant anesthesia is generally the safest and most effective way to maintain anesthesia that will last 30 minutes or more – but inhalants are only as safe as the anesthetist is. Inhalant anesthetic drugs should never be used as the sole anesthetic since **this group of drugs causes significant DOSE-DEPENDENT hypotension, hypothermia, and hypoventilation**. Our goal should always be to keep the vaporizer at the *lowest possible setting*. We often need to add extra analgesia to allow a decrease in the vaporizer setting.

Analgesic drugs & techniques:

Myth: *Analgesia is not necessary while the patient is under general anesthesia.* In fact, analgesia in anesthetized patients is extremely important for both improving the safety of anesthesia (because the patient can be maintained at a lower concentration of inhalant anesthetic) and decreasing the degree of postoperative pain (the more aggressive we are at treating intraoperative pain, the more comfortable the patient will be postoperatively). Aggressive treatment of acute pain may also lead to a decreased incidence of chronic pain. Intraoperative analgesia can be supplied by using boluses, infusions or local injections.

1) Boluses of opioids or alpha-2 agonists: Easy to administer; may provide only short duration analgesia

2) Infusion of opioids, lidocaine, ketamine or alpha-2 agonists
- **Advantages**: Can provide anything from mild to profound analgesia for any duration necessary
- **Disadvantages**: Requires a little more work than bolus administration
- **Myth**: *Infusions are hard and expensive.* Infusions are EASY (all you need is a dosing sheet or spreadsheet so that you don't have to do math) and CHEAP.

3) Local anesthetic drugs
- **Advantages:** Easy to use, effective, inexpensive;
- **Disadvantages:** Really none
- **Myth**: *Local blocks are hard to do and there will be adverse effects if I miss the injection spot.* Local blocks are EASY! Just use your knowledge of anatomy (and look in a book that describes local blocks☺. And if you miss the injection spot, the analgesia won't be very good but it is VERY UNLIKELY that the local anesthetic was deposited anywhere that it might cause harm. Just don't overdose – as with any drug, overdose can cause adverse effects.

Recovery

Recovery is an oft-overlooked phase of anesthesia and yet it is equally as important as the other 3 anesthesia phases.

Myths:

1) *Once the vaporizer is turned off, the patient is fine.* Actually, most deaths occur in the recovery phase of anesthesia☹. WHY? The patient may be a little deeper than we think – especially if it is very young, very old, or diseased (these groups of patients require lower dosages of anesthetic drugs). In recovery we tend to remove all monitoring and support so a patient that was doing 'okay' under anesthesia may suddenly decompensate without support (oxygen, fluids, etc…) and we aren't monitoring to know that it is happening. We can greatly improve this statistic by spending a little extra time in recovery!

2) *Hypothermia isn't a big deal.* Hypothermia is not at all benign and actually causes a variety of complications including clotting dysfunction, increased risk of infection, tissue hypoxia, acidosis, abnormal cardiac electrical conduction, myocardial ischemia, etc... (Noble 2006). Hypothermia also causes cerebral effects that decrease the patient's anesthetic needs. Unfortunately, the decreased anesthetic need is not always recognized and the delivery of anesthesia is not changed, resulting in an overdosage of anesthetic drugs. Although shivering in recovery may increase the body temperature, the intensive muscle movements associated with shivering causes discomfort and increases oxygen consumption by as much as 200% (Sessler 2002). In fact, in human medicine, an active area of research centers on prevention of shivering in the postoperative period. Finally - and importantly - hypothermia is the main cause of prolonged recoveries from anesthesia in small animal patients.

3) *Excitement in recovery is normal.* A BRIEF period of mild to moderate dysphoria right at extubation may be normal as the patient goes back through Stage II of anesthesia (the normal excitatory phase). But prolonged (>1-2 mins) or severe excitement is not normal and should not be tolerated. Is it pain or dysphoria? It doesn't matter – for the sake of the patient, the other patients within earshot and the owners/technicians/veterinarians/staff that are in ear shot – TREAT IT!!! First address analgesia and consider an opioid, but if the opioid isn't effective – or if an opioid has recently been administered, use alpha-2 agonists. This 'rescue' from bad recovery is one of my favorite uses of the alpha-2 drug class. These drugs are sedative/analgesics so it doesn't matter if the patient is experiencing dysphoria or pain – we are treating both! Dose for this use: 1-3 microg/kg IV or 3-5 microg/kg IM (higher end of either dose for cats) will achieve 10-30 mins of light-moderate sedation and analgesia.

4) *It is better for a patient to be painful than risk the adverse effects of NSAIDs since this is not a very safe drug class*. In fact, when compared to the number of dosages used, the number of adverse effects is VERY low. And because this drug class treats pain at its source (inflammation), it is a very powerful drug class.

- ***Non-steroidal anti-inflammatory drugs***
  - **Advantages**: CONTROL INFLAMMATION! Easy to use, not controlled
  - **Disadvantages**: Not appropriate for patients with renal, hepatic or GI disease

5) *NSAIDs should not be administered to cats*. This appears to be 'true' only in the US. Cats in the rest of the world do very well on NSAIDs. Could it be that we aren't dosing NSAIDs properly in the US?

Get the Nerve: Local Anesthetic Blocks

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Local anesthetic drugs are extremely effective, inexpensive and easy to use. When local anesthetic drugs are administered, pain impulses originating in the periphery are blocked and prevented from reaching the central nervous system. This blockade has several positive consequences:

- The sensation of pain is alleviated or even eliminated for the duration of the block. Local anesthetic drugs work by blocking sodium channels in nerve membranes. Decreased permeability to sodium slows the rate of depolarization so that the threshold potential is not achieved and an action potential is not propagated, thus the pain impulse is not propagated. Local anesthetics bind more readily to 'open' channels, thus rapidly firing nerves are more susceptible to blockade.
- The analgesia allows the patient to be maintained under a lighter plane of anesthesia and this makes the anesthetic episode safer for the patient. In fact, local anesthetic drugs decrease the minimum alveolar concentration (MAC) of all anesthetic gases.
- The likelihood that 'wind-up' or hypersensitization will occur is greatly decreased because the portion of the pain pathway called 'transmission' is blocked. Transmission involves the conductance of pain impulses from the peripheral nociceptors to the dorsal horn neurons in the spinal cord. The neurons in the dorsal horn are responsible for central sensitization. By blocking input to these neurons, central sensitization (or 'wind up') is less likely to occur.

Furthermore, local anesthetic blocks are extremely cost effective and can increase profits to the clinic.

Commonly used local anesthetic drugs in veterinary medicine include

- *Lidocaine*
  - Onset of action: rapid; approximately 1-2 mins (less than 5 minutes)
  - **DOSE:** 4-6 mg/kg in the dog and 2-4 mg/kg in the cat
  - Duration of action: 60-120 minutes
  - Convulsive dose in dogs: 11-20 mg/kg; Lethal dose in dogs: 16-28 mg/kg
  - 'Toxic dose' in cats reported as 6-10 mg/kg
- *Bupivacaine*
  - Onset of action: approximately 5-10 minutes (up to 20 minutes)
  - Duration of action: 4 to 6 hours
  - **DOSE:** 1-2 mg/kg in the dog and 1 mg/kg in the cat
  - Convulsive dose in dogs: 3.5-4.5 mg/kg
  - Lethal dose in dogs: 5-11 mg/kg
  - Data is mostly anecdotal in the cat but the general feeling is that 3 mg/kg is the toxic dose
- *Mepivacaine*
  - Onset of action: 2-5 minutes (up to 10 minutes)
  - Duration of action: 2-3 hours
  - **DOSE:** 3-5 mg/kg in the dog and 2-3 mg/kg in the cat
  - Used primarily for diagnostics in equine lameness but effective for all blocks
  - Lethal and convulsive dose in dogs: 29 mg/kg
  - No toxic dose published for cat

Adverse events caused by local anesthetic drugs

- Adverse events are extremely rare but can include any of the following:
- Local tissue effects – swelling, bleeding, inflammation, 'tingling'? (unknown if this occurs in animals)
- Anaphylaxis – rare, more common with esters (but still rare)
- Central nervous system – muscle tremors, seizure, coma

- At lower concentrations, depression of inhibitory neurons occurs and can cause cerebral excitation, which may lead to seizures. At higher concentrations, profound CNS depression with subsequent coma, respiratory arrest and death can occur. The latter is more likely following IV boluses of large doses.

- Cardiovascular system – the myocardial conduction system is sensitive to local anesthetics and IV boluses can result in cardiovascular collapse. ONLY LIDOCAINE CAN BE ADMINISTERED IV.
- Methemoglobinemia – rare, but can occur in cats.

Commonly used local anesthetic blocks in veterinary medicine

For many of the blocks listed below, a suggested volume of drug is listed based on the amount of drug that can physically be injected into the site. However, with all blocks, the total dose that the patient can receive should be calculated and the cumulative dose (add up the dose or volume injected for each block) should not exceed this total dose.

A. General blocks

- *'Field' block (also called incisional block or line block)*
  - Blocking the 'field' of surgery. Local anesthetic drugs can be administered around the incision or directly into the incision. It is NOT true that lidocaine in an incision causes a delay in healing.

- *Indwelling catheter block (long duration field block)*
  - Indwelling, or 'soaker', catheters should be considered for large wounds or incisions that may be difficult to block or that may require continuous or intermittent delivery of drug for several days.
    - The catheters can be buried in or near incisions and local anesthetic infused through the catheter to provide more long-term analgesia.
    - Very useful for surgeries with large incisions, eg: amputations, mastectomies, etc…
    - Local anesthetic drugs can be infused via a pump or administered by intermittent injection (eg, q 6-8 hour injections of bupivacaine at 1-2 mg/kg).
    - The catheter is generally removed in 48-96 hours but can be left in longer.

B. Blocks on the Head

- *Oral blocks (Figure 1)*

  Blocks listed below will cause unilateral desensitization from the site of injection rostrally to midline.
  - Maxillary or infraorbital nerve block – cranial approach
    - The infraorbital nerve exits the infraorbital foramen, which can be palpated as a depression in the buccal mucosa dorsal to the root of the maxillary 3rd premolar (just cranial to the root of the 4th premolar or carnassial tooth in the area where the gingiva on the maxillary bone and the gingiva on the lip join together).
    - Block the nerve by injecting local anesthetic under the gingiva just rostral to the foramen or insert the tip of the needle into the infraorbital canal and inject. Injecting into the foramen insures more caudal spread of the block but is not necessary if the oral surgery site is rostral to the foramen. Also, the foramen can be difficult to locate or to enter in small dogs and cats & infusion rostral to the canal is still useful as there will be some caudal migration of the local anesthetic into the canal.
    - A vessel runs with this nerve so aspirate, then slowly infuse drug
    - Volume that can be injected is approximately 0.1 to 1.0 ml, depending on the patient's size.

  - Caudal Maxillary
    - Insert the needle percutaneously along the ventral border of the zygomatic arch approximately 0.5 cm caudal to the lateral canthus of the eye. The needle is kept horizontal and directed medially and slightly cranially (in an angle that would draw an imaginary line with the

premolars on the opposite side of the head) until it hits bone. At this site, the maxillary nerve enters the pterygopalatine fossa.
- An alternate technique is to approach the pterygopalatine fossa from the ventral margin of the orbit or from inside the mouth just caudal and medial to the last molar.
- A second alternate technique is to approach the pterygopalatine fossa from the bony orbit. The needle would be placed at the midpoint of the ventral rim of the bony orbit and inserted straight down between the globe and the bone.
- For all 3 techniques, aspirate and inject. The volume that can be injected is approximately 0.1 to 1.0 ml, depending on the patient's size.

- Mandibular nerve block
  - The mandibular foramen or the mandibular nerve can often be palpated on the lingual side of the mandible just rostral to the angle of the mandible and just caudal to the last molar in approximately the middle 1/3rd of the mandible (as measured from top to bottom).
  - Regardless of whether or not the nerve or foramen can be palpated (often difficult to palpate in very small patients), the landmarks described above will be utilized for deposition of local anesthetic drug.
  - The nerve ENTERS the mandible at the mandibular foramen and cannot be blocked between the mandibular foramen and the mental foramen.
  - **Intraoral technique:**
    - With the patient's mouth supported in the open position (ie, use a mouth gag, roll of tape or some other method to ensure that the patient doesn't close its mouth while your hand is in the oral cavity), direct the tip of the needle to the site described above.
      - **REMEMBER:** Rigid mouth gags should NOT be used in cats. They can cause occlusion of the maxillary artery with resultant blindness and/or neurologic complications.
    - Aspirate, then slowly infiltrate (0.2 -2.0 mls). The foramen cannot be entered so the drug is merely infused under the gingiva at the site of the nerve.
  - **Extraoral technique:**
    - Landmarks are the same as those described above but the approach is from the outside, through the skin at the angle of the mandible. This technique is easier than the intraoral technique in cats and in some small dogs.
    - Pass the needle through the skin along the medial aspect of the mandible to a point where the tip of the needle is at the site of the foramen (again, aiming for a site just caudal to the last molar on the lingual side of the mandible).
    - With a finger in the oral cavity the needle can be felt under the gingiva.
    - When the site near the mandibular foramen is reached, aspirate and inject the local anesthetic drug (0.2-2.0 mls).

- Mental nerve block
  - The mandibular nerve EXITS the mandible at the middle mental foramen which can be palpated just ventral to the root of the 2nd premolar, immediately caudal to the labial frenulum.
  - Insert the needle tip just cranial to the foramen, aspirate and slowly infuse 0.1-0.5 mls local anesthetic. Apply digital pressure over injection site for 30-60 seconds in order to ensure maximum caudal/distal diffusion of the drug into mandibular canal.

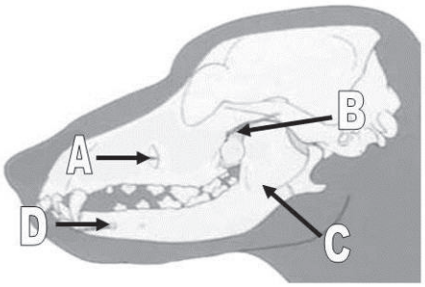


Figure 1: Diagram of a dog's skull showing the locations of a variety of local anesthetic blocks. Infraorbital block (A), caudal maxillary block from the zygomatic arch (B), inferior alveolar nerve or mandibular block (C), and mental nerve block (D). Landmarks for cats are the same as for dogs. Diagram used with permission from Pfizer Animal Health.

- *Auriculotemporal and greater auricular nerve block (Figure 2)*
  - Blockade of these nerves will desensitize the inner surface of the auricular cartilage and the external ear canal
  - Insert 23 ga. 1-1 ½ inch needle subcutaneously rostral to the vertical ear canal and directed towards the base of the 'V' formed by the caudal aspect of the zygomatic arch and the vertical ear canal
  - Insert the same sized needle subcutaneously ventral to the wing of the atlas and caudal to the vertical ear canal and directed parallel to the vertical ear canal
  - Inject 0.5-1.5 ml (depending on size of dog) at each location

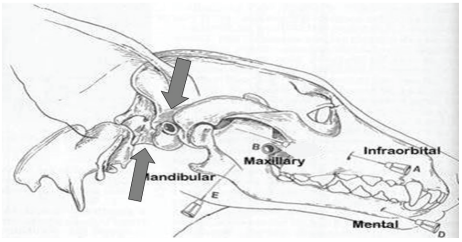


Figure 2: Landmarks for auriculotemporal and greater auricular nerve block. Lumb & Jones Veterinary Anesthesia & Analgesia; 4th edition; 2009

C. Blocks of the thorax, abdomen and genital-urinary system

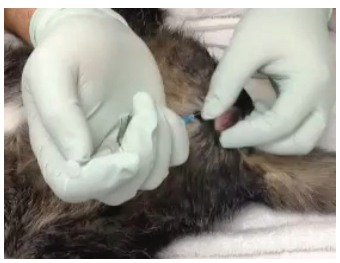
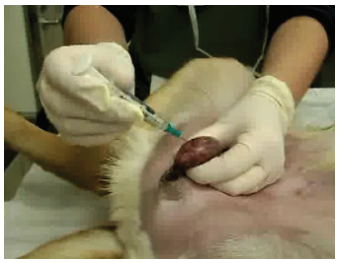
- *Testicular block (Figure 3)*
  - Isolate the body of the testicles
  - Inject lidocaine or bupivacaine into the body of the testicle until you feel 'pressure' or until the 'dose' (see below) has been injected
    - The drug will migrate up the spermatic cord.
  - The dose will be volume limited due to the size of the testicular tissue
    - Calculate 1 mg/kg bupivacaine or 4 mg/kg lidocaine and the volume that will 'fit' is about ½ of the calculated volume
    - This will generally be 0.2-2.0 ml per testicle in dogs and cats
  - For an incision directly over the testicle (cats), continue infiltrating as the needle exits the testicular body to block the skin and subcutaneous tissue.
  - For an incision in another location (dogs), inject local anesthetic in skin and subcutaneous tissue at the incision site.
  -  

Figure 3: Testicular block in a cat (left) and a dog (right).

- *Ovarian block or peritoneal 'block'*
  - The mesovarium can be infiltrated with lidocaine.
  - The volume will be about 0.5 mls per side in small dog or cat and up to 3.0 mls/side in large dog (can use a volume up to the maximum recommended dose of either lidocaine or bupivacaine).
  - Elevate ovary, infiltrate mesovarium, elevate opposite ovary, infiltrate mesovarium, remove first ovary, remove the second ovary and proceed with the ovariohysterectomy.

  - Alternatively, the peritoneal cavity can be 'bathed' with local anesthetic.
    - After completing the OHE, dilute 2-4 (cat) – 4-6 (dog) mg/kg lidocaine OR 1-2 (cat) – 2-4 (dog) mg/kg bupivacaine to 2-3 times the volume with sterile saline and 'bathe' the peritoneal cavity with the mixture by instilling it into the abdomen. Close the incision as usual.

- *Lumbosacral epidural analgesia*
  - **Opioids** are most commonly used but local anesthetic drugs can be used in conjunction with opioids.
    - 0.1 mg/kg morphine (preservative-free is gold standard but morphine with preservative is commonly used in veterinary medicine)
    - Dilute to 1 ml/4.5 kg with bupivacaine, sterile saline or sterile water
  - Provides up to 24 hours of analgesia with little to no systemic effects. The opioids will cause sensory blockade but will not cause motor blockade. The local anesthetics can cause motor blockade, however, the motor effects are generally minimal or absent by the time the patient recovers from anesthesia to the point that it is ambulatory.
  - Consider for any pain in caudal half of patient. Examples include, rear limb soft tissue or orthopedic surgery, abdominal exploratory and bladder surgeries, surgeries on the tail or perineal region, etc…
  - Technique:
    - Place the anesthetized patient in sternal or lateral recumbency
      - Legs can be placed forward or to the back. I prefer forward in cats and small dogs.
    - Locate the wings of the ilium and palpate the lumbo-sacral (LS) space (almost directly in line with the wings of the ilium on the mid-line).
    - Clip and scrub this region. Wear gloves and use a small drape or glove wrapper.
    - Insert an epidural needle into the caudal portion of the LS site with the needle angled at approximately 45^{o} from vertical.
    - Slowly advance the needle until the epidural space is entered.
      - 'Hanging' drop often works (aspiration of fluid in the hub of the needle as the epidural space is entered).
      - Several 'pops' will be felt.
      - 'Walking off' the bone is the most definitive determination of proper placement of the needle in between vertebrae.
    - STOP as soon as the space is entered and slowly inject the drug.
      - The drug should inject easily if the needle is in a space.
        - Stop injecting and take your thumb off the plunger. the fluid should momentarily continue to flow if the tip of the needle is in the epidural space. This is the most definitive determination that the needle is in the lumbosacral space.
      - If the drug does not inject easily, back up a VERY tiny amount and try again.
    - Once drug has been injected, remove needle and proceed with surgery.
      - If local anesthetic drugs have been used, may want to lay patient with surgical side down for about 5 minutes.
    - Opioid epidurals do NOT affect motor function of the rear limb or diaphragm. Local anesthetic drugs can affect motor function but rarely do (volumes that are described here do not migrate far enough cranially to affect the diaphragm so ventilation is not impaired).

- Complications include ineffective or incomplee block (by far the most common complication), epidural hematoma or abscess, hyperalgesia (VERY rare). Contraindications include bleeding disorders (to prevent hematomas) and skin disease over the LS space (to prevent abscesses). Abnormal pelvic anatomy (either from congenital lesions or trauma) may make epidurals difficult.
- Epidural catheters are fairly easily placed in larger dogs and can be maintained for several days to allow continuous or intermittent delivery of analgesic drugs.

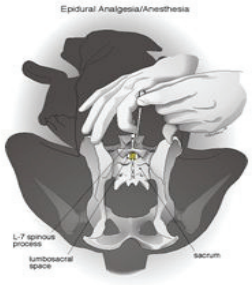


Figure 4: Diagram of the landmarks for an epidural injection into the lumbosacral space. Diagram used with permission from Tranquilli WJ, Grimm, KA, Lamont LA. Pain Management for the Small Animal Practitioner. Teton New Media Jackson, WY, 2000.

- *Sacrococcygeal or intercoccygeal epidural*
  - This block is often used to provide analgesia for tail amputations, perineal urethrostomies, and placement of urinary bladder catheters for urethral obstructions.
  - Move the tail up and down in a 'pumping' motion while palpating the sacrococcygeal region of the patient. The first movable space at the caudal end of the sacrum is either the sacrococcygeal or intercoccygeal space. Either site is appropriate for injection.
  - Insert a 22-G needle through the skin ON MIDLINE at a 45-degree angle to the skin surface.
  - Proceed slowly until needle enters the space (generally hit bone and 'walk off' the bone).
  - Hanging drop technique often works. Should have no resistance on injection.
  - Use lidocaine for rapid onset (0.1-0.2 ml/kg 2% lidocaine), can add an opioid (same as for lumbosacral epidural) for long-term analgesia. Don't inject air, air bubble may cause incomplete block since this is a very small space.

- *Intercostal block*
  - Inject local anesthetic in the tissues caudal to the proximal portion of the ribs. Inject local anesthetic in 2-3 rib spaces in front of and 2-3 rib spaces behind the area that needs to be desensitized.

D. Blocks of the limbs

- *Metacarpals/metatarsals/digits block (Figure 5)*
  - Four different ways to block
    - Three point (or four point)
      - Locate the carpus and the accessory carpal pad
      - Inject 0.1-0.3 mls subcutaneously at three sites:
      - 1) medial to the accessory carpal pad (blocks median nerve and palmar branch of the ulnar nerve);
      - 2) lateral and proximal to the accessory carpal pad (blocks dorsal branch of the ulnar nerve); and
      - 3) on the dorsal-medial portion of the carpus (blocks superficial branches of the radial nerve).
    - Ring block
      - Similar to three-point block but use a subcutaneous 'line' of local anesthetic all the way across the dorsum of the paw and another 'line' all the way across the ventrum of the paw just above the location of the accessory carpal pad to provide a 'ring' of local anesthesia that desensitizes the nerves described above.

- Interdigit or 'digital' block
  - Block between each toe
- 'Splash block'
  - 'Splash' local anesthetic into incision
  - Not as effective as other methods

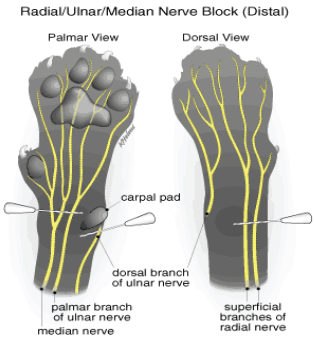


Figure 5:- Diagram of a cat's distal forelimb showing the locations for placement of local anesthesia for desensitization of the meta-carpals/tarsals & digits. Diagram used with permission from Tranquilli WJ, Grimm, KA, Lamont LA. Pain Management for the Small Animal Practitioner. Teton New Media Jackson, WY, 2000.

- *Brachial plexus block*
  - Locate the point of the shoulder, the first rib and the transverse processes of the cervical vertebrae.
  - Insert a 2-3-inch needle (an epidural needle will work) at the point of the shoulder to the point where the tip of the needle is even with the first rib. Keep the needle horizontal during placement so that the tip does not enter the thoracic cavity.
  - Aspirate, then inject 1/3 of the local anesthetic (1 (cat) or 2 (dog) mg/kg bupivacaine diluted with saline to a total 1 ml solution per 4.5 kg body weight) at this site, slowly withdraw the needle to the middle of the area to be blocked, aspirate and inject 1/3 of the local anesthetic. Withdraw the needle to a site just before it exits the skin, aspirate and inject the remaining 1/3 of the local anesthetic.

- *Intra-articular block*
  - This block is used for analgesia following intraarticular anesthesia. Inject 1-5 ml local anesthetic into the joint prior to surgery and repeat the injection after the joint has been sutured closed.
  - If local anesthetics are concerning, use opioids! There are opioid receptors in the synovium and they are upregulated in inflammation. This seems like the joint's way of screaming, 'give me opioids!

D. Other uses of local anesthetic drugs

- Lidocaine constant rate infusions are effective and safe in a large variety of patients.
- Lidocaine patches have been used over incisions or painful cutaneous lesions in veterinary patients. In humans, lidocaine patches are used for deeper muscle pain and they may be effective for this type of pain in our patients too. But our patients would likely have to be shaved to get patch contact with the skin and this isn't usually practical.
- There are a variety of creams & gels that may or may not work. Some of the local anesthetic creams work on the skin if they are placed on the skin and covered with a bandage for 30-45 minutes. These can be used to desensitize the skin for IV catheter placement. Lidocaine gel (you can make your own by just mixing some lidocaine into sterile lubricant) is an excellent lubricant for passing a urinary catheter.

References: Skarda, RT. Local and regional anesthetic and analgesic techniques: dogs. In: Lumb and Jones' Veterinary Anesthesia, Third Ed., Thurmon, Tranquilli, & Benson, eds., Williams and Wilkins, p 426-447, 1996. Tranquilli WJ, et al. Pain Management for the Small Animal Practitioner. Teton New Media Jackson, WY, 2000.

New Ways to Help: Osteoarthritis Treatment Update

Tamara Grubb DVM, PhD, DACVAA

Acute versus Chronic pain

Acute and chronic pain differ in ways other than their duration. *Acute pain* typically follows some tissue insult such as surgery or trauma and the pain resolves as the injury heals. Acute pain is called 'protective pain' because its role is to protect the patient from further tissue damage by limiting use of injured tissues. Acute pain tends to be responsive to treatment with conventional drug therapy including NSAIDs, alpha-2 agonists, and opioids. *Chronic pain* can exist after the original injury has healed as a result of pathophysiologic changes in the central nervous system. Since there is no longer an injury to 'protect', chronic pain serves to no purpose and is called 'pathologic' or 'maladaptive' pain. Chronic pain can be difficult to treat and poorly responsive to conventional analgesic therapy. Effective treatment may require multiple pharmacologic and non-pharmacologic treatment modalities (i.e., various analgesic drugs, acupuncture, massage, physical therapy, weight control, etc...). Left untreated, chronic pain causes a deterioration of the animal's quality of life and may result in adverse behavioral changes, including aggression.

As is the case in human medicine, osteoarthritis (OA) is the main cause of chronic pain in dogs and cats. Based on the population of aged dogs in many countries, it is estimated that 1 in 5 adult dogs is likely to have some form of OA. OA is most often seen in large-breed dogs, patients older than 7 years of age, patients having a history of being very active and overweight patients (thus, weight loss is an important part of therapy). Based on radiographic evidence, 22% of our general cat population (Godfrey DR. J Small Anim Pract. 2005;46(9):425-9) and 90% of cats over 12 years old (Hardie EM, et al. J Am Vet Med Assoc. 2002;220(5):628-32) may have OA. Fortunately, chronic pain due to OA - if diagnosed early - is often responsive to weight loss, controlled exercise, non-steroidal antiinflammatory drugs (NSAID) or piprants, and/or disease modifying agents (eg, chondroitin sulfate). If diagnosed after the disease has become moderate to severe, multimodal therapy will probably be required and even aggressive therapy may not completely eliminate all pain. Thus, it is imperative that we emphasize the signs of OA to our clients and to our staff members who may be involved in patient physical examinations.

Cancer is the second most common cause of chronic pain in animals. Although geriatric pets are most frequently affected, cancer can occur at any age. Patients will almost always require a multi-modal approach to pain therapy and may also require a variety of non-pharmacologic analgesic therapies (eg, acupuncture) as well as a number of analgesic adjunctive medications (e.g. NMDA antagonists). Neuropathic pain, a type of pain caused by a true lesion in the nervous system, is increasingly recognized in veterinary patients. Unfortunately, neuropathic pain can be extremely severe and is also quite difficult to control. Often there is no relief of neuropathic pain from traditional analgesic drugs like NSAIDs and opioids.

Treatment of chronic pain

As stated, treatment of chronic pain is not always easy and often requires a combination of therapies ('multimodal analgesia'). This combination may include multiple pharmaceuticals, pharmaceuticals plus non-pharmacologic therapy (eg, acupuncture, massage, etc..) or both. Often, finding an effective treatment takes time and must proceed on a 'trial and error' basis. It is important to remember – and important to explain to the client - that chronic pain is a very individual disease and treatment protocols almost always require modification for each individual patient. Treatment of chronic pain is most effective when the clinic staff operates as a pain management team. However, a pain management strategy for treating chronic pain will not work unless the pet's owner is also a part of the team. The owner should be educated as to the underlying condition that causes pain, as well as to the effects and side effects of the analgesic therapy. Furthermore, the owner must be committed to long-term therapy and to assessing the extent of their pet's pain and relief of pain from analgesics. Various pain assessment forms are available for the owner to use at home and one is included in Table 1. Also, owners should be advised that adequate pain control involves more than just treatment of the pain itself. Weight loss is extremely

important in overweight patients and alteration of the pet's environment (eg, eliminate need for pet to climb stairs, cover slick floors with mats or rugs to provide better footing, etc…) and activity level (eg, more controlled activity like leash walking is often the best for a pet in pain) are often part of the treatment plan.

TABLE 1: Analgesic assessment for the owners of pets in chronic pain to fill in at home. (modified from 'Pain Management for the Small Animal Practitioner'. Tranquilli et al; published by Teton New Media, Jackson, WY)

	DATE			
PAIN INTENSITY How bad was your pet's pain today?	Severe Moderate Mild None	Severe Moderate Mild None	Severe Moderate Mild None	Severe Moderate Mild None
PAIN RELIEF How much pain relief was achieved by the medication?	Complete Good Moderate Slight None	Complete Good Moderate Slight None	Complete Good Moderate Slight None	Complete Good Moderate Slight None
SIDE EFFECTS Did the medication upset your pet in any way? Please describe.				

Analgesic drugs

A good review of the pharmacokinetics of oral analgesics used for the treatment of chronic pain in dogs and cats has been published (KuKanich 2013).

Multimodal therapy

Effective treatment of moderate to severe chronic pain almost always requires multimodal therapy. What options are available when the patient is unable to take NSAIDS or, more commonly, when the pain advances to a pain state that is uncontrollable by NSAIDs used alone? In that instance, opioids, N-methyl-D-aspartate (NMDA) antagonists, and novel drugs like gabapentin should all be considered as potential therapies. In addition, non-pharmacologic therapies (eg, acupuncture, massage, physical therapy, TENS, etc…) should be strongly considered. Dosages for drugs used to treat chronic pain, along with considerations for the use of the drugs, are listed in Table 2.

NSAIDs

Non-steroidal anti-inflammatory drugs (NSAIDs) are the mainstay of treatment of chronic pain. This is an appropriate choice since most forms of chronic pain do have an inflammatory component. NSAIDs provide analgesia AND treat pain at its source (inflammation). Controlling the pathology of the pain leads to more effective pain relief. NSAIDs are the only drugs that have statistically shown consistent relief of chronic pain. Multiple NSAIDs are approved for treatment of chronic pain in dogs. There are no FDA approved NSAIDs for treatment of chronic pain in cats, but there are guidelines and clinical reports demonstrating safety and efficacy of NSAIDs when administered at the correct dose to cats.

The meloxicam dose most commonly used for chronic pain in cats is 0.03-0.05 mg/kg/SID. This can be administered daily or less frequently, if possible. Dosages as low as 0.01 mg/kg/SID may be effective (Gunew MN, et al. J Feline Med Surg. 2008;10(3):235-41) and perhaps even beneficial – or at least not harmful - in some cats with chronic kidney disease (Gowan RA, et al. J Feline Med Surg. 2012;14(12):876-81; Gowan RA, et al. J Feline Med Surg. 2011;13(10):752-61). There are no studies on the use of robenacoxib for chronic pain but there is a published study reporting safety when the drug was used for 42 days (King JN, et al. J Vet Pharmacol Ther. 2012;35(3):290-300.). Anecdotally, the label dose is commonly used SID or less frequently for treatment of chronic pain in cats.

Piprants
Piprants are prostaglandin receptor antagonists and grapiprant is currently the only drug in this class. Grapiprant antagonizes the EP4 receptor of PGE2. This receptor mediates pain and inflammation associated with OA. Because other prostaglandins are not blocked, those involved in homeostasis are not affected and the adverse effects commonly associated with traditional NSAIDs (eg, gastrointestinal upset & ulceration and renal & kidney damage) are minimal to nonexistent. At the time this manuscript was written, grapiprant was not yet FDA-approved in cats but a safety study has been published (Rausch-Derra LC, Rhodes L. Am J Vet Res. 2016;77(7):688-92.).

Gabapentin
Gabapentin is commonly used to control seizures in both human and veterinary patients. In addition to the antiseizure activity, gabapentin has been shown to be effective in treating neuropathic pain. Neuropathic pain is pain from nervous system pathology and includes conditions that cause direct pathology of the nervous system (eg, herniated discs, nerve root tumors), pressure on nerves (eg, osteophytes near nerves) or nerve damage (eg, trauma, surgery – especially when large nerves are cut). In addition, the pathologic changes that occur in the pain pathway in response to chronic pain stimulation cause neuropathic pain. Although no research manuscripts are available regarding the use of gabapentin in dogs and cats for the treatment of chronic pain, many practitioners are using the drug for control of various pain syndromes. The dosage generally ranges from 1-10 mg/kg PO BID to QID but dosages as high as 50 mg/kg have been anecdotally reported. Generally, gabapentin therapy is initiated at 3-10 mg/kg PO BID and dosages increased as necessary. The most common side effect is sedation and the dose of gabapentin should be reduced in patients that become sedate. Gradually increasing the dose over time generally eliminates the chance of sedation. Recommended gabapentin treatment guideline:

- Start at 5 mg/kg for mild pain and 10 mg/kg BID for moderate to severe pain.
    - If the patient has renal or hepatic disease, the starting dose may be as low as 3 mg/kg BID (see more under adverse effects).
- If no pain relief occurs in 3-5 days, use the same dose TID.
- If no pain relief occurs in another 3-5 days or if TID dosing is not possible, increase the dose by roughly 25% per dose.
- Continue escalating every 3-5 days until one of the two endpoints is reached (sedation or pain relief).
- If sedation is reached before pain relief, return to the previous (non-sedating) dose and maintain at that dose for 7 days.
- If the patient is comfortable, stay at that dose. If not comfortable, try increasing again. Gradually increasing the dose over time often decreases the incidence of sedation.
- If sedation without pain relief occurs a second time, we presume that gabapentin will not be effective and change therapeutic plans. Often the plan still includes gabapentin but with more multimodal therapy.
- The If the patient is to be removed from gabapentin therapy (eg, the patient is ‘cured’ or the gabapentin is not working), the drug should be gradually withdrawn over a period of one to three weeks (depending on the duration of therapy) to prevent potential rebound pain.
    - Have the owner continue to monitor the patient. Drug efficacy is sometimes easier to identify when the drug is being withdrawn.

If the patient is to be removed from gabapentin therapy (eg, the patient is ‘cured’ or the gabapentin is not working), the drug should be gradually withdrawn over a period of one to three weeks (depending on the duration of therapy) to prevent rebound hyperalgesia. Gabapentin has a variety of uses in chronic pain and scenarios for addition of gabapentin should include:

- Patients with painful backs/necks
- Any patient with known nerve damage
- Patients with difficult to diagnose, difficult to characterize pain
- Patients with long standing chronic pain

Opioids

Tramadol is probably the most commonly used opioid for treatment of chronic pain in veterinary patients. Tramadol is a centrally acting analgesic drug that is structurally related to both codeine and morphine and does have some opioid effects. However, tramadol also inhibits both serotonin and norepinephrine uptake. These varied activities are complementary and synergistic for analgesia and have led to the classification of tramadol as a 'nontraditional centrally acting analgesic'. However, tramadol provides analgesia that is moderate at best and the drug should be used as part of a multimodal protocol rather than as a stand-alone drug. This is further evidenced by the fact that absorption of tramadol is highly variable in dogs and it is not possible to predict which dogs might absorb the drug poorly, resulting in inadequate analgesia for that patient. In dogs, the systemic availability following 11 mg/kg of orally administered tramadol was 65 ± 38% and the half-life (t½) was 1.71 ± 0.12 hrs (Kukanich & Papich, 2004), which is much shorter than the t½ in human beings. Furthermore, dogs produce very little of the intermediate (M-1) metabolite that is likely responsible for a good deal of tramadol-mediated analgesia. When compared to dogs, bioavailability was greater (93±7%) and the t½ was longer (204±8 mins) in cats following 5 mg/kg tramadol administered orally (Pypendop & Ilkew, 2008; Papich & Bledsoe, 2007). Furthermore, cats produced a significant concentration of the active M-1 metabolite, which also had a long t½. Thus, there are more opioid mediated effects, including analgesia and dysphoria, from administration of oral tramadol in cats when compared to dogs.

The tramadol dose for the dog and cat is 2-5 mg/kg BID to QID. Because of the high bioavailability and production of the active metabolite in cats, a starting dose of 2 mg/kg BID is recommended. Dogs, conversely, generally require TID-QID dosing for effective pain control and dosages of up to 10 mg/kg are used anecdotally. Tramadol can cause opioid-mediated side effects in dogs, including sedation and mild cases of anorexia, nausea and constipation. Tramadol could potentially cause serotonin reuptake syndrome when combined with other selective serotonin reuptake inhibitors (SSRIs; fluoxetine (Reconcile® or Prozac®), paroxetine (Paxil®), sertraline (Zoloft®) and fluvoxamine (Luvox®)) or serotonin-norepinephrine reuptake inhibitors (SNRIs; Cymbalta (duloxetine), Effexor (venlafaxine)), although the use of tramadol at appropriate dosages has not been reported to cause serotonin reuptake syndrome (reports are all due to a significant tramadol over dosage). Serotonin receptor-antagonists and reuptake inhibitors (SARIs; trazodone) might also interact with tramadol.

Other opioids used in veterinary medicine include transdermal fentanyl and oral formulations of codeine, codeine + acetaminophen (DOGS ONLY), morphine, oxycodone, hydrocodone and methadone. These opioids are more potent than tramadol and should be considered anytime that pain is severe or when pain has advanced beyond the point that it can be controlled by tramadol. These opioids are DEA scheduled (fentanyl, codeine and morphine are Class II, codeine+acetaminophen is Class III) and have a greater potential to cause adverse effects (primarily sedation, nausea and, eventually, constipation) than tramadol but are more likely to control severe pain. Research trials have shown poor evidence that orally delivered opioids are effective for analgesia because of their low bioavailability (KuKanich 2013) but clinical use supports their efficacy in some patients. Buprenorphine (Class III) can be administered bucally for both acute and chronic pain in cats but new information has shown that absorption is not as good as was once thought (Giordano, et al. 2010), so recommended dosages have been increased for this route of delivery to 0.03-0.05 mg/kg BID-QID.

Amantadine

Amantadine is an antiviral drug that also antagonizes the N-methyl-D-aspartate (NMDA) receptors, an action which prevents or reverses the development of central sensitization but does not provide direct analgesia. In humans, the NMDA-receptor antagonists are being extensively researched and have been used for treatment of acute, chronic and 'specialized' (eg, neuropathic and phantom limb) pain conditions. Newer NMDA-receptor antagonists (eg, memantine) are available in human medicine. The role of amantadine in pain management has been reported in dogs by Lascelles et al (2008). Effective pain control was achieved when amantadine was combined with an NSAID and dosed at 5 mg/kg orally for 21 days. A recent literature search yielded no other veterinary publications describing the use of amantadine for analgesia. Amantadine has a variety of uses in chronic pain and scenarios for addition of amantadine include:

- Anytime pain of 'wind-up' could be an issue
- NSAIDs suddenly 'not working' after controlling pain long-term
- Any long standing untreated pain
- Moderate to severe cancer pain

Amantadine should be dosed at 5-7 mg/kg SID-BID (BID is recommended) for at least 3 weeks.

Ketamine
Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist and plays a role in both anesthesia & analgesia. Activation of the NMDA receptors in the dorsal horn of the spinal cord are, in large part, responsible for the pain of central sensitization (or 'wind up). By antagonizing these receptors, the pain pathway can be returned to 'normal'. Meaning that the patient may still feel pain (thus ketamine must be part of a multimodal protocol) but that the pain is not exaggerated and is more likely to be controlled by traditional analgesic drugs like NSAIDs and opioids. To achieve this effect, ketamine must be administered as an infusion. The analgesic effects in chronic pain have been well-documented in humans (Remerand et al. 2009; Sigtermans et al. 2009), although, as with any treatment of any chronic condition, a ketamine infusion does not always produce analgesia (Sen et al. 2009). This may be because the pain in those patients is not caused or augmented by central sensitization. In veterinary medicine, ketamine improved postoperative analgesia after forelimb amputation for up to 3 days (Wagner et al. 2002). There are no publications to guide ketamine infusions in dogs and cats for chronic pain but an infusion of 2-6 microg/kg/min is fairly common. The duration of the infusion is not known. Ideally, the infusion would be administered until the patient demonstrates decreased pain but this is unlikely to be practical. Anecdotal reports include everything from 2 to 24 hours but the common range is 2-6 hours. The infusion is repeated 'as needed' – generally every 30 days. As stated, this is part of a multimodal protocol and the goal is to return quality of life to the patient but not necessarily to eliminate any other analgesic therapies.

Other drugs
Because chronic pain is so difficult to treat, new drugs – or new applications for old drugs – are continually being investigated. Currently, other drugs to consider for treatment of chronic pain include antidepressant drugs (eg, the tricyclic antidepressants, SNRIs, SSRIs, etc.), bisphosphonates and newer generations of currently used drugs like pregabalin (newer generation of gabapentin) and tapentadol (newer generation of tramadol).

Nonpharmacologic Therapy
Techniques reported useful for treatment of OA-mediated pain include everything from simple heat/cold therapy to more advanced techniques like physical therapy/rehabilitation, acupuncture and massage. In addition to the modalities just listed, modalities like therapeutic ultrasound, transcutaneous electrical nerve stimulation (TENS), pulsed radio frequency and low-level laser may all contribute to pain relief but, as with nutraceuticals, most of the evidence of efficacy is weak at best. However, physical therapy/rehabilitation and acupuncture have more positive evidence than the other modalities and many pain practitioners incorporate these techniques into their OA treatment plans. An advantage of the simpler nonpharmacologic therapies is that owners can often be trained to utilize basic techniques at home and the pet can then benefit from more consistent therapy. Owners can be taught to utilize ice packs, heat compresses, basic exercise and physical therapy maneuvers, basic massage, and acupressure. As stated with nutraceuticals, lack of evidence of efficacy does not mean that these treatment modalities are ineffective in all patients and the modalities should be considered as a viable part of multimodal analgesia, especially in patients where other therapies have failed, or as stand-alone treatment when pharmacologic therapy is inappropriate for the patient or when the nonpharmacologic therapy is effective when used alone.

Special diets, dietary supplements, nutraceuticals & other disease-modifying compounds
Most of the diets and food supplements are designed to modify the disease progression of OA and are thus called 'disease modifying osteoarthritis agents' (DMOAA). The idea of disease modification is a step in the right

direction for disease elimination, but evidence supporting the OA-modifying efficacy of most diets, dietary supplements and nutraceuticals is fairly sparse and not always scientifically based. A good review of a number of these products is available (Fox 2009) and the author of that review states, 'Perhaps the best advice for pet owners is to spend their money where the science is strong' (Fox 2009).

However, it does appear that some of compounds may modify the progression of OA, especially diets rich in eicosapentaenoic acid (EPA) (Fox 2009) and at least one of the polysulfated glycosaminoglycan (PSGAG) chondroprotective compounds (Fox 2009). In fact, there is one injectable) PSGAG available that is FDA-approved for the treatment of OA in dogs (Adequan®). It is commonly used in cats at the same dose used in dogs. An advantage of this compound is that it can be administered SQ by the owner at home, which means that some patients may be more likely to get treated since the cat doesn't have to come to the hospital. However, because any improvement that does occur is fairly slow, these compounds should be used as adjunctive therapy to NSAIDs or other rapidly-acting, more potent analgesic drugs when pain is moderate to severe. As a caveat to this discussion, because chronic pain has many facets and inciting causes, some of the DMOAAs with little evidence may still work in a particular patient. Lack of evidence does not necessarily mean lack of efficacy for an individual patient, but does decrease the likelihood that the efficacy would be apparent in a global population of patients.

Conclusion

Chronic pain can drastically alter a patient's quality of life and can, unfortunately, be difficult to treat. In order to obtain adequate pain control, multimodal therapy should be utilized in every patient with moderate to severe pain. Also, unfortunately, the number of drugs and techniques that are available to treat chronic pain is fairly limited and knowledge of the use of these drugs and techniques in dogs and cats is even more limited. However, because chronic pain is a major problem in human medicine as well as veterinary medicine, research into the relief of chronic pain is extensive. Hopefully, new drugs and techniques developed for humans will rapidly become available to our veterinary patients.

Some common scenarios with treatment recommendations *(see table for dosing info):*

1. A patient with mild OA has been on an NSAID for a week and the NSAID isn't working to control pain.
   - Solution: Try another NSAID. Individual sensitivity exists in animals just like it exists in human beings. ALL NSAIDs work globally, but each individual may respond better to one NSAID than to another.
2. A patient (dog or cat) with mild OA has been on an NSAID for an extended duration of time and the NSAID was controlling pain adequately until recently. Now, despite the fact that the disease doesn't seem to be worsening, the patient is fairly painful.
   - Solution: Add amantadine to the current therapy. The most common explanation for this scenario is that the chronic stimulation of the NMDA receptors in the dorsal horn of the spinal cord has produced central sensitization. The NSAID should remain to treat the inflammatory component of OA.
3. A patient (dog or cat) with moderate OA or cancer pain is painful even on an NSAID.
   - Solution: Add gabapentin to the NSAID and send home tramadol (or another opioid), either on a continuous basis or an 'as needed' basis. The opioids in cancer patients are generally administered on a continuous basis. If this is a cat, consider using OTM buprenorphine as the opioid.
4. A patient with disc herniation is very painful but is not a candidate for surgery.
   - Solution: Add gabapentin to the NSAID (or steroid) treatment and use tramadol (or another opioid) either as continuous therapy or on an 'as needed' basis. For severe pain, hospitalize the patient for several hours of a ketamine infusion.
5. A cat has pain of OA and elevated renal enzymes but the owner would like to try to improve the cat's quality of life.
   - Try a joint health modifier like Adequan or Cosequin. These are often very successful in cats. NSAIDs may also be appropriate as evidenced by cats with confirmed renal failure receiving meloxicam for chronic OA pain with no detrimental renal effects (Gowan et al 2012).

TABLE 2: Dosages for drugs other than NSAIDs used to treat chronic pain in dogs and cats. Not all drugs / dosages are approved for use. PO=oral, SC=subcutaneous, IM=intramuscular, IV=intravenous, OTM=oral transmucosal. SID=once daily, BID=twice daily, TID=three times daily, QID=four times daily.

Drug	Dog Dosage	Cat Dosage	Comments
Opioids			Chronic use of opioids may cause constipation.
Tramadol (50 mg tablets)	2-5 mg/kg (up to 10 mg/kg?) PO BID - QID. Frequent dosing recommended due to low bioavailability.	2-5 mg/kg PO BID-TID. Start with 2 mg/kg BID because of high bioavail-ability in the cat.	Tramadol is an 'opioid like' drug that has other mechanisms of action. The pharmacokinetics in the dog are somewhat erratic so the drug is best used as multimodal therapy with NSAIDs or other analgesic drugs.
Oral morphine (10,15,30 mg tablets)	0.5-2 mg/kg PO TID - QID (can be dosed as often as q2-4hrs)	0.25-0.5 mg/kg PO TID-QID (can be dosed as often as q3-4 hrs)	Higher doses may induce sedation or dysphoria. Nausea & vomiting may also occur but a tolerance to these effects generally develops within 1 week.
Sustained release oral morphine (15, 30, 60, 100, 200 mg tablets)	2-5 mg/kg PO BID - QID	Difficult to dose due to size of tablets (tablets should not be cut)	Higher doses may induce sedation or dysphoria. Increase the frequency of administration prior to increasing dose if duration is not long enough
Codeine (15, 30, 60 mg tablets)	1-2 mg/kg PO q6-8 hrs	0.1-1.0 mg/kg PO 4-8 hrs	Higher doses may induce sedation or dysphoria. Nausea & vomiting may also occur but a tolerance to these effects generally develops within 1 week.
Codeine (30 or 60 mg) plus acetaminophen (300 mg)	1-2 mg/kg (codeine) PO q 8-12 hr	**TOXIC TO CATS - DO NOT USE**	Multimodal therapy improves analgesia over either drug used alone. DO NOT EXCEED 10-15 mg/kg acetaminophen per dose.
Transdermal fentanyl (25, 50, 75, 100 µg/hr)	3-5 ug/kg/hr	3-5 ug/kg/hr	May induce sedation or dysphoria. Addition of an NSAID may improve analgesia.
Methadone (5, 10 mg tablets)	0.1-0.5 mg/kg IM, SC q 2-4 hrs	0.1-0.5 mg/kg IM, SC q 2-4 hrs	Side effects same as other opioids. Only injectable dosing currently published.
Buprenorphine (0.3mg/ml inject.)	0.01-0.03mg/kg SC, IM, IV; 0.03-0.05 OTM	0.01-0.03 mg/kg SC, IM, IV; 0.03-0.05 OTM	May cause mild opioid side effects. Volume too large to be practical in anything larger than a cat or small dog.
Other drugs or compounds			
Amantadine (Various capsules, liquid)	2-5 mg/kg PO SID-**BID** for at least 21 days	2-5 mg/kg PO SID-**BID** for at least 21 days	Does not provide analgesia directly but helps prevent / treat wind-up due to NMDA receptor antagonist activity. Use in multimodal protocol.
Ketamine (100 mg/ml)	2-4 microg/kg/ min for several hours. Optimal duration of infusion is unknown.	2-4 microg/kg/min for several hours. Optimal duration of infusion is unknown.	Can be used to 'break' the cycle of severe pain. Does not provide analgesia directly but helps prevent / treat wind-up due to NMDA receptor antagonist activity. Use in multimodal protocol.
Gabapentin (multiple tablet	1-10 mg/kg PO BID-QID; up to 40	1-10 mg/kg PO BID-QID; up to 40	Effective for treatment of neuropathic pain. Best used as part of a multimodal protocol.

or capsule sizes; liquid has xylitol)	mg/kg (start with 3-10 mg/kg)	mg/kg (start with 3-10 mg/kg)	Increase the dose by about 25% every 3-7 days until patient is more comfortable or sedate. If sedate, go back to previous dose.
Polysulfated Glycosamino-glycan (eg, Adequan)	Inject 2mg per lb given only by intramuscular (IM) injection twice a week for up to 4 weeks (a maximum of 8 injections)	Inject 2mg per lb given only by intramuscular (IM) injection twice a week for up to 4 weeks (a maximum of 8 injections)	Licensed by the FDA for control of OA pain in dogs (not licensed in cats). Clinically most effective for mild pain or as part of a multimodal protocol.

What Are They Hiding? Pain Assessment in Dogs and Cats

Tamara Grubb, DVM, PhD, Diplomate ACVAA

Introduction: the 5th vital sign

Pain is called the 5th vital sign in human medicine (vital signs: heart rate, respiratory rate, arterial blood pressure, body temperature, pain) and is often called the 4th vital sign in veterinary medicine (because we don't often measure blood pressure in a routine physical exam). Why is pain the '5th vital sign'? Because pain is the main reason that humans seek medical care. And because of the importance of unrecognized pain:

Pain is a stressor and impacts the entire body through physiologic responses to stress;
Healing is faster when pain is adequately treated;
Unrelieved pain can delay healing and turn acute pain into a chronic problem;
Chronic pain is 'pathologic pain' with no protective value.

What does that have to do with veterinarians?

Why do we care in veterinary medicine? Because our patients feel pain too. The pain pathway is the equivalent in all mammals so if a stimulus would cause pain in a human, it would also cause pain in an animal. And perhaps pain is not the main reason that animals 'seek' veterinary care, but the importance of unrecognized pain is the same in our patients as it is in human patients. However, animals are very likely to try and hide pain since pain could be considered a 'weakness' and, no matter how long animals have been domesticated, the instinct for survival still exists and that instinct dictates that animals hide weaknesses – or they may be killed by stronger animals. So we must anticipate pain, look for signs of pain and 'ask' our patients if they are in pain.

Anticipating Pain

The best way to control pain in our patients is to anticipate the level of pain that might occur from the surgery, diagnostic test, traumatic event, etc… that will be/has been experienced by the patient. Since all mammals have a similar pain pathway, we can scientifically say that an experience that would cause pain in a human will indeed cause pain in an animal. Although true that animals may not cerebrally process pain like humans do, it is a certainty that they do indeed feel pain and pain intensity in humans is most likely parallel to pain intensity in animals. Thus, we can use charts like those provided by Dr. Karol Mathews (Mathews KA, Vet Clinics of North America, Small Animal Practice 2000;30:729-755.) to anticipate the degree of pain that our patients will feel based on the degree of pain expected from with the procedure, surgery, injury, disease, etc...

Looking for Pain

However, sometimes we don't anticipate well and we need to look for pain. And even if we have utilized excellent analgesia, we should still assess our patients for pain since pain is a very individual experience and the analgesic protocol may not be adequate for all individual patients. Let's go back to the vital signs. We don't 'ask' the patient to 'tell' us the other vital signs, so why would we 'ask' them to 'tell' us their pain level? We must LOOK for pain. We can use the other vital signs to aid in pain assessment. Since pain is a stressor, we can look for physiologic signs of stress: tachycardia, tachypnea, hypertension, arrhythmias, etc… However, a change in physiologic parameters without any other change may not indicate pain. Conversely, changes in behavior or signs of pain like limping may indicate pain even if physiologic changes have not occurred. A partial list of signs that might indicate pain are listed in Table 1. Of course, these signs can be altered by any stress, including hospitalization, doctors with white coats, barking dogs, etc… so they must be assessed in conjunction with other signs of pain.

Vocalization is often used to determine the presence of pain, and this can be useful, but vocalization is often breed specific (eg, Huskie dogs and Siamese cats) and, especially in the postoperative setting, can be due to dysphoria. Vocalization can include growling or hissing and, of course, are more specific for pain if they occur following a painful event – especially if the patient didn't growl or hiss before the painful event.

We can also look for changes in posture and gait, which can often be quite specific for pain. Changes in posture like 'tucked' abdomen or 'hunched' back usually indicate pain. Head down, neck stretched, ears back or flat and tail down are also all signs that could indicate pain. Body posture while lying down is also important. For instance, cats generally sleep 'curled' and cats that are laying stretched out may be experiencing pain, but again this should be linked to a potential painful condition or event, not just a happy cat stretched out in the sun. Of course, lameness is usually indicative of pain, although mechanical lameness can occur if healed fractures or articular injuries cause abnormal anatomical changes to the limb. But lameness should always be investigated.

Lameness may become worse with exercise (pain of unstable joints) or worse with sedentary activity (like old dogs with musculoskeletal pain that are more painful after a night's sleep) so it is important to get a history from the owner regarding the timing of the animal's lameness. Walking with a very stiff or abnormal gait may also occur with pain.

One physical change that was not attributed to animals until recently is change in facial 'expressions'. However, with the publication of the 'rat grimace scales' (Sotocinal SG, et al. *Molecular Pain* 2011, 7:55), the ability to identify changes in facial expressions in animals has been validated and expressions related to pain have been described in other species. These should be used as part of the overall pain assessment and are included in some pain scales, like the Colorado State scales discussed below.

Other signs that might be linked to pain include changes in eating, grooming or defecation/urination habits. For instance, cats that are litter box trained but suddenly stop using the box for defecation/urination may have pain that precludes them from wanting to climb into the box. Of course, all other sources of changes in defecation/urination (eg, urinary bladder infection, gastrointestinal disease, new cats in the house, etc..) must be ruled out. These indices might also be related to behavior and **one of the most useful signs of pain is change in behavior**. Of course, we can't be sure that a change in behavior necessarily means pain, but a change in behavior that coincides with a painful event (eg, surgery or trauma) should be investigated. Animals that were friendly may become aggressive or defensive and those that were solitary may seek human companionship and comfort. The animal's behavior may even seem normal until the painful area is approached or touched and then fear or aggression may be exhibited. Animals that don't exhibit normal sleep behavior, especially those that don't want to lie down and sleep after a painful surgery, are very likely painful.

Ask the Patient if it feels Pain

Finally, the most useful way to determine whether or not an animal is in pain is to administer an analgesic drug and evaluate the response to the drug. For acute pain, an opioid is often the best option because of the rapid onset and 'high' potency of the drug. For chronic pain, an NSAID is often the best choice, but a dose of an opioid can be used to make a rapid decision. If the patient's behavior returns to normal after treatment, then the diagnosis has been made – PAIN, and now we can move on to developing a treatment plan that will provide the patient with pain relief. If the patient's behavior does not return to normal but pain is still a likely diagnosis, try another dose of the analgesic drug and add a drug from another drug class (eg, use opioids and NSAIDs together). Relief of severe pain often requires multimodal therapy and may require higher than expected drug dosages. Lack of response to aggressive analgesic therapy can be used as a diagnostic tool since continued abnormal behavior would unlikely be due to pain if analgesic therapy is adequate but the patient doesn't improve. Pain is ruled out and further diagnostics are begun.

Scoring Systems

One of the best ways to detect pain is to use pain scoring systems, especially systems that combine physiologic, physical and behavioral signs. In human medicine, pain scoring systems are used to determine the level of pain as the 5th vital sign, although these systems are generally not as robust as the scoring systems that we are using in veterinary medicine since humans can verbalize their level of pain. No pain scoring system is perfect, especially since we have to rely on a human's perception of what the animal is feeling – or what the animal is trying to hide. There are many scoring systems that range from simple numeric scales with no descriptors to more complex

scales with physiologic, postural and/or behavioral indices to evaluate. Thus, each clinic can choose the one that works best for them. Ideally, the same person will score the animal before and after a painful procedure (like surgery) or before and after pain relieving treatment. Using the same person to score the patient improves the usefulness of the scoring system. Systems are available for both acute and chronic pain. One easy to use descriptive scale is the Colorado State University pain scale, which is available for both dogs and cats (Figures 1 & 2). Another commonly used scale is the Glasgow Composite Short Form, which is not as intuitive as the CSU scale but has been validated to identify pain in the research setting in both dogs and cats (Figures 3 & 4). Another validated pain scale for cats is the UNESP-Botucatu scale from Brazil. The scale is located at an excellent website (http://www.animalpain.com.br/en-us/avaliacao-da-dor-em-gatos.php) that includes a series of videos of painful cats for scoring practice. Other scales, including facial grimace scales, are available.

Owners know the normal behavior of their pets better than anyone and owners see their pets in an environment very different from the stressful environment of the animal hospital. Thus, we should get a good history of the animal's behavior from the owner when investigating pain. And, especially with chronic pain, the owner should be asked to participate in an evaluation of their pet's pain – and pain relief. Scoring systems like those in Figures 5 and 6 can easily be used by pet owners.

The CSU, Glasgow and Botucatu scales can be downloaded at the following sites:
CSU Canine: http://www.csuanimalcancercenter.org/assets/files/csu_acute_pain_scale_canine.pdf
CSU Feline: https://www.csuanimalcancercenter.org/assets/files/csu_acute_pain_scale_feline.pdf
Glasgow Canine: http://www.isvra.org/PDF/SF-GCPS%20eng%20owner.pdf
Glasgow Feline: https://novacatclinic.com/wp-content/uploads/2016/06/CMP_feline_eng.pdf
UNESP-Botucatu: http://www.animalpain.com.br/assets/upload/escala-en-us.pdf

SUMMARY

Animals feel pain and pain can add to the patient's morbidity, but animals are masters at hiding pain so we must learn to look for the pain. Using physiologic, physical and behavioral signs of pain, especially when combined in a pain scoring system, can help us to identify patients that need analgesic therapy. An even better way to identify pain is to administer an analgesic drug and monitor the patient's response to treatment.

Table 1: Examples of signs that might indicate pain in dogs and cats.

Physiologic Signs	**Behavior Signs**	**Expression/ Vocalization**	**Posture/ Body position**	**Gait/ Locomotion**	**Other**
Tachycardia	Any change in behavior	Howling (dog)	Head down	Lameness	Failure to groom
Tachypnea, Panting	Aggression	Whimpering (dog)	'Hunched' body or 'tucked' abdomen	Reluctant to move	Excessive grooming of painful site
Hypertension	Hiding/ avoidance	Excessive barking (dog)	Tail down	Walks with stiff gait	Failure to go outside to urinate or defecate
Arrhythmias	Seeks comfort, won't leave owner	Growling (dog or cat)	Ears 'flat' or out to side (cat)	Walks with more weight on front or back legs	Failure to use litter box
	Guards painful area – may snap if painful area touched	Hissing (cat)	Laying in straight position rather than curled (cat)	Pacing	Change in facial 'expressions'
	Won't lie down, won't sleep	Purring (cat)			Anorexia

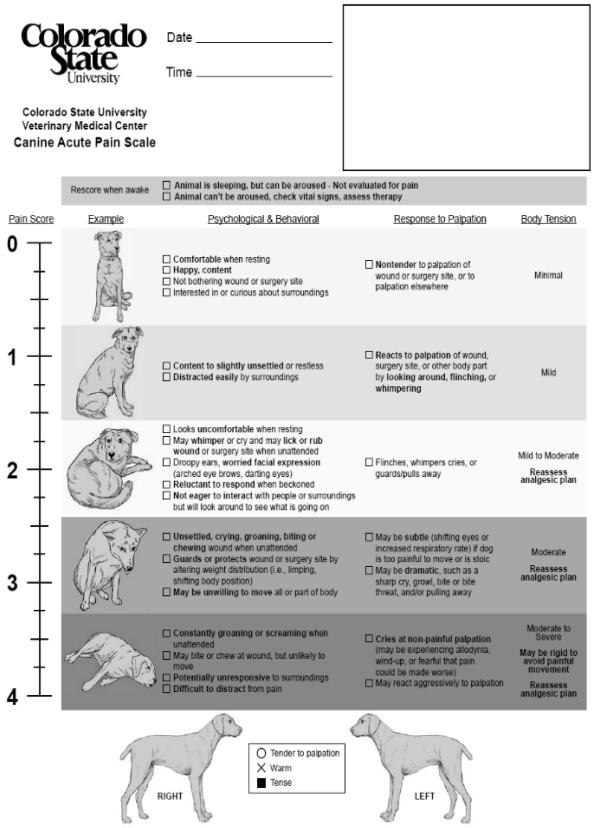


Figure 1: Colorado State University canine pain scale

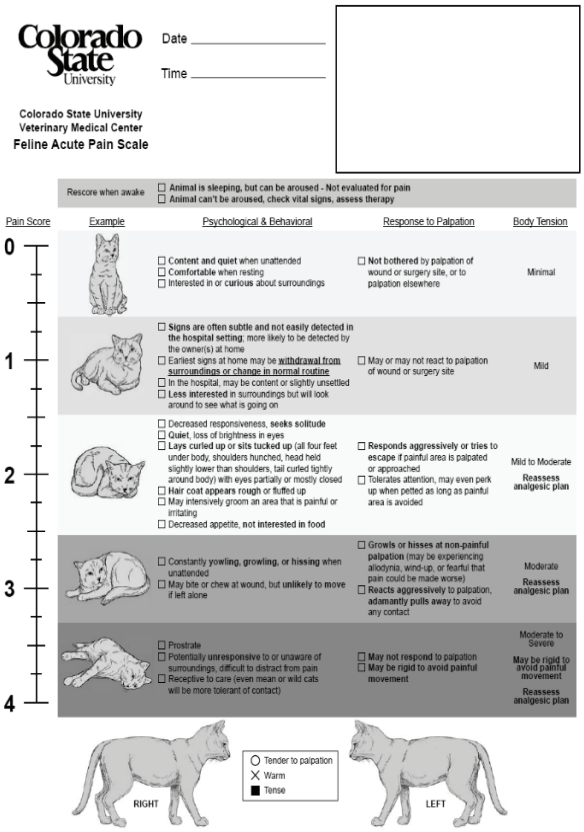


Figure 2: Colorado State University feline pain scale

SHORT FORM OF THE GLASGOW COMPOSITE PAIN SCALE

Dog's name _____

Hospital Number _____ Date / / Time

Surgery Yes/No (delete as appropriate)

Procedure or Condition_____

_____

In the sections below please circle the appropriate score in each list and sum these to give the total score

A. Look at dog in Kennel

Is the dog?

(i)		(ii)	
Quiet	0	Ignoring any wound or painful area	0
Crying or whimpering	1	Looking at wound or painful area	1
Groaning	2	Licking wound or painful area	2
Screaming	3	Rubbing wound or painful area	3
		Chewing wound or painful area	4

In the case of spinal, pelvic or multiple limb fractures, or where assistance is required to aid locomotion do not carry out section **B** and proceed to **C**
Please tick if this is the case ☐ then proceed to C.

B. Put lead on dog and lead out of the kennel.

When the dog rises/walks is it?

(iii)	
Normal	0
Lame	1
Slow or reluctant	2
Stiff	3
It refuses to move	4

C. If it has a wound or painful area including abdomen, apply gentle pressure 2 inches round the site.

Does it?

(iv)	
Do nothing	0
Look round	1
Flinch	2
Growl or guard area	3
Snap	4
Cry	5

D. Overall

Is the dog? (v)		*Is the dog?* (vi)	
Happy and content or happy and bouncy	0	Comfortable	0
Quiet	1	Unsettled	1
Indifferent or non-responsive to surroundings	2	Restless	2
Nervous or anxious or fearful	3	Hunched or tense	3
Depressed or non-responsive to stimulation	4	Rigid	4

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Total Score (i+ii+iii+iv+v+vi) = _____

Figure 3: Glasgow canine pain scale. Validated in research studies to identify pain.

Glasgow Feline Composite Measure Pain Scale: CMPS - Feline

Choose the most appropriate expression from each section and total the scores to calculate the pain score for the cat. If more than one expression applies choose the higher score

LOOK AT THE CAT IN ITS CAGE:

Is it?

Question 1

Silent / purring / meowing	0
Crying/growling / groaning	1

Question 2

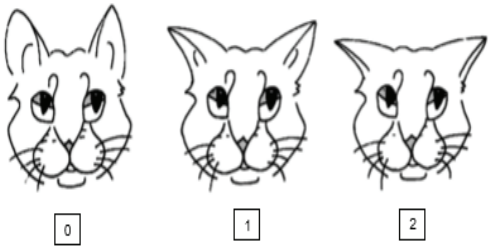
Relaxed	0
Licking lips	1
Restless/cowering at back of cage	2
Tense/crouched	3
Rigid/hunched	4

Question 3

Ignoring any wound or painful area	0
Attention to wound	1

Question 4

a) Look at the following caricatures. Circle the drawing which best depicts the cat's ear position?



0 1 2

b) Look at the shape of the muzzle in the following caricatures. Circle the drawing which appears most like that of the cat?

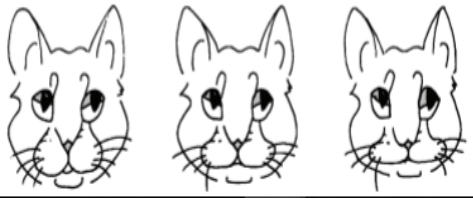


Figure 4: First page of Glasgow feline pain scale. Validated in research studies to identify pain.

Score	C-SOM Term	Descriptor
1	No Problem	
2	Mildly Problematic	Mild; Owner can detect impairment while others might not
3	Moderately Problematic	Intermediate; Easily detected by Owners; observable to others
4	Severely Problematic	Serious;Very obvious to any observed; requires evaluation or treatment
5	Impossible	

Figure 5: The Client-Specific Outcomes Measurement (C-SOM) is a pain scoring system for owners.

DATE				
PAIN INTENSITY How bad was your pet's pain today?	Severe Moderate Mild None	Severe Moderate Mild None	Severe Moderate Mild None	Severe Moderate Mild None
PAIN RELIEF How much pain relief was achieved by the medication?	Complete Good Moderate Slight None	Complete Good Moderate Slight None	Complete Good Moderate Slight None	Complete Good Moderate Slight None
SIDE EFFECTS Did the medication upset your pet in any way? Please describe.				

Figure 6: Another example of an owner-based pain assessment system (modified from 'Pain Management for the Small Animal Practitioner' by Tranquilli, Lamont and Grimm; published by Teton New Media, Jackson, WY)

Mews Flash: Update on Cat Anesthesia and Analgesia

Tamara Grubb, DVM, PhD, Diplomate ACVAA,

Cat Facts

- Often nervous or fractious
  - Increased circulating catecholamines = Increased dose of anesthetic drugs required
- Small body size
  - May be difficult to dose, to fit to monitoring & anesthetic equipment & to keep warm
- Species-specific drug metabolism
  - May not metabolize drugs the same as dogs do (eg, NSAIDs)
- Species-specific response to drugs
  - May respond differently than dogs do (eg, opioids)

These differences add to the fact that cats are at higher risk than dogs for anesthesia-related deaths (risk factor of 0.11% vs 0.05%, respectively, in healthy patients; Brodbelt Vet J. 2009;182(2):152-61).

Anesthesia

Anesthesia can be divided into 4 separate (but continuous) and equally important phases: Preanesthesia, induction, maintenance and recovery.

Preanesthesia

As with other species, appropriate diagnostics and stabilization should occur prior to anesthesia and premedications should be administered to improve the safety of anesthesia by allowing a decrease in the dosages of induction and maintenance drugs and by providing preemptive analgesia.

Preoperative drugs or drug classes and key points:

Opioids	Analgesia, reversible, minimal adverse effects
Alpha-2 Agonists	Analgesia, reversible, titratable sedation; increased cardiac work
Acepromazine	Light to moderate sedation, long duration; not reversible
Benzodiazepines	Very safe but not much sedation

Cat specific information on premedications

- Full opioid agonists (bind to mu and kappa) receptors provide the most profound analgesia but are more likely to cause excitement in cats than in other species. This class of opioids may be used alone for premedication in some dogs but is almost always combined with a sedative in cats.
- Buprenorphine and butorphanol are unlikely to cause excitement but also don't provide analgesia as profound as that provided by the full agonists.
- Butorphanol only lasts about 90 minutes in the cat (Lascelles BD, Roberston SA. AJVR 2004;65(8):1085-1089); buprenorphine lasts 4-8 hours (Steagall PV, et al. J Vet Intern Med. 2014;28(3):762-70).
- Transmucosally administered buprenorphine (this is just the regular buprenorphine applied on the oral mucosa at the standard dose) is a great way to allow owners to provide analgesia for cats at home. Buprenorphine serum concentration after administration by this route was once thought to be equal to serum concentration after IV administration but this was because of sampling. In that study, blood from the jugular vein was analyzed for drug concentration. If a drug is administered for absorption from the oral mucosa, the highest concentration is in the jugular vein (Hedges AR, et al. J Vet Pharm Therap 2014;37(2):145-150). So this route is still good, just not as brilliant as we thought it was. **TIP**: Increase the dose for OTM administration to 0.03-0.05 mg/kg BID-TID.
- Opioids (primarily full agonists) can cause hyperthermia in cats (Posner LP, et al.VAA 2010;37(1):35-43). The hyperthermia is usually mild and self-limiting but body temperature should be monitored postoperatively and any cat that seems agitated in recovery should be checked for hyperthermia.

- Simbadol is buprenorphine in a higher concentration than regular buprenorphine that is FDA-approved for cats. It is labeled for subcutaneous administration (regular buprenorphine is very poorly absorbed after SQ administration) that provides analgesia for 24-hours. It is a DEA Class III drug, just like regular buprenorphine (which is not FDA-approved in animals).
- Dexmedetomidine (specifically Dexdomitor) is one of the few drugs FDA-approved for use in cats. This is one of my favorite drugs – provides sedation AND analgesia and the effects are reversible!

Induction
Induction should occur rapidly & smoothly with drugs dosed 'to effect'.

Induction Drugs and Key Points

Propofol	ADV: Easy to titrate to effect and cleared by multiple routes; DISADV: Dose-dependent cardiovascular & respiratory depression.
Alfaxalone	Similar to propofol for both advantages and disadvantages. Can be administered IM but volume is large.
Ketamine	ADV: Minimal to no change in cardiovascular or respiratory function in patients with healthy hearts; DISADV: Cleared in part unchanged by the kidney – especially in cats.
Telazol	Similar to ketamine/benzodiazepine; very potent.
Etomidate	ADV: No cardiovascular changes – safest drug for patients with cardiovascular disease; DISADV: Causes muscle tremors, dysphoria, vocalization if sedation isn't adequate.
Inhalants	Not ideal for use as a routine induction drug. Causes dose-dependent cardiovascular and respiratory depression.

Cat specific information on induction drugs

- Propofol may cause Heinz bodies with repeat administration (meaning repeated over several days) and was once thought to be a limiting factor for propofol. However, the same thing happens with repeat dosages of ketamine (Bley CR, et al. JAVMA 2007;231(9):1347-53). Turns out it is probably just a cat response, maybe not so much a propofol problem.
- Propofol can be safely used in cats with hepatic lipidosis (Posner LP, et al. JAVMA 2008;232(12):1841-3), even though propofol itself is a lipid.
- The preservative in propofol (Propoflo28) is NOT toxic to cats (Taylor PM, et al. J Feline Med Surg 2012;14(8):516-26). This type of propofol is preferred to the old propofol because the preservative allows the bottle to be used for 28 days after opening whereas the old propofol without a preservative could only be used for 6 hours after opening. This propofol CAN BE USED IN CATS! It isn't FDA approve in cats, but most drugs aren't☹.
- Alfaxalone is labeled for IM administration in cats in some countries outside the US. A low dose (0.5-1.0 mg/kg) combined with an opioid is appropriate for sedation in geriatric or compromised cats (not very sedating in healthy cats) but the IM label dose (10 mg/kg) is a HUGE volume and can cause dramatic hyperreactivity with prolonged recovery (Grubb et al. J Fel Med Surg 2013;15(10):858-865).
- Inhalant induction (mask or chamber induction) is a risk factor for anesthesia-related death and should NOT be the routine method of anesthesia induction (Brodbelt Vet J. 2009;182(2):152-61).

After induction comes intubation. Cat specific information on intubation:

- Intubate carefully.
- Apply a drop of lidocaine on each arytenoid. Cats are more prone than dogs to laryngospasm. The lidocaine reduces the likelihood of laryngospasm. Alternatively, or additionally, titrate a small dose of induction drug – laryngospasm is often related to inadequate anesthetic depth for intubation.
- Inserting an endotracheal tube was a risk factor for anesthesia-related death in cats (Brodbelt Vet J. 2009;182(2):152-61) – but it isn't the tube that is a risk factor, it is poor intubation technique that is a risk factor.
- Disconnect patients from breathing systems before repositioning them – especially cats. The twisting of

the tube in the trachea as the patient is repositioned can cause tracheal damage.

- Don't use a rigid mouth gag for intubation (or for dentistry, or anything else) in cats. These mouth gags cause excessive opening of the mouth which can cause occlusion of the maxillary artery, which is the main source of blood supply to the retina and brain in cats (Martin-Flores M, et al. Vet J 2014;200:60-64). Occlusion of this artery secondary to mouth gag use has been linked to blindness and neurologic dysfunction, which was profound enough to warrant euthanasia in some cats (Stiles J, et al. Vet J 2012: 2012;193(2): 367-73).

Maintenance

Maintenance is not only about anesthetic drug delivery but also about analgesia, monitoring and support.

- As with other species, inhalant anesthetic drugs are commonly used for procedures lasting > 30 mins.
  - Isoflurane, sevoflurane, desflurane
  - Easily cleared from the body, minimal metabolism, easy to change anesthetic depth
  - Dose-dependent cardiovascular and respiratory depression
- Injectable drugs are also commonly used in cats for short procedures. These are often administered IM since really small cat veins can make IV injection difficult. Common protocols include:
  - Ketamine + an opioid + an alpha-2 agonist
  - Telazol + an opioid + an alpha-2 agonist

Analgesia

To decrease the dose-dependent impact on cardiovascular and respiratory function, keep the inhalant DOSE LOW! The best way to do that is to use analgesia. Analgesic drugs/techniques commonly used during the maintenance phase of anesthesia include:

- Boluses of opioids or alpha-2 agonists
- Local anesthetic blocks
- Constant rate infusions (opioids, ketamine, alpha-2 agonists, combinations; lidocaine is controversial in cats)

Monitoring

- Anesthesia causes depression of ALL organ systems
  - CNS, cardiovascular & respiratory depression most immediately life threatening so our monitoring is focused on these systems
- Monitor the basics
  - MM color, CRT, jaw tone, body temperature, etc…
- Use electronic monitoring equipment

Monitors and cat specific concerns

ECG	Can be hard to detect the small complexes. Increase the amplitude.
Blood pressure - oscillometric	Can be hard to get a reading. Blood pressure is the same as in the dog, but the really small vessels are hard to detect.
Blood pressure - Doppler	Usually the best way to get a blood pressure reading in really small patients. Systolic blood pressure as determined by the Doppler may be closer to MAP than SAP in cats (Caulkett et al. Vet Surg 1998;27:370-377). For patient safety, assume it as systolic and carefully assess the cat. Treat if necessary.
SpO_2	Great! But cats very likely to get cold (small body size) and hypothermia-mediated vasoconstriction decreases likelihood of getting a reading.
ET CO_2	Sidestream may provide average rather than true end-tidal reading in patients with small tidal volumes and high respiratory rate

Support – if it isn't right – FIX IT!

- Hypotension (MAP<60 mmHG)
  - Decrease the vaporizer setting.
  - Give a bolus of crystalloids or colloids
  - Utilize positive inotropic drugs.
  - CAT TIP: Be careful with fluids!
    - Administration of fluids was listed as a risk factor for anesthesia-related death (Brodbelt Vet J. 2009;182(2):152-61). But it isn't the fluid that kill cats – it's the amount of fluid that kills cats!
    - Calculate – and administer – the volume of fluids very carefully. Best to draw up the desired amount in a syringe or small chamber (like a buretrol) vs trying to deliver a small volume from a fluid bag.
- Hypoventilation ($ETCO_2$>45-50 mmHg)
  - Occurs more often than we think
  - Has many causes
  - Breathe for the patient!
- Hypothermia
  - Prevent: decrease anesthesia time, etc…
  - ACTIVELY WARM the patient!!!
  - CAT TIP: Cats are very likely to be hypothermic. Hypothermia can lead to:
    - PROLONGED RECOVERY from anesthesia
    - Impaired metabolism (adds to prolonged recovery)
    - Decreased need for anesthetics
    - Immune system depression
    - Coagulation dysfunction, sludging of blood
    - Decreased cardiac contractility, arrhythmias
    - Increased oxygen consumption (shivering)
    - Respiratory impairment
    - Etc…
  - Be aggressive with warming
    - Prevention easier than rewarming
      - Temperature starts dropping AT INDUCTION
    - Forced air blanket most effective
    - Warm patient's environment
      - Surgery room, recovery cage, etc…
    - Use warm fluids, warm scrub solution (and MINIMAL scrub solution), warm lavage solution, etc…
    - MINIMIZE ANESTHESIA TIME

Recovery

- Most unexpected anesthetic deaths occur in recovery.
- Monitoring and support should continue as long as the patient needs that level of care.
- MAKE SURE CATS ARE WARM!!
- Pain and dysphoria needs to be addressed. A rough recovery is NOT acceptable. Think pain first and re-dose the opioids – but take the body temperature first and make sure the cat is not hypothermic. May need to include a sedative. Alpha-2 agonists are excellent because they provide both sedation AND analgesia.
  - NSAIDs in cats? Cats have pain of inflammation! But we do have to dose NSAIDs carefully. Both meloxicam and robenacoxib are approved for preoperative use in cats. Cats seem to be more likely than dogs to suffer NSAID-related adverse effects so administration of NSAIDs postoperatively, after turning off the inhalant so hypotension is unlikely, is also a good option.

Common Anesthetic Protocol EXAMPLES

Healthy cat (American Society of Anesthesiologists [ASA] I-II) inhalant drug based protocol

- Preanesthesia: 0.1mg/kg hydromorphone OR 0.2-0.3 mg/kg morphine IM PLUS 10-15 microg/kg of dexmedetomidine OR 0.03-0.05 mg/kg acepromazine IM. Start NSAIDs now if appropriate.
- Induction: Any of the injectable drugs are good choices
- Maintenance: Isoflurane, sevoflurane or desflurane administered to effect; provide analgesia appropriate for the procedure (local blocks, CRI, etc…); monitor and support
- Recovery: Sedation and analgesia as indicated by the procedure and patient. Commonly, administer another bolus of the opioid used for premedication +/- sedation if the patient is stressed or excited. Administer Simbadol and dispense transmucosal buprenorphine. Start or continue NSAIDs.

Healthy cat (ASA I-II) injectable drug based protocol

- Preanesthesia: Any opioid at the appropriate dose PLUS 10 microg/kg dexmedetomidine PLUS 5-10 mg/kg ketamine all combined in the same syringe and administered IM. Start NSAIDs now if appropriate. Telazol protocols are also commonly used.
- Induction: The ketamine (or Telazol) in the combination listed above is the induction drug, if the patient is deeply sedated but not asleep, a bolus of any of the injectable drugs are good choices
- Maintenance: The ketamine (or Telazol) in the combination listed above can be the maintenance drug for SHORT (eg, castration) procedures. If the anesthesia is inadequate or the procedure is prolonged, more ketamine can be administered IM or IV or an inhalant can be used. Isoflurane, sevoflurane or desflurane administered to effect; provide analgesia appropriate for the procedure (local blocks, CRI, etc…); monitor and support
- Recovery: Sedation and analgesia as indicated by the procedure and patient. Commonly, administer another bolus of the opioid used for premedication +/- sedation if the patient is stressed or excited. Start or continue NSAIDs +/- Simbadol and/or transmucosal buprenorphine.
- This is the protocol commonly called ‘kitty magic’ and a common formula is 0.1-0.2 MLS/4.5 kg cat of each of these drugs: dexmedetomidine, buprenorphine and ketamine. The drugs are combined in the same syringe and administered IM (decrease the dose by about 25% for IV administration). Use the low-end dosing for deep sedation and the high end for anesthesia.

ASA III cat

- Preanesthesia: 0.1 mg/kg hydromorphone OR 0.1-0.2 mg/kg morphine IM. Opioids aren’t particularly sedating in cats so probably need to add 0.2 mg/kg diazepam or midazolam (if very calm cat), 1-5 microg/kg dexmedetomidine or 0.01-0.02 mg/kg acepromazine IM (if anxious or stressed but not in cats with hepatic disease – may not be able to metabolize drug) or 0.5-1.0 mg/kg alfaxalone (if really sick cat)
- Induction: Any of the injectable drugs are good choices. Propofol or alfaxalone would be ideal because they can most easily be titrated ‘to effect’.
- Maintenance: Isoflurane, sevoflurane or desflurane administered to effect; provide analgesia appropriate for the procedure (local blocks, CRI, etc…); monitor and support
- Recovery: Sedation and analgesia as indicated by the procedure and patient. Commonly, administer another bolus of the opioid used for premedication +/- sedation if the patient is stressed or excited. Continue support and monitoring for at least several hours. Start NSAIDs, if appropriate. Also Simbadol and/or transmucosal buprenorphine, if appropriate.

ASA IV-V cat

- Preanesthesia: The patient should have a catheter in place and should be on IV fluids as part of stabilization. Administer 2-5 microg/kg fentanyl through the catheter. IF NO CATHETER, try 0.2 mg/kg butorphanol (not great analgesia but decent sedation in sick cats) PLUS 0.2 mg/kg diazepam or midazolam.
- Induction: Any of the injectable drugs are good choices and should be administered within 1-5 minutes of the premed fentanyl bolus. Can also administer 0.2 mg/kg diazepam or midazolam to decrease dose of induction

drug. Some patients are sick enough that they can be intubated with the opioid and benzodiazepine alone. If not, propofol or alfaxalone would be ideal because they can most easily be titrated 'to effect'.

- Maintenance: Isoflurane, sevoflurane or desflurane administered to effect – LOW DOSE; provide analgesia appropriate for the procedure (local blocks, CRI, etc…); monitor and support
- Recovery: Analgesia as indicated by the procedure and patient. Continue support and monitoring for as long as it takes to insure that the patient is stable. NSAIDs are generally not used in this category of patients because of the potential for NSAIDs to exacerbate disease effects (eg, renal compromise, GI ulceration, etc…). Simbadol or transmucosal buprenorphine may be appropriate.

NOTE ON TRAMADOL: Tramadol appears to be more effective in cats than dogs but it TASTES BAD. I prefer to use buprenorphine for both acute and chronic pain since we have more proof of efficacy with buprenorphine.

Treating Intraoperative Hypotension

Tamara Grubb DVM, PhD, DACVAA

Hypotension, or low blood pressure, (mean arterial blood pressure [MAP] <60 mmHg in small animals or <70 mmHg in horses) is the second most commonly reported anesthetic complication (hypoventilation is the most common anesthetic complication). Hypotension often occurs secondary to excessive anesthetic depth. Hypotension leads to decreased blood flow (and therefore decreased oxygen delivery) to organs and tissues and the consequence of hypotension depends on which organ or tissue is affected. Organs with high oxygen consumption are most vulnerable to damage and this includes the kidneys, brain and myocardium.

Unfortunately, many of the anesthetic drugs that we use (primarily the inhalant anesthetics) contribute to hypotension. Also, our patient profile has changed over the last several decades and we are more likely to be anesthetizing patients that are not in the 'young, healthy' category and these patients (neonates, geriatrics, patients with advanced disease, etc…) are much more likely to develop hypotension under anesthesia.

Causes of hypotension

- The cardiovascular system is just like any other system with fluid that needs to be circulated. The system requires a pump (the heart), some fluid (blood) and pipes (blood vessels). Adverse changes in any of these components can be caused either by the patient or by the anesthetist, and can cause a decrease in pressure. Changes include:
  - Inadequate pump function (heart rate too slow or too fast; heart muscle (myocardium) not contracting normally. Causes:
    - Patient disease (cardiovascular disease or disease that causes cardiovascular changes)
    - Anesthetic drugs: Contractility primarily inhalants; rate primarily opioids; propofol can affect rate & contractility
  - Inadequate circulating blood volume. Causes:
    - Patient disease (dehydrated, blood loss, protein loss)
    - Vasodilation causes the blood not to circulate. The blood is still there but because the vessels are large, there is no driving force to make the blood move around the body. So there is inadequate volume that is circulating. Causes: anesthetic drugs, inhalants; acepromazine might contribute if the dose is high or if the patent is already vasodilated (like a patient that has been hemorrhaging or is in shock)
    - Evaporation from airways & body cavities (this is normal and is treated by administering IV fluids)
  - Blood vessels excessively dilated. The blood vessels will always dilate a little when inhalant anesthetics are used but excessive dilation is uncommon. Causes:
    - Patient disease (eg, shock)
    - Anesthetic drugs: Primarily inhalants; acepromazine might contribute if the dose is high or if the patent is already vasodilated (like a patient that has been hemorrhaging or is in shock).

Identifying hypotension

- ***Direct measurement of arterial blood pressure*** using a catheter placed in a peripheral artery is the most accurate way to determine blood pressure but is not necessarily the most practical way. In a few practices with a high volume of critical patients, direct arterial blood pressure measurement might be appropriate. However, for most practices, the technique is too time-consuming and cumbersome and is not necessary in most patients. The exception is surgical equine practice. All horses anesthetized with inhalant anesthesia should be monitored using direct arterial blood pressure.
- ***Doppler*** - provides audible indication of blood flow (comforting!), can be used for monitoring heart rate and for determining blood pressure (systolic - so maintain above 90 mmHg). This is my absolute favorite monitor for the price (relatively inexpensive) and utility (extremely useful). However, the monitor does take a bit of work to set up (shave the skin, appropriately place the probe, tape on the probe, manually measure blood

pressure) and some experience to use the unit well. TIP: We are underutilizing this tool! Use for measuring blood pressure in anesthetized patients, in patients with hypertensive disease (eg, renal disease, hyperthyroidism, etc…) and in patients with likelihood of hypotension (eg, hypothyroidism or shock from trauma, etc...). Use for heart rate in exotic species - works great in pocket pets, birds, snakes, etc.... All you have to do is find an artery!

- ***Oscillometric blood pressure monitors*** - these units are easier to use than Dopplers (just put the cuff on and press start) and generally provide consistent readings in medium to large patients. However, readings may not be consistent in small patients (eg, cats), patients with arrhythmias, patients that are moving (or shivering) and extremely hypotensive patients. Thus, having a Doppler AND an oscillometric unit is often a wise choice.
- ***Recommendation:*** Every clinic should be monitoring blood pressure in as many patients as possible. Blood pressure is one of the most important, and most frequently changed, parameters in the anesthetized patient. If you don't have a blood pressure monitor, get one. If you have one and aren't using it, start using it as often as possible.
- ***TIP:*** The width (but not the length) of the blood pressure cuff is crucial to getting appropriate blood pressure measurements. The cuff width should be approximately 40% of the circumference of the limb that the cuff will be placed on. Cuffs that are too wide cause falsely low readings while cuffs that are too narrow cause falsely high readings.
- ***TIP:*** The height of the cuff in comparison to the heart is also crucial and the cuff should be placed level with right atrium. A cuff that is above the level of the right atrium will cause falsely low blood pressure readings while one that is below the level of the right atrium will cause falsely high blood pressure readings.
- ***From the literature:*** In cats, the 'systolic' blood pressure measured oscillometrically or by Doppler is probably not actually systolic pressure but is a pressure that is somewhere between systolic and mean. Thus, we should strive to get a value >60 mmHg but perhaps it doesn't have to be as high as 90 mmHg.

Step by Step Treatment of Hypotension *(See the flow chart at the end of the notes)*

- **STEP 1: Stabilize the patient.** Treatment of hypotension should start BEFORE the patient is anesthetized. Factors that are known to contribute to hypotension include increasing American Society of Anesthesiologists (ASA) score, low preoperative blood pressure and high dosages of induction drugs. We can compensate for this by:
  - Stabilizing the patient and (hopefully) decreasing the ASA score.
  - Improving preoperative blood pressure by administering IV fluids.
  - Premedicating the patient with a sedative or analgesic drug so that high dosages of induction drugs are not necessary.
- **STEP 2: Decrease the dose of inhalant.** The anesthetic gases contribute more to hypotension than any other drug that we use in anesthesia. Decreasing the inhalant dose (ie, turning down the vaporizer) generally improves the blood pressure. In order to decrease the inhalant dose, extra analgesia may be required. Analgesia is best supplied by:
  - Boluses of opioids
  - Local or regional anesthetic blockade
  - Constant rate infusion of analgesic drugs
- **STEP 3: Give a fluid bolus:** Fluids 1) replace fluid deficits that were already present (eg, dehydration, blood loss); 2) replace fluids that will be lost during surgery (eg, urine production, evaporation from the airway, evaporation from open body cavities, blood loss); and 3) counteract some of the effects of inhalant-induced vasodilation by filling the vessels, which decreases 'pooling' of the blood in the vessels and causes the blood circulate better.
  - Normally we start with crystalloid fluids because crystalloids have an electrolyte composition that is similar to body fluids (ie, high in sodium). Thus we are replacing lost fluid with a fluid that has a similar composition to that of the lost fluid. That is why we call crystalloids ***replacement fluids***.
  - Fluids should be administered at an appropriate rate (anywhere between 3-20 mls/kg/hour depending on the patient) and boluses should be used to increase blood pressure.

- The volume of the bolus will depend on the patient. Here are some guidelines:
  - Large bolus (5-20 mls/kg) if the patient is severely hypovolemic, dehydrated or is losing a lot of fluid intraoperatively (losing blood, evaporation from a large open body cavity, etc…). Can be repeated as needed to rehydrate the patient and replace losses. If the blood pressure does not increase with fluid boluses or if the pressure is REALLY low (MAP<40 mmHg), add Step 4 (colloids).
  - Medium bolus (5 ml/kg) if the patient is already hydrated and not losing a lot of fluids (most of our patients fit in this category). Can be repeated 2-3 times but if the patient is well-hydrated and the losses are being replaced, continuing to give crystalloids probably won't help the pressure so move on to Step 4 (colloids).
  - Small bolus (2-5 ml/kg) if the patient has cardiovascular disease (the heart can't pump a lot of extra fluid) or low protein (we don't want to cause further dilution of the patient's protein – remember that crystalloids do not contain protein). Boluses usually not repeated. Move on to Step 4 or even Step 5 depending on the patient.

- **STEP 3: Check the heart rate (HR) and fix if necessary**. ***Yes, this is also Step 3!!*** As the fluids are being administered, check the heart rate and decide if it is too slow or too fast and fix it.
  - A low heart rate can contribute to hypotension because heart rate is a component of blood pressure (Blood Pressure = Cardiac output [**HR** x contractility of the heart muscle x amount of blood in the heart] x Systemic vascular resistance [which is the tone of degree of constriction of the blood vessels])
    - Both atropine and glycopyrrolate are appropriate. If possible, administer the anticholinergic IM. The heart rate increases by a greater magnitude when the anticholinergic is administered IV. Increased heart rate = increased cardiac work.
    - Atropine dose: 0.04 mg/kg; Glycopyrrolate dose: 0.01 mg/kg
    - REMEMBER: Don't increase the HR just because it is low – ONLY increase it if blood pressure is also low. Alpha-2 agonists (eg, dexmedetomidine or Dexdomitor) cause low heart rates but HIGH pressures.
  - A really high heart rate can also contribute to hypotension because the heart does not have time to fill up with blood if it is beating too fast. If it can't fill up with blood, it doesn't have any blood to push into the circulation, so blood pressure goes down.
    - Treat a really high heart rate by treating the condition that is causing it. Causes: pain, hypoxemia (low oxygen), hypercarbia (high carbon dioxide), inadequate circulating volume (eg, blood loss), etc…

Now let's look at our patient! In many patients, these steps will return the blood pressure to normal. We wait about 5-10 minutes after making the changes above and, if the blood pressure is increasing (the blood pressure may not be normal yet, but it should be increasing), then we can wait another 5-10 minutes before making further changes. HOWEVER, if it is not increasing in 5-10 minutes, we need to move to the next step. What is the next step? It depends on the patient (see the flow chart at the end of the notes for more information). If the patient is still dehydrated, still losing a lot of fluid or is responding to the crystalloid boluses, keep giving boluses! If not, let's move on to the next step.

- **STEP 4: Increase the circulating volume:** We can use colloids to do this. Remember that crystalloids replace lost fluids and crystalloids are distributed to all the places where fluid might be lost (circulation, tissues, etc….) and this helps blood pressure if fluid loss is the only problem. BUT, sometimes the patient really needs more volume in the vessels and colloids are big molecules which stay in the vessels and do not distribute to all of the tissues. Because this increased volume improves perfusion of the organs, we call colloids ***perfusion fluids***.
  - The volume of the colloid bolus will depend on the patient. Here are some guidelines:
    - 2-5 ml/kg if the patient has a healthy heart (most of our patients fit in this category). Can be repeated for a total dose of 20 ml/kg.
    - 2 ml/kg if the patient has cardiovascular disease (the heart can't pump a lot of extra fluid whether it is crystalloids or colloids) or low protein (we don't want to cause further dilution of the patient's

protein – remember that colloids do not contain protein). Usually not repeated in these patients. Move on to Step 5.

Again, wait 5-10 minutes. If no improvement, either repeat the colloid bolus (if appropriate) or go to Step 5 (ie, improve contractility). If you know the patient has a heart that is not healthy and not contracting normally, Step 5 should be initiated within 10-20 minutes of starting anesthesia. If you think that the patient's heart is healthy but you have done all of the other steps and the blood pressure did not improve, then the patient either doesn't have a healthy heart OR the inhalant anesthetics are causing a major impact on myocardial contractility. Either way, go to Step 5.

- **STEP 5: Improve contractility:** If volume expansion and increased heart rate are ineffective or if the heart is not capable of appropriate contraction (eg, in patients with myocardial disease or diseases that affect myocardial contractility – like hypothyroidism or sepsis), a positive inotrope should be utilized. Positive inotropes increase the heart's contractility.
    - The most commonly used inotropes are *dopamine* and *dobutamine* (dosage 1-10 microg/kg/min for both drugs; Table 1) and both must be administered as constant rate infusions.
    - Dobutamine is slightly more potent at the beta receptors (greater contractility) but dopamine has a slight alpha effect (some vasoconstriction).
    - If both drugs are available and one fails to increase the blood pressure, it is appropriate to try the other drug or even to administer both simultaneously.

ALMOST ALL of our patient's will respond to these 5 steps. Rarely do we need to go to Step 6, but if the patient is excessively vasodilated (eg, patients in shock), then Step 6 will be necessary to improve blood pressure.

- **STEP 6: Decrease vasodilation.** If cardiac contractility is presumed normal or if dopamine and/or dobutamine fail to increase blood pressure, a vasopressor should be used.
    - *Norepinephrine* (0.05-0.4 microg/kg/min; generally start 0.1 microg/kg/min and increase as needed) activates beta receptors and has a very potent effect at the alpha receptors. Norepinephrine is useful in septic patients and in patients receiving beta-blocking drugs like propranolol or atenolol. The profound vasoconstriction could lead to tissue ischemia but this is unlikely to be of clinical concern in most patients when dosages within the normal range are administered.
    - *Phenylephrine* (1.0-2.0 micg/kg bolus and 1.0 microg/kg/min infusion - increase as needed) activates primarily alpha receptors. It is often used with dobutamine for potent beta effects in combination with the phenylephrine-induced alpha effects. Less likely than norepinephrine to cause increased heart rate.
    - *Epinephrine* (0.05-0.4 microg/kg/min; generally start at 0.1-1.0microg/kg/min) provides potent effects at both beta and alpha receptors but also increases cardiac work, myocardial oxygen consumption and the potential for arrhythmias (especially in some anesthetized patients). As with norepinephrine, the profound vasoconstriction could lead to tissue ischemia. Epinephrine is generally reserved for patients that do not respond to other support.
    - *Vasopressin* is potent nonadrenergic vasoconstrictor that has no inotropic effects. Vasopressin stimulates specific V1A receptors in the smooth muscle of the vasculature, leading to vasoconstriction. Boluses (0.2-0.8 U/kg IV) or an infusion can be administered to treat catecholamine-resistant hypotension. Vasopressin is especially useful in patients with septic shock since the patients are generally profoundly vasodilated and catecholamines may be ineffective in the acidic environment of the blood and tissues. As with the other vasoconstrictive drugs, profound vasoconstriction could lead to tissue ischemia.

Final notes on fluid therapy

Crystalloids and colloids are the main fluids used during anesthesia but don't forget to replace what is lost. So if a patient has lost a lot of protein or blood, then plasma, packed red blood cells, or whole blood should be administered. Also remember that fluid therapy is not benign. Fluids should be thought of similarly to the way we think about drugs. That is, they are a tool that can be used – and abused --- and abuse can lead to adverse effects. Excessive fluids create increased work for the heart and can cause edema. Fluids should be administered to meet, but not exceed, the patient's needs. Also, specific fluids can have specific adverse effects. For example, plasma

can cause an anaphylactic reaction, colloids can cause clotting dysfunction, etc… Monitor fluid therapy by monitoring 1) the total dose of fluids administered; 2) blood pressure changes in response to fluids; 3) packed cell and total protein; 4) presence of edema; 5) harsh lung sounds; 6) urine production (if possible); etc….

Summary for treating hypotension:

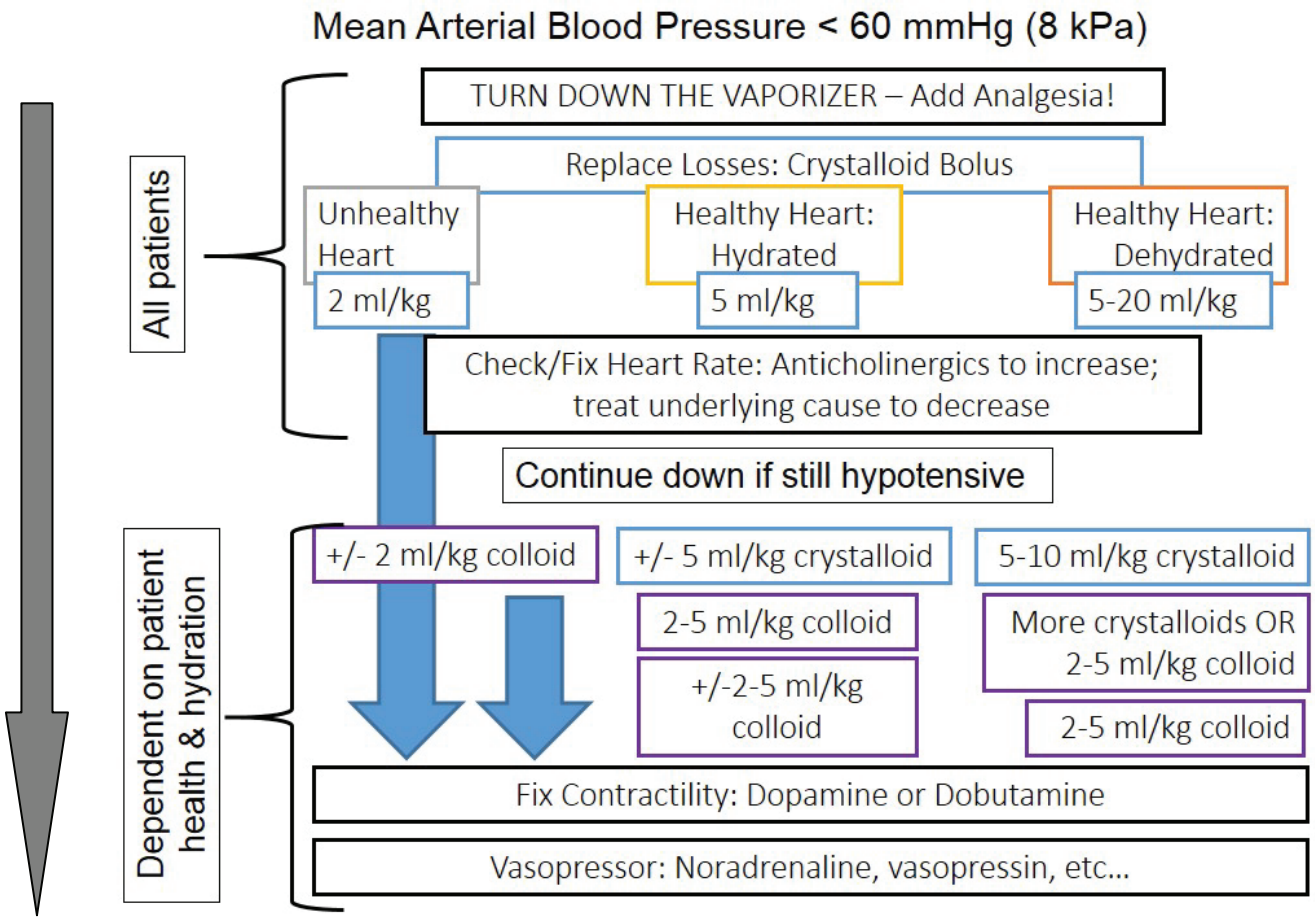
1. **Stabilize** the patient prior to anesthesia.
2. **Turn down the vaporizer** – may need to add analgesia.
3. **Replace fluid losses.** Increase the rate of fluid administration and/or administer fluid boluses of crystalloids.
3. **Check the heart rate** and fix if too high or too low.
4. If steps 1, 2 and 3 are not producing an increase in blood pressure within 5-10 minutes, increase the perfusion pressure by **increasing the circulating volume** with a bolus of colloids.
5. If steps 1-3 do not produce an increase in blood pressure or if the patient is likely to have decreased cardiac contractility (eg, patients with cardiac disease or disease that affects contractility), **increase contractility** with an infusion of a positive inotrope like dopamine or dobutamine.
6. If these steps fail or if the patient is in an extreme vasodilatory state (like septic shock) **decrease the vasodilation** with a vasopressor like norepinephrine, epinephrine or vasopressin.

Table 1: Dobutamine / Dopamine Infusion

Add 4.0 mls (50.0 mg) of dobutamine (12.5 mg/ml) or 1.25 mls (50.0 mg) of dopamine (40 mg/ml) to 250 mls saline. The concentration of either CRI will be 200 microg/ml (3.3 microg/drop with 60 drop/ml set). The standard dose of either drug is 1-10 microg/kg/min. For mild to moderate hypotension start either drug at 2 microg/kg/min and for profound hypotension start at 5 microg/kg/min. If no response in 3-5 minutes, increase the rate by 1-2 microg/kg/min every 3-5 minutes until the blood pressure starts to improve or the maximum dose is reached. If the maximum dose is reached and there is no response either the drug is not effective (expired?) or the problem is not cardiac contractility. In this case, check for other causes of hypotension (eg, bradycardia, inadequate fluid volume, vasodilation, etc…).

The following chart works for a 60 drop/ml set and the number in the column is equal to the drops/min (which also works out to be the mls/hr with a 60 drop/ml set). Appropriate dosing in patients over 40 kg needing high dosages of dopamine or dobutamine will require a 10 or 15 drop/ml set. For really small patients, the infusion can be made more dilute so that more drops/min can be administered. The easiest way to dose any sized patient is to use a syringe pump and program the dose into the pump.

Weight/kg	**1**	**2.5**	**5**	**7.5**	**10**	**12.5**	**15**	**20**	**25**	**30**	**35**	**40**
Dose in microg/kg/min	**Drops/min using a 60 drop/ml set.** Number of drops/min have been rounded up or down, as appropriate. Because the dose is a range and not an absolute value, rounding does not jeopardize safety. The actual drops the patient gets per minute will also have to be rounded – for example 61 drops/min is hard to count but 60 drops/min=1 drop/sec is quite easy.											
2	1	1	3	5	6	8	9	12	15	18	21	24
4	1	3	6	9	12	15	18	24	30	36	42	48
5	2	4	8	11	15	19	23	30	38	45	53	61
6	2	5	9	14	18	23	27	36	45	54	63	73
8	3	6	12	18	24	30	36	48	61	72	85	97
10	3	8	15	23	30	38	45	61	76	91	106	121



Progressively move down the flow chart until hypotension is resolved.

Anesthesia & Analgesia for Fractious/Aggressive Dogs & Cats

Tamara Grubb DVM, PhD, DACVAA

Start Treatment at Home

Ideally, treatment of the fractious/aggressive patient should start at home before the patient leaves its house or yard. Having a calmer patient to anesthetize is not only extremely beneficial for the patient but also make our job easier and safer. The dose of drugs needed to sedate/anesthetize patients escalates as fractiousness/aggression escalates and, since the adverse effects of most sedative/anesthetic drugs are dose-dependent, this can lead to a dangerous potential for drug overdose.

The cause of the fractiousness/aggression should be analyzed and the specific cause treated, if possible. Fear and anxiety commonly cause fractiousness and aggression, as does pain. Fear/anxiety can exacerbate pain and pain – and the anticipation of pain – can exacerbate fear/anxiety. Treatment at home may mean long-term therapy (eg, SNRIs or benzodiazepines for fear & anxiety and/or NSAIDs and/or other analgesic drugs for chronic pain) or immediate therapy the day before and day of the veterinary visit (eg, trazodone, gabapentin, sedatives, opioids, etc…). Trazodone and gabapentin are fairly safe and effective for calming dogs and cats prior to their visit to the veterinary clinic. Although either species could have either drug, trazodone seems to be most effective for dogs and gabapentin seems to be most effective for cats. The most effective protocol is to administer a dose of the drug the night before the veterinary visit and again the morning of the veterinary visit at least two hours before the patient leaves home. Both drugs can cause some sedation (which is a benefit in this situation) and, as with all sedatives, can cause ataxia in older or weak patients. Paradoxical excitement has been reported for both drugs but is extremely uncommon and not seen by the author. For patients that need deeper sedation acepromazine can be added to the protocol. Oral alpha-2 agonists might also be beneficial. Longer term treatment with benzodiazepines (eg, lorazepam) may be required in some patients. Short acting benzodiazepines (eg, diazepam) administered immediately prior to the visit may cause paradoxical excitement and are not recommended. Again, pain should also be treated. Gabapentin plays a role in pain relief so it can serve two roles. NSAIDs, oral opioids and other drugs should be considered, depending on the source of pain and patient health.

Administer drugs, even if a small treat is necessary to entice the patient to take the drugs. What happened to nothing to ear after midnight? That is more about big meals than small treats and anesthetists should always induce patients quickly and intubate to protect the airway regardless of whether the patient is NPO or not. Sometimes the patients find things to eat unbeknownst to the owner. And perhaps our fasting protocols are too long. Fasting times are now generally much shorter in humans and this may be our direction in animals.

At the Hospital

Once in the hospital, the patient should spend minimal (or no) time in noisy lobbies, should be placed in a quiet exam room, and should be handled by veterinarians/technicians/staff with appropriate training and compassion for the behavior status of the animal. The use of pheromones, music and other calming techniques may also benefit the patient. When it is time to examine or treat the patient, gentle handling may be sufficient if the patient has mild fear/anxiety or pain or even moderate fear/anxiety or pain that has responded to therapy at home. DON'T BE AFRAID TO SEDATE THE PATIENT and DON'T WAIT UNTIL THE SITUATION HAS IRREVOCABLY ESCALATED if the patient is showing signs of fractiousness/aggression. This is dangerous for everyone, including the patient, and early use of sedatives/analgesics can prevent a bad situation. If the situation has already escalated beyond what can be controlled by sedation/analgesia, consider either general anesthesia immediately (even if no exam has been done) or rescheduling the appointment.

Drugs – and more importantly the drug dosages – for sedation/anesthesia/analgesia should be chosen based on the patient's degree of fear/anxiety or aggression, level of pain, and sedation/anesthesia risk level (ASA Status, **Table 1**). Also consider the anticipated degree of restraint required, invasiveness of the procedure that the pet is at the hospital for and degree of pain that will be caused by the procedure. There is no 'one size fits all' in these

situations. 'Appropriate drugs' and 'appropriate dosages' will be very patient and situation dependent and the protocols presented here are guidelines, but each veterinarian should choose individualized protocols using their clinical experience. IMPORTANT POINT TO REMEMBER: Response to drugs can be quite varied in patients with fear/anxiety, fractiousness/aggression and/or pain. Expect an unpredictable response – especially in unpredictable patients – and be ready to escalate your protocol – or to send the patient home and try another day.

Sample Protocols based on Patient ASA, Fear/Aggression and Pain Levels

Dosages for drugs listed in the protocols are listed in **Table 2**. Unless indicated otherwise, drugs are generally administered IM to decrease stress from restraint for IV injection. The subcutaneous route of administration is not recommended because the absorption is too slow and results in low circulating concentrations of the drug.

Low Fear/Anxiety, Mild Pain, ASA I-II (low risk)

- Dexmedetomidine low dose
  - Low end range: large cats and dogs, older patients
  - High end range: smaller patients, younger patients, if used solo (without opioid)
- AND/OR dose of acepromazine
  - Not an anxiolytic so may add a benzodiazepine to the protocol if not using alpha-2 agonist
  - ADD if long duration sedation is necessary
  - NOT REVERSIBLE, NO ANALGESIA
- +/- the opioid of your choice
  - Match the opioid to the degree of pain; butorphanol &/or buprenorphine may be appropriate for mild pain

Low Fear/Anxiety, Mild Pain, ASA III-IV (moderate to high risk)

- Midazolam OR alfaxalone
- PLUS opioid appropriate for level of pain. DO NOT ADMINISTER BENZODIAZEPINES ALONE – may cause paradoxical excitement.
- If the patient is extremely fractious, consider microdose of dexmedetomidine
  - This level of fear/anxiety is likely more detrimental than a microdose of a reversible drug
  - Staff safety must be considered along with health status of the pet

Moderate Fear/Anxiety or Pain, ASA I-II

- Start calming therapy pre-visit
  - Dexmedetomidine higher dose (Dosing caveats same as for ASA I-II)
  - +/- acepromazine or midazolam (Comments are the same as for ASA I-II)
- Midazolam is an excellent addition as a true anxiolytic (but not likely to need BOTH ace & midazolam)
- +/- the opioid of your choice
  - Match the opioid to the degree of pain
    - Moderate-high pain: morphine, hydromorphone, methadone, oxymorphone
- If the procedure is painful, use other analgesics as appropriate for the procedure
  - Eg, local anesthetic blockade, constant rate infusion, etc…

Moderate fear/anxiety/fractiousness or Pain, ASA III-IV

- Start calming/sedating therapy pre-visit
- Midazolam OR Alfaxalone
- PLUS Opioid (standard doses – low end of range) appropriate for degree of pain
- If painful procedure, use other analgesics as appropriate for the procedure

Severe Fractiousness/Aggression, Any ASA

- START CALMING/SEDATING TREATMENT PRE-VISIT
- DO NOT put personnel in danger or stress the patient any further - Go straight to sedation/anesthesia

Protocol 1:

- High dose dexmedetomidine (can use LABEL DOSE)
- PLUS an opioid appropriate for the level of pain
- Will get calmer patient in about 20 mins – but may still need IV or IM anesthetic drugs (Protocol 2)

Protocol 2:

- Next step if previous protocol not effective OR first step if patient is dangerous
- Add ketamine to protocol above
  - 1-2 mg/kg may provide dissociation without anesthesia; often called 'ketamine stun'
  - 5-10 mg/kg added for true anesthesia – often used in cats but volume too high for most dogs
- OR Add Telazol to protocol above
- Combine all drugs in same syringe, administer together IM by quick hand injection, pole syringe or dart.

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TABLE 1: American Society of Anesthesiologists (ASA) Risk for Anesthesia Related Adverse Events

ASA#	Risk
1	Low; free from disease or conditions that would impact anesthetic drug/management choices
2	Low; with mild disease or conditions that might impact anesthetic drug/management choices
3	Moderate; has disease or condition that will moderately impact anesthetic drug/management
4	Severe; disease or condition will profoundly impact anesthetic choices, patient may die
5	Profound; patient has life-threatening disease and may die with or without anesthetic intervention

TABLE 2: Sedative, Analgesic and Anesthetic Drugs

Note: Not all of the drugs in these charts are FDA-approved for use in dogs and cats. Drugs like the alpha-2 agonists and acepromazine are often used at lower than the FDA-approved dose as profound sedation is not always necessary. However, all of the dosages in this chart are commonly used and are referenced in the veterinary literature. A variety of drugs/protocols are available, choices should be made based on the veterinarian's experience. Drugs are presented in alphabetical order in each category.

DRUG & DOSAGE (mg/kg)	ADVANTAGES	DISADVANTAGES/ CONCERNS	COMMENTS
Drugs to Administer at Home			
ACEPROMAZINE **Dog** & **Cat**- 0.025-0.05 oral transmucosal	Inexpensive	Effects are not consistent with PO administration	Effects are highly variable
BENZODIAZEPINES	True anxiolytics	May take days – weeks for full effect	Variety used for anxiolysis
CLONIDINE **Dog** & **Cat**- 0.01 to 0.05	Oral alpha-2 agonist	Bradycardia	Little to no information for using in this context
DEXMEDETOMIDINE GEL (see label for dose)	Effective for mild calming	Unlikely to be potent enough for aggressive patients	FDA-approved for noise phobia, not fractiousness and aggression
GABAPENTIN **Dog**- 10-20; **Cat**- 50-100/cat	High safety margin	No major concerns	Effective for calming, mild to moderate sedation
TRAZODONE **Dog**- 5-7 (up to 15); **Cat**- 50 mg/cat	High safety margin	No major concerns	Effective for calming, mild to moderate sedation
Sedative/Analgesic Drugs for In-Hospital Use			
ACEPROMAZINE **Dog**- 0.01-0.03 IV or IM (up to 0.2 IM); **Cat**- 0.03- 0.05 (up to 0.2 IM);	Mild to moderate sedation for several hours; can be given orally or	Not anxiolytic, analgesic or reversible; duration may be longer than	If anxiolysis rather than sedation is required, a benzodiazepine should be added to the protocol. No absolute contraindications but use with

Can be used alone but best used in combination with opioids and/or other sedatives.	transmucosally but higher doses will be required & onset of effects are slow	desired	caution in patients with hepatic disease, clotting dysfunction, or hypotension; recent evidence proves that ace does NOT cause seizures.
ALFAXALONE 0.5-1.0 IM	Mild to moderate sedation for 20-40 minutes	Mild cardiovascular & respiratory depression	Alfaxalone is an anesthetic induction drug that can be used IM for sedation. It is best used with opioids and in cats & small dogs since the injectate volume can be very large for medium-large patients.
ALPHA-2 AGONISTS *Dexmedetomidine* **For light to moderate sedation**: **Dog:**0.001-0.003 IV or 0.003-0.01 IM; **Cat:**0.001-0.005 IV or 0.005-0.015 IM; **For deeper sedation:** **Dog:**0.008-0.03 IV or 0.01-0.04 IM; **Cat:**0.02-0.04 IM; Use low end of dosing range if used in conjunction with opioids or other sedatives, for older patients & patients with low level of fear/anxiety; Use high end of range if used alone, for younger patients and patients with higher level of fear/anxiety or aggression. *Medetomidine* Dosages are roughly double the mg/kg dexmedetomidine dosages.	Provide analgesia & sedation; effects are reversible rapid onset; titratable sedation from mild to profound; decreased stress as evidenced by decreased cortisol release	Cardiovascular effects including hypertension and increased cardiac work due to vasoconstriction; sudden, brief arousal can occur with painful stimulus – alleviated by concurrent opioid administration.	Generally the best drugs for patients exhibiting moderate to profound fear/anxiety and/or fractiousness/aggression; most predictable effects when used in combination with opioids. Dosages in this handout are based on, but not exactly the same as, the FDA-approved label dosages. See the product insert for more information on dosing. Can reverse drug effects once procedure is complete and patient is in a calm, quiet area where restraint is possible if needed. Contraindication: do not use in patients with cardiovascular disease. An oral dexmedetomidine paste is available for treatment of noise phobia that might also be effective for mild calming in some patients.
BENZODIAZEPINES *Midazolam* **Dog or Cat:** 0.1 -0.2 IM or IV *Diazepam* **Dog or Cat:** 0.1-0.2 IV only	Minimal to no adverse physiologic effects; enhance calming when used in combination with true sedatives; midazolam can be administered IM	True sedation is minimal; may not be not effective if patient is already exhibiting fear/anxiety/ aggression and paradoxical excitement can occur if used alone!	Never use alone. Use in combination with an opioid and/or true sedative for those exhibiting fear/anxiety/ aggression and/or aggression. Be cautious with reversal as it may cause sudden arousal. Generally no need to reverse effects.
OPIOIDS: Low Pain *Butorphanol* **Dog & Cat:** 0.2-0.4 IM or IV; *Buprenorphine* **Dog & Cat:** 0.02-0.03 IM or IV; 0.03-0.05 oral transmucosal (slow onset)	Opioids provide mild to potent analgesia depending on the drug and have a wide safety margin; fast onset except buprenorphine (10-30 mins); reversible; many to choose from; variety of routes of administration;	May cause vomiting, slow GI motility and some respiratory depression if used with other respiratory depressing drugs (eg, inhalants); more potent opioids may cause excitement and/or hyperthermia in cats	Combine with a sedative to avoid excitement in cats; with mild pain use butorphanol or buprenorphine; with moderate to severe pain use hydromorphone, methadone, morphine or oxymorphone. No absolute contraindications but use with caution in patients in which vomiting or slowed GI motility would be detrimental.
OPIOIDS: High Pain *Hydromorphone:* **Dog:** 0.1-0.2 IM or IV; **Cat:** 0.1 IM or IV; *Methadone:* **Dog:** 0.3-0.5 IM or			

IV; **Cat:** 0.3 IM or IV; *Morphine:* **Dog:** 0.3-1.0 IM; **Cat**: 0.1-0.3 IM	synergistic with sedatives		
Anesthetic Drugs Any of the anesthetic drugs can be used if IV access is available. Listed here are the anesthetics used IM.			
KETAMINE **Dog & Cat:** 1.0-2.0 IM when used in combination with a sedative may provide dissociation without anesthesia while the same dose IV will provide light anesthesia; 5.0-10.0 mg/kg IM for true anesthesia; IM is a good for route for cats but the volume at this dose may be too high for medium-large dogs **TILETAMINE-ZOLAZEPAM** **Dog & Cat:**1.0-2.0 IM or IV can be added to sedatives/opioids for light to moderate sedation For anesthesia WITH PREMEDS: **Dogs:**5-6 IM; 2-3 IV **Cats:** 6-8 IM; 2-3 IV	Decrease CNS response to circulating neurotransmitters in those already exhibiting fear/anxiety and/or aggression; decrease incidence of sudden arousal to stimulus; ketamine (and maybe tiletamine) can contribute to pain relief.	Duration and/or depth may be longer and/or more profound than desired; ketamine & tiletamine are not reversible; ketamine is painful on injection; prolonged, rough recoveries are possible with tiletamine-zolazepam, especially in dogs.	This is anesthesia so patients should be monitored! There are no absolute contraindications but use with caution in patients with sympathetically driven cardiac arrhythmias or seizures and those with clinically-significant hepatic or renal disease since these drugs are cleared by the liver & kidneys.

Topical Therapy for Infectious and Allergic Dermatoses

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BASIC PRINCIPLES OF TOPICAL THERAPY

- Client education on topical therapy with written discharge instructions is critical for proper use of these products.
- The medical and financial advantages of using topical therapy should be discussed. A topical treatment and maintenance program may reduce the need for long-term continual systemic medications.
- Inform owners that medicated shampoos do not typically lather well so that they do not over apply the products. It is helpful to use a general cleansing shampoo prior to the medicated shampoo to clean the skin and hair coat and reduce the amount of the more expensive medicated product.
- If necessary for the skin disease to be adequately treated, have the hair coat cut short to facilitate application of the topical product. This is especially important for long-term management of infectious diseases in longhaired dogs.
- Contact time, contact time, contact time – at least 10 minutes for most shampoos.
- Monitor for possible irritancy or hypersensitivity reactions.
- Use tepid water for bathing and cool water for rinsing when the skin is inflamed and the patient pruritic.
- At least twice weekly application is indicated initially followed by application as needed – usually every 7-14 days.
- Use sprays, rinses, flushes, mousses or wipes between shampoos for more continual and residual activity.
- Cytology, cytology, cytology – to select the product with the correct active ingredient(s) and to change treatment if necessary at the recheck visit.

SELECTION AND USE OF TOPICAL AGENTS

The main clinical indications for topical therapy are divided into microbial infections (bacterial and fungal) and inflammatory/allergic dermatoses. Antiseborrheic shampoos containing sulfur, salicylic acid, tars and other ingredients for primary scaling disorders (primary idiopathic seborrhea) were commonly used in the past. However, it is now clear that most of these dogs did not have primary scaling disorders but scaling and crusting secondary to infections and allergies. Thus, antiseborrheic shampoos are rarely needed in favor of addressing the specific infection and/or inflammatory dermatosis.

Microbial Infections

This is the most common indication for topical therapy. Clients should be strongly encouraged to use topical products to assist in the treatment and control of recurrent infections. The key to successful long-term management of recurrent infections is to find the cause. The infections are generally associated with underlying allergies (atopic dermatitis, cutaneous adverse reactions to foods, parasitic hypersensitivities, etc.) or endocrinopathies (hypothyroidism, hyperadrenocorticism). However, even patients successfully managed for their allergies on restricted diets, allergy immunotherapy and/or pharmacologic agents such as glucocorticoids, modified cyclosporine (Atopica®, Novartis/Elanco) or oclacitinib (Apoquel®, Zoetis) will have periodic flare-ups and develop cutaneous infections.

<u>Bacterial Pyoderma</u>

The most common organism isolated from pyoderma lesions in dogs is *Staphylococcus pseudintermedius*.

Staphylococcus schleiferi and *S. aureus* are other important pathogens.[1] *Pseudomonas aeruginosa* is rarely isolated from the skin.

The prevalence of staphylococcal resistance has increased worldwide in recent years with some dermatology referral clinics reporting anecdotally that up to 70% of pyoderma referral cases are associated with methicillin- or multi-drug-resistant staphylococci. Although not as common, staphylococcal resistance is also of concern in general practice due to the apparent potential for rapid development of antimicrobial resistance. In a Canadian study, 60 dogs with pyoderma associated with methicillin-sensitive *S. pseudintermedius* (MSSP) were treated with a course of systemic antibiotics.[2] After one course of treatment, follow-up cultures from the skin now revealed carriage of methicillin-resistant *S. pseudintermedius* (MRSP) in 28.3% of the dogs.

Methicillin-resistant *S. pseudintermedius* carriers may be at increased risk of development of infections in certain situations.[1] Risk factors may include antimicrobial administration, hospitalization or surgery within 30 days prior to the onset of infection.[3]

On a positive note, it has been demonstrated that topical therapy may reduce the duration of systemic antibiotic use[4] and that topical therapy alone may resolve superficial bacterial infections.[5] Additionally, in a randomized, blinded study a 4% chlorhexidine digluconate shampoo and solution were as effective as amoxicillin–clavulanic acid in the treatment of canine superficial pyoderma.[6]

In their 2014 guidelines for the diagnosis and antimicrobial therapy of canine superficial pyoderma, the Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases stated that…

"Topical therapy alone (without co-administration of systemic antimicrobial drugs) is encouraged as a desirable and recommended approach to the treatment of superficial bacterial folliculitis (SBF) unless precluded by owner and/or patient factors. This is particularly true in the following circumstances: (i) localized lesions of SBF; (ii) early stages of generalized SBF when lesions are mild; and (iii) to help prevent recurrence of SBF while diagnostic procedures for primary underlying skin disease are pursued."[7]

Chlorhexidine

Chlorhexidine is an antiseptic agent with activity against the common bacteria causing cutaneous infections. It is bactericidal by acting on the cytoplasmic membrane. Stability, bioavailability, adherence characteristics and antimicrobial activity can be significantly affected by the formulation into which chlorhexidine is incorporated.[8,9,10,11]

Dermatologists typically use 3% or 4% chlorhexidine shampoos (ChlorhexiDerm® 4%, Bayer; Hexadine®, Virbac; TrizChlor™ 4, Dechra) in their bacterial pyoderma cases. Ideally, a shampoo should be used at least twice a week initially and then as needed to control recurrence thereafter. *In vitro* antimicrobial data and *in vivo* clinical efficacy data are lacking for most commercial veterinary formulations available in the US. ChlorhexiDerm® 4% Shampoo demonstrated *in vitro* the ability to eliminate 10^{5-7} colony forming units of *S. (pseud)intermedius* with $\leq$1 minute of contact time even when diluted 1/25 with saline.[9] An *in vitro* pilot study further confirmed the anti-staphylococcal efficacy of specific formulations of chlorhexidine and chlorhexidine/miconazole using minimal bactericidal concentrations.[11] This study also determined that neither a chloroxylenol nor an acetic/boric acid shampoo was effective against MSSP or MRSP.

In another study, dogs were bathed with a non-medicated shampoo vehicle or a 3% chlorhexidine/phytosphingosine shampoo (Douxo® Chlorhexidine PS Shampoo, Ceva) weekly for four treatments with assessment of bacterial counts pre-treatment and out to day 26.[10] There were no significant differences in bacterial numbers between placebo and treatment sites prior to therapy and on nearly all subsequent time points,

groups and areas of the skin. Additionally, there was no or only a very small difference in bacterial adherence between areas shampooed with the antimicrobial agents and with placebo at the same time points.

The residual clinical anti-staphylococcal activity of chlorhexidine when formulated with miconazole will be discussed later in this review.

For potentially more sustained activity, a chlorhexidine spray (TrizChlor™ 4, Dechra) or wipe (Douxo® Chlorhexidine 3% PS, Sogeval; TrizChlor™ 4, Dechra), a 0.2% chlorhexidine and 0.2% miconazole flush (Malaseb® Flush, Bayer) or 25 µg/mL nisin impregnated wipes (Preva™ Wipes, Bayer) can be used between shampoos.

Benzoyl Peroxide

Benzoyl peroxide is metabolized in the skin to benzoic acid, which alters pH and acts as an oxidizing agent to damage bacterial cell walls. *In vitro* benzoyl peroxide had inferior anti-staphylococcal activity in comparison to chlorhexidine and chlorhexidine/miconazole based on comparative minimal bactericidal concentrations.[11]

Benzoyl peroxide is clinically effective in staphylococcal pyoderma and is used in shampoos (Benzoyl Plus™, Vétoquinol; DermaBenSs™, Dechra; Pyoben®, Virbac) and a gel (Pyoben®, Virbac). In two separate studies, a 2.5% benzoyl peroxide shampoo was compared to a 3% chlorhexidine shampoo as sole treatment for canine bacterial overgrowth[12] and canine superficial pyoderma[5] with comparable results in the first study while chlorhexidine was more effective in the second study.

Because of its comedolytic, keratolytic and degreasing activity, benzoyl peroxide has most commonly been used in greasy dogs with pyoderma, deep pyoderma and pyoderma associated with demodicosis. These should be its only uses since repeated use of benzoyl peroxide shampoos on dogs with atopic skin disease may cause further disruption of an already defective epidermal barrier and increased percutaneous penetration of potential environmental allergens and microbial pathogens. Moisturizing agents and fatty acids have been added to some benzoyl peroxide shampoos in an attempt to offset epidermal lipid loss and excessive drying, but this approach has not been documented to be effective. It is an irritant in 10% of dogs and may bleach hair and clothing.[13]

Ethyl Lactate

Ethyl lactate (Etiderm®, Virbac) is hydrolyzed in the skin to ethanol and lactic acid, thus lowering the skin pH and acting similarly to benzoyl peroxide. The active metabolites have been shown to penetrate hair follicles and sebaceous glands. One study demonstrated comparable clinical efficacy to benzoyl peroxide in dogs with surface and superficial pyoderma.[14] However, neither immediate nor residual anti-staphylococcal activity of hairs was demonstrated in a recent antibacterial shampoo study.[8] Ethyl lactate was not as clinically effective as chlorhexidine for canine superficial pyoderma[15] and is usually reserved for those patients with sensitive, inflamed and pruritic skin that cannot tolerate other antimicrobial formulations.

Nisin

Nisin is a naturally-derived antimicrobial from *Lactococcus lactis*. It is found in cow's milk and cheese and has been used as a natural food preservative in human foods for decades. Nisin is a 34 amino acid, lanthionine-containing, water-soluble polypeptide which is effective in rapidly killing gram-positive bacteria at low (µg) concentrations.[16] The positive charge of nisin binds the molecule in a perpendicular orientation to the bacterial cell wall followed by rapid formation of pores, leakage of cell contents and bacterial cell death.[17] *In vitro* data demonstrate low MIC_{90s} for nisin against methicillin-resistant strains of *S. pseudintermedius*, *S. aureus* and *S. schleiferi*.[16] Clinical efficacy for staphylococcal overgrowth and superficial pyoderma in dogs has been demonstrated in an open trial.[18] Nisin is marketed in 6" x 8" towelettes (Preva™ Wipes, Bayer) for antibacterial

and cleansing activity. The towelettes have also been used to cleanse contact areas of dogs with environmental allergies in an attempt to help remove pollens from the skin surface after outdoor exposure.

Mupirocin

Mupirocin (Muricin®, Dechra) is an antibiotic isolated from *Pseudomonas fluorescens* with greater than 90% of the formulation comprised of pseudomonic acid A. It is an excellent ointment formulation for localized staphylococcal skin infections with the following beneficial characteristics: bactericidal, enhanced activity at an acid pH, no cross-resistance with other classes of antibiotics and virtually no systemic penetration but excellent local penetration in a relatively short period of time after application.[19] Historically, mupirocin has been used twice daily for focal skin infections such as impetigo, focal superficial and deep pyoderma, callus and pressure point pyoderma, infected chin acne, fold pyoderma, mucocutaneous pyoderma and interdigital abscesses.

Mupirocin is the most commonly utilized topical antibiotic for treatment of humans with methicillin-resistant staphylococcal (MRS) infections. Unfortunately, the prevalence of resistance has risen to over 60% in several published studies.[19] Therefore, it is medically and ethically prudent to reserve use of mupirocin in veterinary patients to those with MRS skin infections documented by culture and susceptibility and not responsive to more conventional topical antiseptics and antibiotics. The use of mupirocin in severe focal deep non-MRS infections such as interdigital abscesses is also justified given the usually slow and incomplete response of these infections to systemic antibiotics and other forms of topical therapy.

Miconazole

Miconazole is a topical imidazole antifungal agent that works by inhibiting the synthesis of ergosterol, a critical component of fungal cell membranes. Although its primary use has been for dermatophyte and yeast infections, it also has activity against some gram-positive bacteria including methicillin-sensitive and methicillin-resistant staphylococci. Results of a study of 112 methicillin-resistant *S. pseudintermedius* isolates from dogs showed an MIC_{90} range of 2-4 µg/mL with the majority at 2 µg/mL.[20] These MICs are well below miconazole concentrations available with topical therapy at 0.2-2% (2,000-20,000 µg/mL). Additionally, miconazole is narrow spectrum, readily available and of low priority for use in human MRS patients.

Anti-staphylococcal activity appears to be somewhat miconazole-specific since ketoconazole does not result in bacterial cell membrane damage or bactericidal activity.[21] Miconazole is minimally absorbed after topical application, rarely sensitizing and nonirritating, even to mucus membranes. Miconazole is available in 1-2% creams and sprays but is also used as a shampoo at 2% in combination with 2% chlorhexidine (Malaseb® Shampoo, Bayer) and as a flush (Malaseb® Flush, Bayer). *In vitro* synergistic antifungal[22] and antibacterial activity[23] have been demonstrated with chlorhexidine and miconazole at equal concentrations in aqueous formulations. In a more recent *in vitro* study, a 1:1 ratio of miconazole and chlorhexidine demonstrated antibacterial synergistic effect for 49/50 isolates of methicillin-resistant *S. aureus* (MRSA), 31/50 isolates of methicillin-sensitive *S. aureus* (MSSA), 12/49 isolates of MRSP and 23/49 isolates of MSSP.[24]

If properly formulated, chlorhexidine may have residual activity by adherence to the skin surface and hair coat. A European study assessed residual *in vitro* anti-staphylococcal activity of hairs plucked from 42 dogs up to 7 days after receiving the last of four antibacterial shampoo applications over 10 days.[8] Six different shampoos were studied. When compared to a non-medicated placebo shampoo base, a 3% chlorhexidine shampoo (Pyohex®, Dermcare Vet) and a 2% chlorhexidine and 2% miconazole shampoo (Malaseb®, Dermcare Vet in Germany, Bayer in the US) demonstrated significant residual activity out to 7 days after the last shampoo. A 0.8% chlorhexidine shampoo (Dermazyme® Losham with ActiBac, Ceva) and a 4% chlorhexidine shampoo (Hexocare®, Alfavet) had variable and inconsistent residual activity. The authors suggested that the disappointing results with the 4% chlorhexidine shampoo were probably related to formulation issues. A 10% ethyl lactate shampoo (Etiderm®, Virbac) showed bacterial inhibition in only 2 hair samples from 2 dogs and a 2.5% benzoyl

peroxide shampoo (Peroxyderm®, Vétoquinol) demonstrated no inhibition at any time point.

Additional Antimicrobial Agents

Sodium hypochlorite (bleach) and its active ingredient, hypochlorous acid, have bactericidal and fungicidal activity. Dilute bleach baths and rinses have been used in humans for atopic eczema infected with *S. aureus* including MRSA.[25] Concentrations have varied but have generally been in the range of 0.005% twice weekly for 5-10 minutes. Anecdotally, success has been reported with dilute bleach baths, rinses and sprays in dogs with staphylococcal skin infections but there are no published data documenting clinical efficacy.[13,26] Results of an *in vitro* study suggested that concentrations of 0.05-0.1% with a 15 minute contact time are required to effectively kill MRSP strains isolated from canine skin.[27] Another *in vitro* study demonstrated antimicrobial effectiveness of sodium hypochlorite diluted to 0.00156% for *Staphylococcus pseudintermedius*, *Pseudomonas aeruginosa* and *Malassezia pachydermatis* after 3 and 5 minutes of contact time.[28] Other factors to consider in deciding to use dilute bleach include: commercial bleach comes in various concentrations which must be taken into account when diluting; no safety data have been published on the use of dilute bleach in dogs; activity is affected by organic matter; solutions should be made up fresh before each use; bleaching of the hair coat and materials in the household may occur; surfactants are added to some commercial bleach solutions which may result in cutaneous irritancy; bleach is regulated by the EPA so it is a violation of Federal Law to use in a manner inconsistent with its labeling.

There is a stable, non-toxic, pH neutral, non-bleaching formulation of hypochlorous acid (Vetericyn® VF, Innovacyn) which is commercially available. It has been advocated as a treatment for pyotraumatic dermatitis and to control bacterial overgrowth and secondary infections, including some associated with MRS.[13] However, results of a pilot study showed no difference in clinical or cytologic improvement in dogs with superficial pyoderma when sprayed with this formulation or saline twice a day for 28 days.[29]

<u>*Malassezia* Dermatitis</u>

Malassezia pachydermatis is classified as a lipophilic, non-lipid-dependent, non-mycelial, saprophytic yeast that is commonly found on the skin, in the ear canals and on mucosal surfaces of normal dogs and cats.[30] Skin disease occurs when a hypersensitivity reaction develops and/or with cutaneous overgrowth of the yeast. Cutaneous overgrowth is similar to bacterial pyoderma in that it tends to be recurrent and due to the same list of underlying causes, especially cutaneous allergies. Generalized infection generally warrants both systemic and topical treatment to achieve rapid remission of clinical signs.

Chlorhexidine, Miconazole, Ketoconazole and Climbazole

Chlorhexidine used alone as a 3-4% shampoo may be effective in yeast dermatitis. In the one published clinical study a 3% formulation (Microbex® Shampoo, Virbac) required application three times per week initially versus twice a week for a 2% chlorhexidine and 2% miconazole combination (Malaseb® Shampoo) to achieve comparable clinical and cytologic improvement over the 6 weeks of the study.[31]

In a published evidence-based review of treatments for *Malassezia* dermatitis in dogs, only the combination of 2% chlorhexidine and 2% miconazole shampoo could be recommended with good evidence for efficacy used twice per week.[32] Subsequent to this review, a blinded randomized trial compared a 2% chlorhexidine and 2% miconazole shampoo (Malaseb®) twice weekly, oral ketoconazole daily at 10 mg/kg and the topical and systemic combination in dogs with *Malassezia* dermatitis.[33] Topical therapy alone was as effective as systemic therapy in reduction of yeast numbers and clinical improvement while the combination was superior to systemic treatment alone.

Chlorhexidine has also been combined with 1% ketoconazole (KetoChlor®, Virbac; Mal-A-Ket™, Dechra) and

0.5% climbazole (Douxo® Chlorhexidine PS+Climbazole Shampoo, Ceva). Similar combinations are also found in other formulations including leave-on lotions/conditioners and pledgets/wipes. In European studies, a shampoo with 2% climbazole (product undisclosed)[34] and a wipe with 0.5% climbazole, trisEDTA and 0.3% chlorhexidine (CLX® Wipes, ICF)[35] have been shown to reduce yeast populations on canine skin but with no concurrent assessment of clinical improvement. Neither of these products is available in the United States.

Acetic Acid, Selenium Sulfide and Sulfurated Lime

These ingredients provide alternatives to chlorhexidine and the azole antifungals but are not supported by the same degree of evidence.[36]

Summary of Topicals for Microbial Infections of the Skin

A literature review was published in which the authors evaluated the 9 *in vitro* and 21 *in vivo* studies on topical antimicrobial treatment of skin infections.[36] Recommendations were made based on quality assessment of the studies and categories of evidence for efficacy. Known reported adverse events were also considered when formulating the final recommendations. The authors concluded that there is:

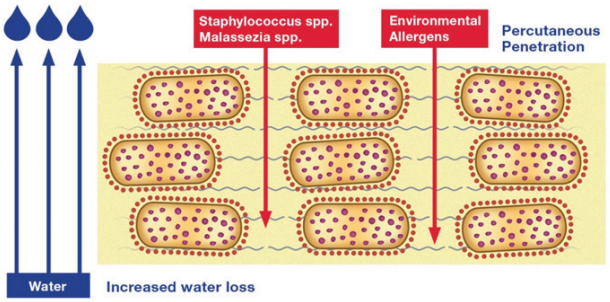
- Good evidence to recommend ≥2% chlorhexidine against bacteria (≥ 1 Double-Blinded, Placebo-Controlled, Randomized study)
- Good evidence to recommend 2% chlorhexidine - 2% miconazole against bacteria and *Malassezia* (≥ 1 D-B, P-C, R study)
- Lesser evidence to recommend 2-3% benzoyl peroxide against bacteria (open trials) and yeast (*in vitro* studies)
- Conflicting evidence on the efficacy of ethyl lactate
- Insufficient evidence to recommend any other topical therapy for cutaneous infections

Allergic Dermatoses

Canine atopic dermatitis is the allergic skin disease for which there has been the most new research directly impacting topical product development and use. Research findings suggest that canine atopic dermatitis (CAD) is a multifaceted disease resulting from a complex interaction between environmental and genetic factors.[37] CAD has been defined as a genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features associated with IgE antibodies most commonly directed against environmental allergens.[38] Since this definition was originally adopted by the International Task Force on Canine Atopic Dermatitis,[37] new research suggests that canine AD is a multifaceted disease determined by a combination of genetic and environmental factors affecting both the immunologic response as well as primary or secondary skin barrier dysfunction.[39] Instead of primarily through the respiratory tract, sensitization to environmental allergens appears to occur more directly in the skin after cutaneous penetration[40] and skin barrier dysfunction may increase the risk of allergic sensitization.[41] This is the likely reason why clinical signs of AD are seen in areas of the skin with contact exposure to environmental allergens.

Studies have demonstrated primary and/or secondary functional, chemical and ultrastructural abnormalities in the epidermis of dogs with atopic dermatitis including: 1) increases in transepidermal water loss (TEWL) as a measure of decreased barrier function,[42,43] 2) abnormal morphology (quantity and organization) of lamellar lipids in the stratum corneum,[44] 3) decreased free and protein-bound ceramides in the epidermis[42,45] and 4) abnormalities in filaggrin expression.[46,47] These abnormalities may be associated with increased environmental allergen and microbial pathogen penetration of the skin barrier leading to cutaneous inflammation and secondary infections associated with atopic dermatitis.

Abnormal Skin Barrier



The evidence summarized above supports primary and/or secondary defects in stratum corneum barrier function in the pathogenesis and clinical abnormalities in CAD. Whether a primary genetic abnormality or a secondary abnormality precipitated by gross or subclinical cutaneous inflammation, this is a clinically relevant problem that is likely to contribute to the dog's disease throughout its life. As such, the defective skin barrier and factors (e.g. inflammation and infection) that contribute to its dysfunction should be treated using appropriate systemic (e.g. antibiotics, glucocorticoids, cyclosporine, oclacitinib, omega-3 fatty acids, allergen-specific immunotherapy, antihistamines) and topical therapy for acute flare-ups of AD and prophylactically in an attempt to decrease frequency and severity of these flare-ups.

Goals of Topical Therapy in Canine Atopic Dermatitis
Gently remove environmental allergens and clean the skin surface
Treat and control recurrent bacterial and yeast skin infections
Treat and control inflammation and pruritus
Hydrate the epidermis
Restore the defective stratum corneum barrier

Cleansing, Moisturizing and Hydrating Agents

Various treatment regimens have been utilized with some success in an attempt to correct the above-mentioned abnormalities.[48] Water itself has cleansing, hydrating and cooling effects, especially when used along with effective emollients and humectants. Shampoos with mild surfactant cleansing systems and cool water baths are utilized 1-2 times per week to gently remove allergens, microbial pathogens and other debris from the skin surface. There is at least some indirect evidence that removal of allergens from the skin surface by shampooing may be effective. Hair clippings and dander samples from 25 dogs were collected before and immediately after washing for analysis of Can f 1 antigen levels. Air sampling for Can f 1 antigen was conducted in some of the homes. Washing twice weekly with a proprietary shampoo maintained reduction in recoverable Can f 1 from the hair (84% reduction; $p<0.0001$), dander (86% reduction; $p<0.0001$) and air samples (61% reduction; $p=0.014$).[49]

Immediately after a shampoo when the skin is still wet, a leave-on aqueous or crème rinse or spray should be applied to potentially increase residual moisturizing and barrier support activity. Forced air dryers should not be used in these patients to prevent further drying of the stratum corneum. Rinses and sprays can also be used on affected areas and CAD predilection sites between shampoos. Cool water rinses, cool water wipes, commercial moisturizing wipes and antibacterial wipes can be used daily as needed on contact areas of the body with the goal to decrease exposure of the defective barrier to environmental allergens and microbial pathogens. This may be beneficial especially after dogs have been outside with allergen exposure during times of high pollen counts.

Cleansing and moisturizing products with various combinations of emollients, emulsifiers, humectants, fatty acids and ceramides are used to address multiple aspects of the defective epidermal barrier. Ingredients incorporated into such products may include various oils, lanolin, propylene glycol, glycerin, urea, lactic acid, ceramides, omega-6 fatty acids and colloidal oatmeal. Pramoxine, diphenhydramine, hydrocortisone and triamcinolone are used when anti-inflammatory and antipruritic activity is desired such as for acute atopic flare-ups. Some of the shampoos in these categories include Allermyl® (Virbac), Cortisoothe® (Virbac), DermAllay™ (Dechra), Dermal-Soothe™ (Vétoquinol), Douxo® Calm (Ceva), Epi-Soothe® (Virbac), HyLyt® (Bayer), and Relief® (Bayer). Rinse and spray options include Cortavance® (Virbac)(currently not approved in the US), DermAllay™ (Dechra), Dermal-Soothe™ (Vétoquinol), Douxo® Calm (Ceva), Epi-Soothe® (Virbac), Genesis® (Virbac), HyLyt® (Bayer), Relief® (Bayer), ResiCort® (Virbac), ResiSoothe® (Virbac).

As stated above, these products are indicated to gently cleanse and moisturize the skin and mechanically remove environmental allergens. It is difficult to critically assess effectiveness of individual ingredients and formulations for barrier restoration at this time since published clinical evidence is lacking. Until such studies are available, selection of specific products is based on the practitioner's experience and clinical observations.

Ceramides and Fatty Acids

Because skin barrier impairment has been linked, in part, to ceramide, cholesterol and fatty acid abnormalities, there has been interest in topical application of these molecules. Ceramide is sphingosine bound to a fatty acid and important in cell membranes and stratum corneum lipid bilayers to maintain barrier integrity. At this time there is evidence that the chemical and structural integrity of the stratum corneum can be improved with a topical ceramide-containing emulsion (Allerderm Spot-On®, Virbac) administered twice weekly.[50,51] Corresponding clinical improvement was not assessed in the studies. An open pilot study in dogs with atopic dermatitis reported variable clinical response with the same product applied twice weekly with benefit at 4-6 weeks and maximum response at 8-12 weeks.[52] A double-blinded, randomized, placebo-controlled study of 32 dogs with atopic dermatitis assessed this product applied three times weekly for 4 weeks.[53] The Canine Atopic Dermatitis Extent and Severity Index (CADESI) in the treated but not the placebo group improved at day 28 while TEWL was variable and pruritus was not assessed. At the time of this review, this product was no longer marketed in the United States.

Another family of topical products (Douxo® Shampoos, Sprays, Mousses, and Spot-on; Ceva) contains phytosphingosine, a pro-ceramide. An open, non-controlled study using weekly shampoos (Douxo® Calm Shampoo) and twice-weekly mousse (Douxo® Calm Mousse) application was conducted on five atopic dogs over 21 days.[54] Values for skin hydration, total cholesterol, total ceramides and stratum corneum thickness were increased at day 21 but were not statistically different from pre-treatment levels. Neither clinical atopic dermatitis scores nor pruritus was monitored. Results of two non-placebo-controlled studies suggest that in dogs with allergic dermatoses the shampoo (Douxo® Calm Shampoo) and spray (Douxo® Calm Spray)[55] or shampoo and mousse (Douxo® Calm Mousse)[56] work as well as another antipruritic shampoo (Allermyl®) to control clinical signs and pruritus. At the time of this review, there have been no placebo-controlled reports on clinical efficacy of any phytosphingosine-containing veterinary formulations for allergic or inflammatory dermatoses.

A topical spot-on formulation containing plant-derived essential oils and high in polyunsaturated fatty acids (Dermoscent® Essential 6 Spot-on for Dogs, Bayer) was developed to restore the skin barrier and hydrate and deodorize the skin.[57] When added to a canine *in vitro* skin equivalent model, the resultant epidermis was thicker with an increased number of viable cell layers and a more continuous basal membrane. The stratum corneum was more dense and compact and the ceramide percentage in the stratum corneum lipids was significantly increased.[57] This formulation was evaluated in a multicenter, randomized, double-blinded, placebo-controlled field study on 48 dogs with environmentally-induced pruritus and clinical signs consisting of erythema, excoriations, lichenification and alopecia.[58] It was applied as directed once per week for 8 weeks to the dorsal neck. There was significant improvement in mean pruritus score (25% decrease, p=0.036) and clinical score (39% decrease,

p=0.011) in the treated group versus the placebo group. Improvement was seen in both severely and mild-moderately affected dogs. No adverse effects were seen during the study. In an open study in dogs this spot-on (7 dogs applied weekly) and a spray consisting of plant-derived essential oils (Atop 7®, Bayer)(7 dogs applied daily) for 8 weeks demonstrated significant improvement in clinical scores and pruritus in both groups, with no difference between groups.[59]

In a multicenter, open, non-controlled trial with final evaluation of 168 dogs (Dermoscent® Essential 6 Spot-on for Dogs) and 73 cats (Dermoscent® Essential 6 Spot-on for Cats, Bayer) with bad smell, flaking and/or greasy skin, the product was applied once a week on the skin between the shoulders for 4 weeks. In dogs, significant improvement was seen at 28 days in hair shine, odor and skin balance (oiliness) while in cats both hair shine and skin balanced significantly improved. Odor was not evaluated in the cats since no owners reported a bad smell at the start of the trial. *P* values for all parameters were < 0.0001.

Dermoscent BIO BALM® (Bayer) is a thick soy oil-based ointment with naturally-derived plant oils which is used to help reduce superficial dryness and manage rough, calloused skin. It has been used on thickened cracked footpads, the nasal planum and calluses, such as those found at pressure points.[60,61] A randomized, double-blinded placebo-controlled clinical trial was conducted to assess control of idiopathic nasal hyperkeratosis in dogs. Thirty-nine dogs were treated with BIO BALM or a placebo (aqueous gelling agent) applied to the nasal planum daily for 60 consecutive days. Scores for lichenification, extension of area involved, softness and total score were assessed. On day 60, changes from baseline for lichenification, extension, softness and total score were -31.2%, -18.3%, -72.8% and 36.8% in the treated group and -11.9%, 2.3%, -42.1% and -14% in the placebo group, respectively. The total score revealed a 51% overall improvement between groups at 60 days which was significant at *p*=0.0016.[62]

Summary of Topicals for Allergic Dermatoses

- Stratum corneum barrier defects are present in CAD.
- Dogs with AD are sensitized to environmental allergens and clinical signs are exacerbated through the percutaneous route.
- Concurrent triggering factors, especially cutaneous infections, may contribute to further barrier disruption and worsening of clinical signs.
- More research is needed to determine to what degree support of the barrier results in clinical improvement and control of CAD.
- Gentle cleansing and moisturizing shampoos, rinses, sprays and wipes are indicated to help remove cutaneous allergens and provide barrier support for long-term maintenance of AD.
- Shampoos, rinses and sprays with pramoxine and hydrocortisone or a triamcinolone spray are indicated to help relieve cutaneous inflammation and pruritus for flare-ups and long-term maintenance of AD.
- Antimicrobial shampoos, sprays and wipes are indicated to help treat and prevent recurrent infections associated with AD.
- Some lipid emulsion and plant-derived essential oil spot-on and spray formulations have demonstrated *in vitro* and *in vivo* improvement in skin barrier and/or clinical signs and may be an effective alternative to shampoos, rinses and sprays to enhance owner compliance.

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Defective Skin Barrier in Canine Atopic Dermatitis
What's Wrong and Can We Fix It?

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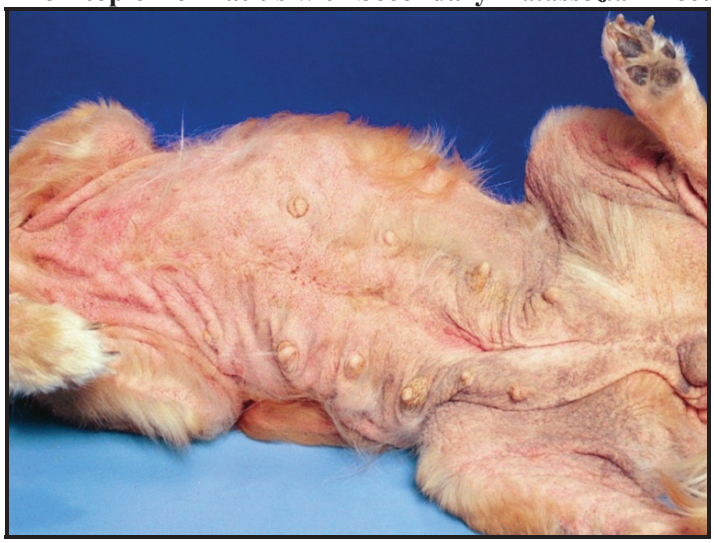
Allergic pruritic skin disease of dogs had been equated with allergic upper respiratory disease since the mid-1960's.[1] Whether cutaneous signs and respiratory signs occurred together or separately, the disease erroneously became referred to as allergic inhalant dermatitis (AID). It was thought that dogs would become sensitized to environmental allergens through the respiratory tract, allergen-specific IgE antibodies would be produced in genetically predisposed individuals and these antibodies would bind mast cells and basophils in the dermis. Upon re-exposure to the offending allergen, mast cells and basophils would degranulate resulting in the release of inflammatory cytokines leading to erythema and pruritus.[1]

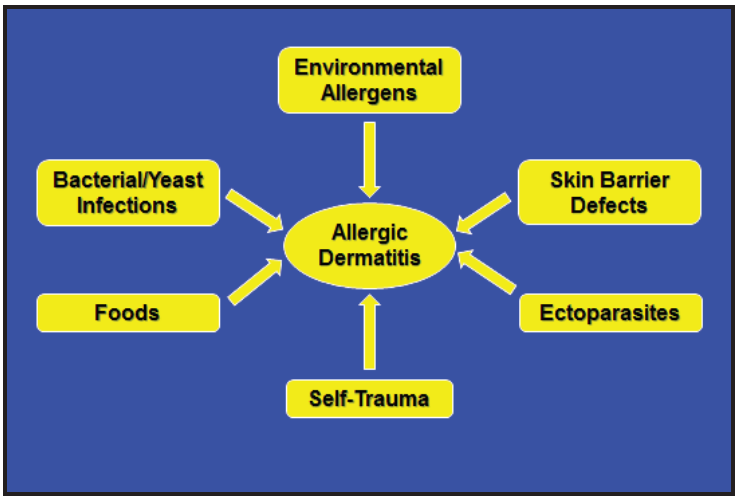
In fact, respiratory disease is rarely seen with canine allergic skin disease. Thus, the term AID has been replaced with canine atopic dermatitis (AD) now defined as a genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features associated with IgE antibodies most commonly directed against environmental allergens.[2] Since this definition was adopted by the International Task Force on Canine Atopic Dermatitis in 2006,[2] new research suggests that canine AD is a multifaceted disease determined by a combination of genetic and environmental factors affecting both the immunologic response as well as primary or secondary skin barrier dysfunction.[3] Instead of through the respiratory tract, sensitization to environmental allergens appears to occur directly in the skin after cutaneous penetration[4] and skin barrier dysfunction may increase the risk of allergic sensitization.[5] This is the reason why clinical signs of AD are seen in areas of the skin with contact exposure to environmental allergens.

Canine Atopic Dermatitis with Secondary *Malassezia* Infection



Kenneth Kwochka, DVM, DACVD

In addition to genetic and environmental factors and skin barrier abnormalities, concurrent allergic diseases and triggering factors may contribute to the severity of allergic skin disease in general.

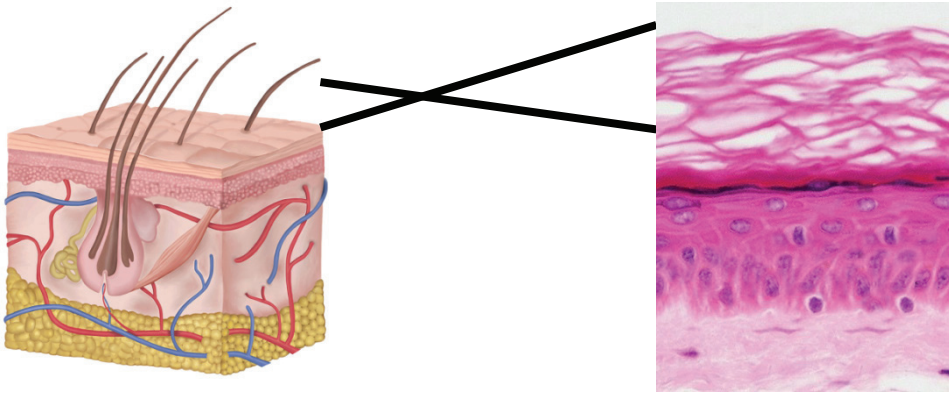


Secondary bacterial colonization and infection is of special concern because 1) bacterial pyoderma is commonly seen in clinical practice, 2) 60% of recurrent pyoderma may be associated with canine AD[6] and secondary infections aggravate clinical signs,[7] 3) staphylococcal colonization is increased in atopic skin,[8] 4) staphylococcal antimicrobial resistance is increasing in veterinary practice,[9] and 5) staphylococcal colonization has been demonstrated to disrupt human skin barrier function and further contribute to inflammation.[10]

The Skin Barrier in Canine Atopic Dermatitis

The stratum corneum is the primary protective layer of the skin responsible for control of water loss, referred to as transepidermal water loss (TEWL), and protection from penetration of environmental allergens and microbial pathogens.

Canine Stratum Corneum



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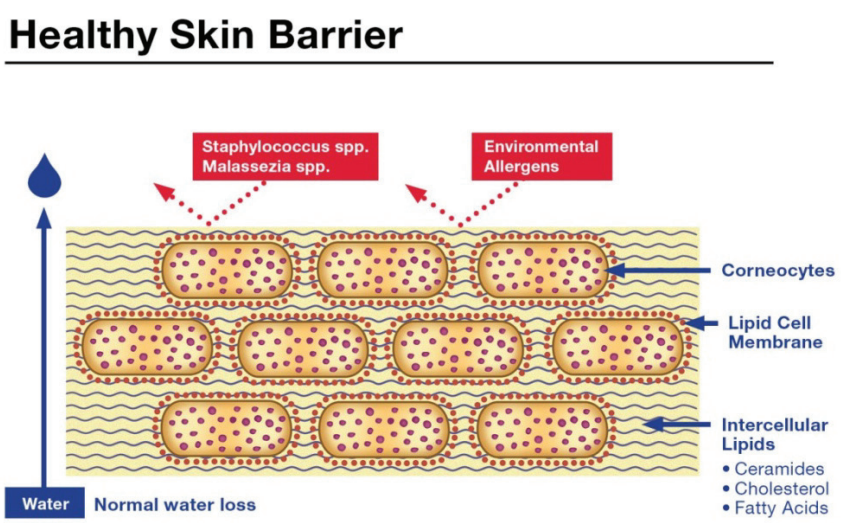

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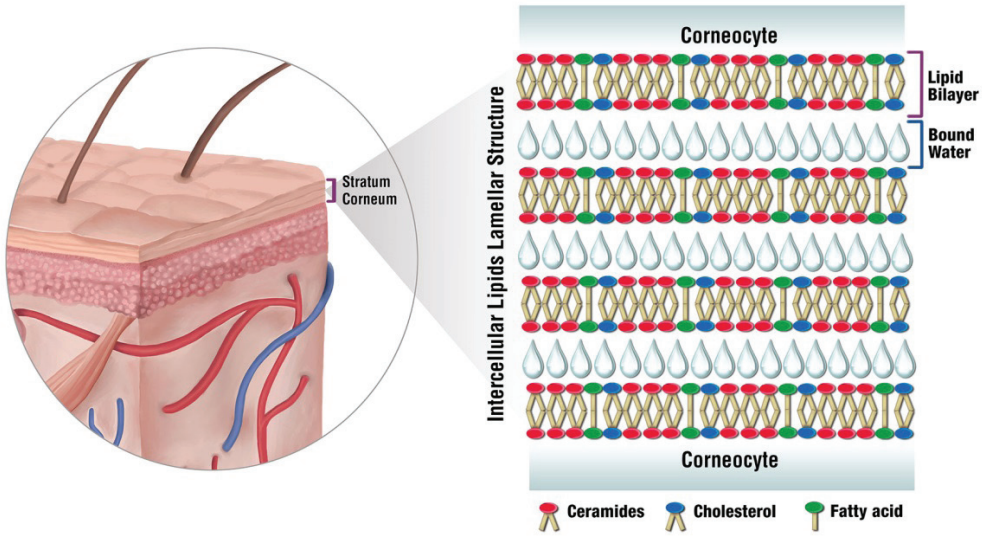
The evidence to support stratum corneum dysfunction in canine AD has been critically reviewed,[3,11] and primary or secondary functional, biochemical and ultrastructural abnormalities have been documented:

1) In spite of technical limitations associated with measuring water loss through the skin of dogs, increased TEWL as a measure of potential barrier dysfunction has been documented in dogs with spontaneous[12] and experimental[13] AD. Lesional skin and AD predilection sites show greater water loss than visibly normal skin.

2) Intercellular stratum corneum lipids are important for normal barrier function. The lipids are comprised of ceramides, cholesterol and free fatty acids and highly-organized into multilayered lipid lamellae.

<u>Stratum Corneum Intercellular Lipid Lamellae</u>



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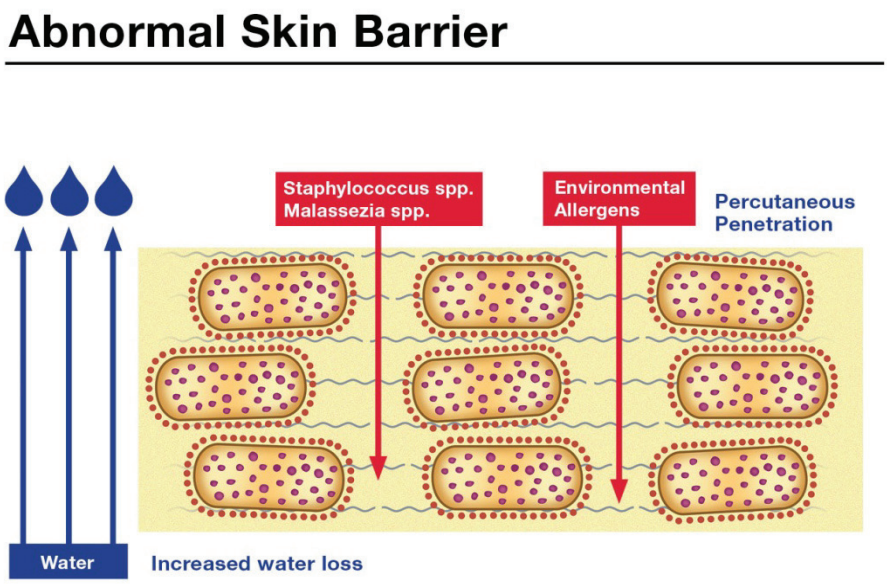
In the non-lesional skin of dogs with AD, there is a decrease in the amount of lipid present and disorganization of the normal lamellar pattern and corneocytes.[14,15] These abnormalities are worsened with allergen challenge in dogs with experimental AD.[16]



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3) Ceramides are waxy lipids important in cell membranes and stratum corneum lipid bilayers to maintain barrier integrity. Total ceramides[12] and some ceramide subclasses[17] are reduced in the non-lesional stratum corneum of dogs with AD. This ceramide reduction has been associated with increased TEWL.[12]

4) Filaggrin is an epidermal protein that is incorporated into the corneocyte lipid envelope, which is partly responsible for the skin barrier function. Expression of this protein is decreased with atopic inflammation in some dogs but genetic mutations in filaggrin have yet to be documented.[18,19]

5) Removal of stratum corneum layers by tape stripping results in increased TEWL[20] and stronger cutaneous allergen sensitization[5] in dogs, thus documenting the importance of an intact stratum corneum for barrier function.

Clinical Relevance of the Abnormal Skin Barrier to General Practice

The evidence summarized above supports primary and/or secondary defects in stratum corneum barrier function in the pathogenesis and clinical abnormalities in dogs with AD. Whether a primary genetic abnormality or a secondary abnormality precipitated by gross or subclinical cutaneous inflammation, this is a clinically relevant problem that is likely to contribute to the dog's disease throughout its life. As such, the defective skin barrier and factors (e.g. inflammation and infection) that contribute to its dysfunction should be treated using appropriate systemic (e.g. antibiotics, glucocorticoids, cyclosporine, oclacitinib, omega-3 fatty acids, allergen-specific immunotherapy, antihistamines) and topical therapy for acute flare-ups of AD and prophylactically in an attempt to decrease frequency and severity of these flare-ups.

Goals of Topical Therapy in Canine Atopic Dermatitis
Gently remove environmental allergens and clean the skin surface
Treat and control recurrent bacterial and yeast skin infections
Treat and control inflammation and pruritus
Hydrate the epidermis
Restore the defective stratum corneum barrier

Cleansing, Moisturizing and Hydrating Agents

Water itself has cleansing, hydrating and cooling effects, especially when used along with effective emollients and humectants. Shampoos with mild surfactant cleansing systems and cool water baths are utilized 1-2 times per week to gently remove allergens, microbial pathogens and other debris from the skin surface. Immediately after a shampoo when the skin is still wet, a leave-on aqueous or crème rinse or spray should be applied to potentially increase residual moisturizing and barrier support activity. Forced air dryers should not be used in these patients to prevent further drying of the stratum corneum. Rinses and sprays can also be used on affected areas and AD predilection sites between shampoos. Cool water rinses, cool water wipes, commercial moisturizing wipes and antibacterial wipes (Preva, Bayer) can be used daily as needed on contact areas of the body with the goal to decrease exposure of the defective barrier to environmental allergens and microbial pathogens. This may be beneficial especially after dogs have been outside with allergen exposure during times of high pollen counts.

Cleansing and moisturizing products with various combinations of emollients, emulsifiers, humectants, fatty acids and ceramides are used to address multiple aspects of the defective epidermal barrier. Ingredients incorporated into such products may include various oils, lanolin, propylene glycol, glycerin, urea, lactic acid, ceramides, omega-6 fatty acids and colloidal oatmeal. Pramoxine, diphenhydramine, hydrocortisone and triamcinolone are used when anti-inflammatory and antipruritic activity is desired such as for acute atopic flare-ups. Some of the shampoos in these categories include Allermyl (Virbac), AvenaLyt (Bayer), Cortisoothe (Virbac), DermAllay (Dechra), Dermal-Soothe (Vétoquinol), Douxo Calm (Sogeval), Epi-Soothe (Virbac), HyLyt (Bayer), and Relief and Relief HC (Bayer). Rinse and spray options include DermAllay (Dechra), Dermal-Soothe (Vétoquinol), Douxo Calm (Sogeval), Epi-Soothe (Virbac), Genesis (Virbac), HyLyt (Bayer), Relief (Bayer), ResiCort (Virbac), ResiSoothe (Virbac).

As stated above, these products are indicated to gently cleanse and moisturize the skin and mechanically remove environmental allergens. It is difficult to critically assess effectiveness of individual ingredients and formulations for barrier restoration at this time since published clinical evidence is lacking. Until such studies are available, selection of specific products is based on the practitioner's experience and clinical observations.

Antimicrobial Agents

As described above, secondary bacterial colonization and infection is an important contributing factor to skin barrier disruption and aggravation of clinical signs of canine AD. Secondary *Malassezia* overgrowth, infection and hypersensitivity reactions may also play a role in patients with AD.[21,22] Because of increasing staphylococcal resistance to commonly used systemic antibiotics, topical antimicrobial therapy is strongly recommended to minimize the repeated use of systemic antibiotics including helping prevent recurrence of superficial bacterial folliculitis while diagnostic procedures for primary underlying skin diseases are pursued.[23]

A recent literature review was published which evaluated the 9 *in vitro* and 21 *in vivo* studies on topical antimicrobial treatment of skin infections.[24] The authors concluded that there is good evidence to recommend $\geq$ 2% chlorhexidine against bacteria, 2% chlorhexidine - 2% miconazole against bacteria and *Malassezia* and good but lesser quality evidence to recommend 2-3% benzoyl peroxide against bacteria and yeast. However, benzoyl peroxide has potent keratolytic and degreasing activity and should not be considered for initial or long-term use in dogs with AD due to the potential to further disrupt the stratum corneum barrier.

Shampoos are commonly used 2-3 times a week with a 10 minute contact time until resolution of infection and then every 7-14 days as needed to prevent recurrence.[24] On non-shampoo days and when owners cannot bathe their pets, sprays, mousses, rinses, lotions and wipes are recommended. Some of the products in these categories include those with chlorhexidine: ChlorhexiDerm 4% (Bayer), Douxo Chlorhexidine PS (Sogeval), Hexadene (Virbac), TrizChlor 4 (Dechra); chlorhexidine and miconazole: Malaseb (Bayer), MiconaHex + Triz (Dechra); chlorhexidine and ketoconazole: KetoChlor (Virbac); and nisin: Preva Wipes (Bayer).

Ceramides and Fatty Acids

Skin barrier impairment, as described above, has been linked in part to lower levels of ceramides, cholesterol and free fatty acids. Therefore, there has been interest in topical application of these and other molecules which may result in normalization of the epidermal lipids and clinical improvement in canine AD. Some therapeutic studies have demonstrated improvement in barrier structure, biochemistry and function and some have demonstrated improvement in clinical condition, but direct correlation between barrier improvement and clinical signs has yet to be documented.

The lipid composition and ultrastructural integrity of the stratum corneum can be improved with a topical ceramide, cholesterol and free fatty acid-containing emulsion (Allerderm Spot-On, Virbac) administered twice weekly for 3 weeks.[15,25] Corresponding clinical improvement was not assessed in the studies. An open pilot study in dogs with atopic dermatitis reported variable clinical response with the same product applied twice weekly with benefit at 4-6 weeks and maximum response at 8-12 weeks.[26] A yet unpublished double-blinded, randomized, controlled study of 32 dogs with atopic dermatitis assessed this product applied three times weekly for 4 weeks.[27] The Canine Atopic Dermatitis Extent and Severity Index (CADESI) in the treated group was significantly decreased when compared to the control group at day 28 while TEWL was variable and pruritus was not assessed. At the time of this review, this product was no longer marketed in the United States.

A topical formulation containing plant-derived essential oils and polyunsaturated fatty acids (Dermoscent Essential 6, Laboratoire de Dermo-Cosmétique Animale) was developed to replenish the lipid film and hydrate and deodorize the skin. When added to a canine *in vitro* skin equivalent model, the resultant stratum corneum was more dense and compact, and the ceramide percentage in the stratum corneum lipids was significantly increased.[28] The spot-on formulation of this product was evaluated in a multicenter, randomized, double-blinded, placebo-controlled field study on 48 dogs with atopic dermatitis.[29] It was applied as directed once per week for 8 weeks to the dorsal neck. There was significantly more improvement in pruritus and CADESI scores in the treated group than in the placebo group. Improvement was seen in both severely and mild-moderately affected dogs. No adverse effects were seen during the study. Additionally, results of an open study in dogs with AD used this spot-on (7 dogs applied weekly) and the corresponding spray (7 dogs applied daily) for 8 weeks demonstrating significant improvement in CADESI scores and pruritus in both groups, with no difference between groups.[30]

Phytosphingosine, a sphingoid lipid base derived from yeast, is found in several formulations (Douxo Calm Shampoo, Spray, Mousse; Douxo Seborrhea Spot-on; Sogeval). Results of an unpublished blinded, randomized, non placebo-controlled study suggested that in dogs with allergic dermatoses the shampoo and/or spray work as well as an antipruritic shampoo (Allermyl, Virbac) used as a positive control.[31] There have been no reports on clinical efficacy of the other formulations.

For most of the ceramide, essential oil and fatty acid spray and spot-on products, the recommendation is to apply 1-2 times weekly to focal or multiple clinically affected areas of the skin for at least the first 4 weeks and then as needed for long-term management. They should be considered as adjunctive therapy initially and then utilized long-term prophylactically in an attempt to reduce the frequency and severity of allergic flare-ups.

Summary

- Stratum corneum barrier defects are present in canine AD.
- Dogs with AD are sensitized to environmental allergens and clinical signs are exacerbated through the percutaneous route.
- Concurrent triggering factors, especially cutaneous infections, may contribute to further barrier disruption and worsening of clinical signs.
- More research is needed to determine to what degree support of the barrier results in clinical improvement and control of canine AD.
- Gentle cleansing and moisturizing shampoos, rinses, sprays and wipes are indicated to help remove cutaneous allergens and provide barrier support for long-term maintenance of AD.
- Shampoos, rinses and sprays with pramoxine and hydrocortisone are indicated to help relieve cutaneous inflammation and pruritus for flare-ups and long-term maintenance of AD.
- Antimicrobial shampoos, sprays and wipes are indicated to help treat and prevent recurrent infections associated with AD.
- Lipid emulsion and plant-derived essential oil spot-on and spray formulations have demonstrated *in vitro* and *in vivo* improvement in skin barrier and/or clinical signs of AD and may be an effective alternative to shampoos, rinses and sprays to enhance owner compliance.

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Omega-3 & Omega-6 Fatty Acids in Veterinary Medicine: Mechanism of Action, Clinical Indications & Quality

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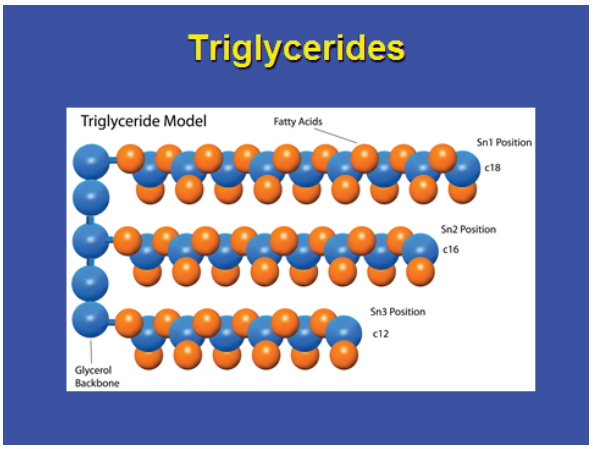
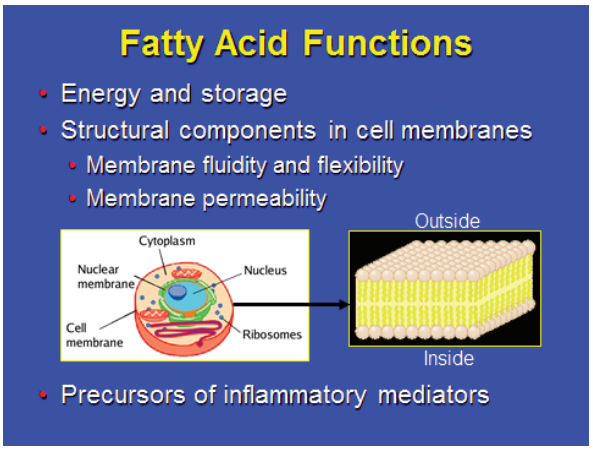
FATTY ACID BASICS [1]

A fatty acid is a carboxylic acid with a long aliphatic tail. Most naturally-occurring long-chain fatty acids have 13-21 carbons. Those of interest for this discussion are polyunsaturated with two or more double bonds. Fatty acids are usually derived from dietary triglycerides or phospholipids. When they are not attached to other molecules such as glycerol, they are known as free fatty acids.



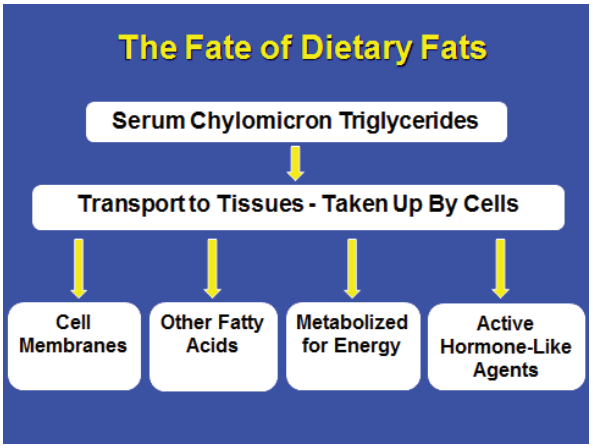
Fatty acids are important sources of energy, but for this discussion their most important functions are as structural components of cell membranes and as precursors of important inflammatory mediators.



Fatty Acid Digestion and Metabolism

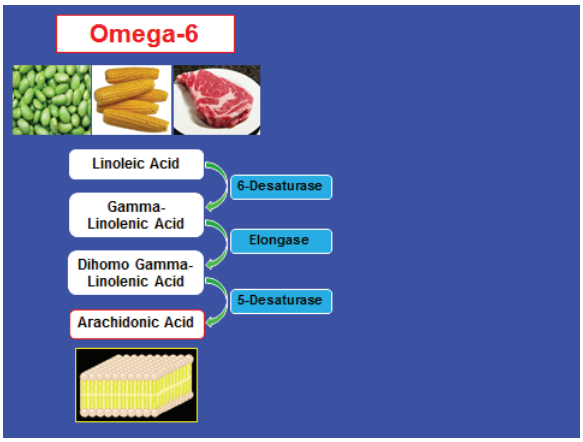
- Ingested from foods as triglycerides or phospholipids
- Triglycerides are degraded, emulsified and hydrolyzed by gastric lipase, bile salts and pancreatic lipase
- Free fatty acids absorbed and re-packaged as triglycerides in chylomicrons for serum transport to tissues
- Released and taken up by cells in body tissues

- Exert their biological effects

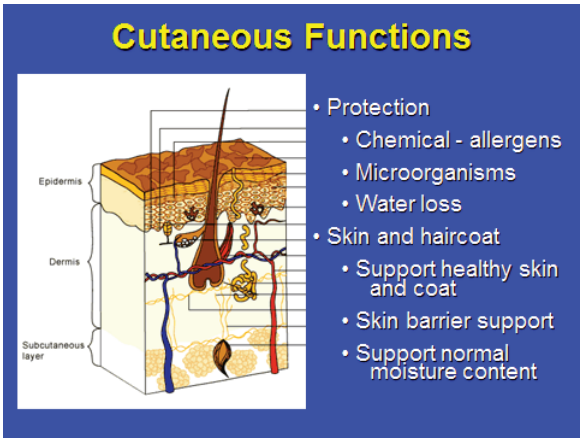


Omega-6 Fatty Acids

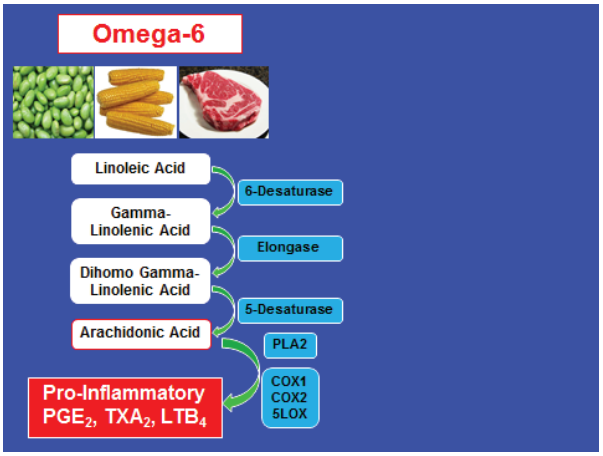
Omega-6 fatty acids are polyunsaturated with the first carbon-carbon double bond at the sixth carbon (n-6) from the methyl end of the molecule. They are essential for all stages of life in dogs and cats because they cannot be synthesized in the body and their deficiency is associated with well-defined clinical abnormalities or suboptimal physiologic processes. Linoleic acid (LA) is the main dietary source. Gamma-linolenic acid (GLA), dihomo-gamma-linolenic acid (DGLA) and arachidonic acid (AA) are important functional metabolites and may also be found in the diet. LA is essential for both dogs and cats and AA is considered by most to be essential for cats.



Omega-6 fatty acids are found in phospholipids in all cell membranes. Additionally, they are incorporated into lamellar bodies (lipid organelles in the viable epidermal cells) and then released into the intercellular spaces in the stratum corneum helping to form the cutaneous barrier. As such, omega-6 fatty acids along with ceramides and cholesterol are important in cutaneous protection of the body providing the first defense against multiple environmental pathogens and allergens.

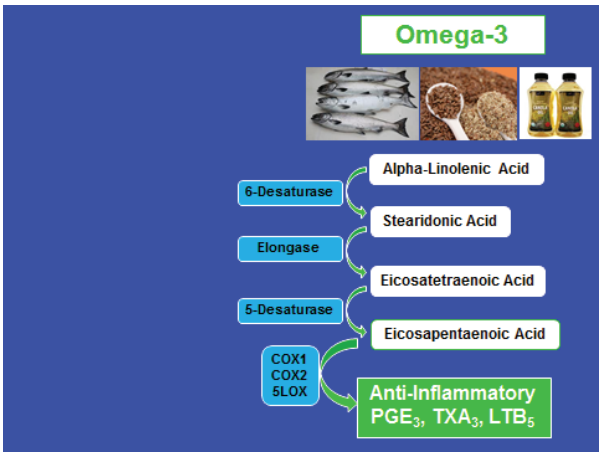


Western diets and most commercial pet foods contain excessive amounts of omega-6 fatty acids. Too much dietary omega-6 may result in more AA synthesis and deposition in cell membrane phospholipids. When AA is released from cell membrane phospholipids by phospholipases A_2 (PLA_2), downstream modification by cyclooxygenases and lipoxygenases leads to production of more pro-inflammatory eicosanoids (LTB_4, PGE_2, TXA_2, etc.). This may be a problem for patients with acute and chronic inflammatory conditions.



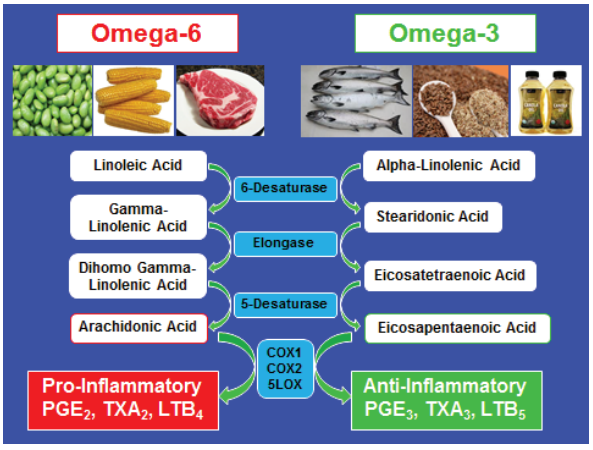
Omega-3 Fatty Acids

Omega-3 fatty acids are polyunsaturated with the first carbon-carbon double bond at the third carbon (n-3) from the methyl end of the molecule. Although they are not required by AAFCO to be in dog and cat foods, they cannot be synthesized in the body and evidence suggests their essentiality for optimal reproductive and growth phases of life (central nervous system and retinal development to be discussed later) and for support of a normal inflammatory response. Alpha-linolenic acid (ALA) is the main plant-derived dietary source. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) may be found in the diet (marine lipids, marine algae) and are also metabolites of ALA. ALA from vegetable sources does not provide the same tissue levels or clinical benefits at comparable doses as directly providing EPA and DHA, since conversion of ALA to the longer chain metabolites in mammalian species is inefficient, less than 10% in dogs and virtually nonexistent in cats. Therefore, using flax, flaxseed oil or other plant oils to provide the omega-3 fatty acids, EPA and DHA, either in the diet or as a supplement, is not optimal in dogs or cats.



Maintenance of a Normal Inflammatory Response

Omega-3 fatty acids compete with omega-6 fatty acids for the same metabolic enzymes, resulting in less production of and displacement of omega-6 fatty acids in phospholipids; most important in many organ systems is EPA in place of AA. This process is sometimes referred to as Competitive Inhibition and Displacement. Resultant EPA mediators (eicosanoids) are neutral, less inflammatory or anti-inflammatory. Counteraction: there is also evidence that eicosanoids produced from EPA can directly counteract those produced by AA. Additionally, downstream endogenous lipid mediators (lipoxins, resolvins, protectins, maresins, etc.) from EPA and DHA have analgesic properties and help signal the termination of acute inflammatory responses in cells and tissues.



CLINICAL INDICATIONS[2]

Cutaneous Health

As discussed in the previous section, linoleic acid (LA, omega-6) is essential for the normal health of the skin and hair coat because of its role as an important structural component of cell membrane phospholipids and the stratum corneum intercellular lipid barrier. For this reason, dietary supplementation with oils high in LA (sunflower, safflower, soy, corn, etc.) has been recommended for dry scaly skin conditions sometimes referred to as seborrhea sicca.[3] This condition may be idiopathic or associated with poor diets, excessively dry environments, underlying endocrinopathies such as hypothyroidism, etc.

This approach may be warranted for dry skin without inflammation. However, the concern is that supplementation of high levels of omega-6s in patients on diets already containing excessive amounts may help the dry scaly skin look better but may further contribute to a pro-inflammatory response in the skin and other organ systems. A commercial omega-6/omega-3 combination product or diet may be a better alternative to omega-6 oil alone since the omega-3 component may help support a normal inflammatory response and/or have a sparing effect on LA.[4]

Alternatively, dermatologists may recommend the use of topical shampoo, rinse and spot-on formulations containing omega-6 fatty acids and other lipid components to directly support the skin and hair coat thus avoiding a systemic pro-inflammatory effect.

Support of Skin Disorders with an Abnormal Inflammatory Response

Several clinical studies have documented efficacy of omega-3[5,6,7] or omega-6/omega-3[8,9,10] combinations as adjunctive therapy for pruritic and inflammatory dermatoses, including the ability to use a lower dose of prednisolone after 2 months[9] and a lower dose of cyclosporine after 12 weeks[10] of supplementation in dogs with atopic dermatitis.

- A recommended dose of omega-3 fatty acids in a fish oil supplement is 180 mg of EPA and 120 mg of DHA per 10 lbs (4.55 kg) of body weight (BW) per day. Efficacy was documented in 16 dogs with idiopathic pruritus or pruritus associated with atopic dermatitis and/or flea allergy in a double-blinded, corn oil-controlled crossover study (6 weeks of treatment with each test article with a 3 week washout).[5] Dogs receiving the fish oil showed significant improvement in pruritus, self-trauma and coat character over time. When compared to the corn oil control over time, fish oil supplementation significantly improved pruritus, alopecia and coat character. Fifty-six percent (56%) of the dogs on fish oil had $\geq$50% improvement in clinical scores compared to only 6% of dogs on corn oil. The dose used in the study corresponds to 66 mg of combined EPA and DHA per kg of BW.

- Another double-blinded, placebo-controlled, randomized trial was conducted in 29 dogs with atopic dermatitis over a 10 week period using a commercial fish oil product, flax oil or mineral oil placebo.[6] The fish oil was administered at 180 mg of EPA and 120 mg of DHA per 5 kg of body weight per day (60 mg of combined EPA and DHA per kg of BW). Both the fish and flax oil groups had significant improvement in post-treatment clinician and owner scores but not dogs treated with mineral oil. It took 2.3 times as much omega-3 fatty acids in the flax oil form as in the fish oil form for similar clinical improvement.

- Sixty-eight (68) dogs with atopic dermatitis were administered a mineral oil placebo (35) or 74.6 mg of combined EPA and DHA per kg of BW (33) for 12 weeks in a double-blinded, placebo-controlled, randomized clinical trial.[7] At both 6 and 12 weeks the treated dogs had significant reductions in their clinical scores (Canine Atopic Dermatitis Lesion Index) and higher overall improvement in owner/investigator visual analog scale scores for pruritus compared to placebo.

- Based on clinical experience and the studies referenced in this section, allow at least 4-6 weeks for an initial effect and 8-12 weeks for a full effect. This recommendation applies to use of omega-3 fatty acids for support of a normal inflammatory response in any organ system, not only the skin.

- It is common to combine an omega-3 fatty acid supplement or diet, an antihistamine and topical therapy in an attempt to manage pruritic dogs with the lowest dose possible of systemic

immunosuppressive drugs. The 2010 International Task Force on Canine Atopic Dermatitis Clinical Practice Guidelines states that "Skin and coat hygiene and care must be improved by bathing with nonirritating shampoos and dietary supplementation with essential fatty acids." No specific formulations were recommended.[11]

Nervous System Development in Puppies and Kittens

The omega-3 fatty acid docosahexaenoic acid (DHA) is needed for optimal neurologic development (especially retinal and auditory) *in utero* and during growth and development in children. The same has been documented for neurocognitive development in puppies and kittens.[12,13,14]

- Fish oil as a source of DHA was fed in diets to 48 beagle puppies from 8 to 52 weeks of age.[12] Low, moderate and high DHA-containing foods were utilized. The high-DHA group (Puppy Growth Formula, Hill's) had significantly better results for reversal task learning, visual contrast discrimination and early psychomotor performance in side-to-side navigation through an obstacle-containing maze than did the moderate-DHA and low-DHA groups. The high-DHA group had significantly higher anti-rabies antibody titers 1 and 2 weeks after vaccination than did other groups. Peak b-wave amplitudes during electroretinography (ERG) were positively correlated with serum DHA concentrations at all evaluated time points.

- DHA is metabolized from ALA in the diet. However, it has been shown that ERG responses and rod sensitivity are improved at 12 weeks of age in puppies fed diets (gestation, lactation and weaning) with DHA from fish oil but not with comparable levels of dietary ALA.[13] An amount of ALA ten (10) times greater than the amount of DHA was needed for the beneficial effects to be seen.

- Female domestic felines throughout pregnancy and lactation were fed either corn and coconut oil diets as their source of fat or diets containing AA and DHA.[14] When kittens from these cats were 8 weeks of age, ERGs were obtained. Kittens on diets devoid of AA and DHA had lower levels of DHA in brain tissue and rod outer segments and significant increases in a- and b-wave implicit times on ERGs. These findings support the importance of DHA in juvenile felines for nervous system and retinal function.

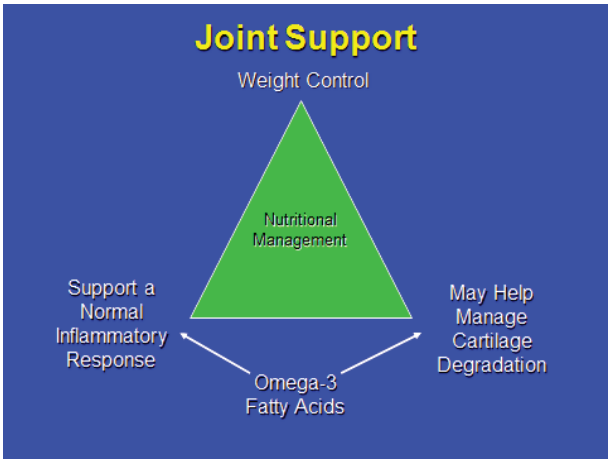
- Based on these and other studies, it is recommended that preformed DHA be provided in the diet during gestation, lactation and post-weaning for optimal neurological development in puppies and kittens. The current dosage recommendation is to follow the 2006 NRC Recommendations for Dogs and Cats.[15]
    - **Pregnant bitch and growing puppy after weaning: 130 mg EPA + DHA per 1,000 kcal of metabolizable energy**
    - **Pregnant queen and growing kitten after weaning: 25 mg EPA + DHA per 1,000 kcal of metabolizable energy**

- 2015 AAFCO Nutrient Profiles do not list a requirement for ALA, EPA or DHA for reproduction, growth or maintenance in dogs or cats. Therefore, one should check labels and/or veterinary technical services at food companies to determine if EPA/DHA is being added and at an appropriate level since there is no requirement to do so.

Support of a Normal Inflammatory Response for Joint Health

A review of the scientific literature by Bauer[2] concluded that COX-2 and 5-LOX may be appropriate targets for the management of symptoms associated with naturally occurring osteoarthritis in dogs and that the omega-3 long-chain polyunsaturated fatty acids may modify the activities of these enzymes.

As described earlier, omega-3 fatty acids antagonistically compete with omega-6 fatty acids which may help balance the production of inflammatory mediators. Additionally, omega-3 fatty acid (but not other fatty acids) incorporation into bovine cartilage chondrocyte membranes resulted in a dose-dependent reduction in the expression and activity of proteoglycan degrading enzymes (aggrecanases) and the expression of inflammation-inducible cytokines IL-1a, TNF-a and COX-2, but not the constitutively expressed COX-1.[16] Thus, omega-3 supplementation may specifically affect molecular mechanisms that regulate the expression of catabolic factors involved in articular cartilage degradation that cause and propagate arthritic disease.



- 127 client-owned dogs with osteoarthritis were fed a therapeutic food with high levels of omega-3 fatty acids and a small amount of glucosamine or a control food for 6 months in a randomized, double-blinded trial.[17] Changes in clinical signs as reported by the veterinarians were not significantly different. Owners reported subjective improvement in ability to rise, play activities and ability to walk.

- The same therapeutic diet was fed for 3 months to 22 client-owned dogs with osteoarthritis and 16 dogs on the control food in a randomized, double-blinded trial.[18] Veterinary assessment revealed significant improvement in lameness, clinical weight-bearing scores and force-plate weight bearing at the end of the 3 months in the treatment but not the control group.

- Dietary supplementation with omega-3 fatty acids has been used adjunctively with carprofen in dogs with osteoarthritis.[19] Results of this study suggest that dietary fish oil omega-3 fatty acid supplementation may allow a reduction in carprofen dosage.

- Based on levels used in the above feeding trials and other published studies, supplementation in the range of 85-100 mg of combined EPA and DHA per kg of BW is suggested by the author. Bauer suggests that even higher dosages may be used depending on severity and chronicity of the disorder up to the NRC safe upper limit in dogs of 370 mg of combined EPA and DHA per $kg^{0.75}$ (metabolic BW basis).[2] Interestingly, veterinary diets marketed for joint health when fed according to label recommendations to a 60 lb (27.3 kg) dog contain as low as 20 to as high as 102 mg of combined EPA and DHA per kg of BW.

- Therapeutic diets with fish oil may also contain ALA which may further contribute to a beneficial effect. However, some diets may contain ALA (generally flax) as the only source of omega-3 fatty acids. This is a concern because of the inefficient conversion to EPA and DHA mentioned

previously.

- In a randomized, blinded, placebo-controlled clinical trial in 40 cats with radiographic evidence of degenerative joint disease, a diet high in EPA and DHA and supplemented with green-lipped mussel extract and glucosamine/chondroitin sulfate was evaluated for pain relief and improvement in activity over a 9-week period.[20] The primary and overall subjective measurements by owners and the veterinarian examination scores revealed that each of the diets significantly improved mobility and reduced pain on manipulation. However, cats fed the test diet had greater objectively measured activity than cats fed the control diet. Cats on the test diet were receiving approximately 105 mg of combined EPA and DHA per kg of BW.

- It should be noted that the NRC has not established a safe upper limit of EPA and DHA for cats as it has for dogs. After a review of the existing literature, Bauer suggested that dosages > 75 mg of EPA and DHA per $kg^{0.67}$ (metabolic BW basis) should be used with caution and under veterinary supervision until further long-term safety studies are performed.[2] For an 8 lb (3.6 kg) cat this would equate to 50 mg of EPA and DHA per kg.

Cardiovascular Support

Heart failure and associated cachexia are known to be associated with an abnormal inflammatory response. An excellent review article was published in 2010 highlighting the beneficial effects of omega-3 fatty acids to support a more normal inflammatory response in cardiovascular disease in dogs.[21]

- A randomized, double-blinded, placebo-controlled study was conducted on 28 dogs with stable chronic heart failure secondary to idiopathic dilated cardiomyopathy.[22] Baseline plasma AA, EPA and DHA concentrations were found to be significantly lower in dogs with heart failure than in controls. Fish oil supplementation (27 mg of EPA and 18 mg of DHA per kg per day) for 8 weeks normalized these deficiencies, significantly decreased IL-1 concentrations, decreased PGE_2 production, improved food intake, reduced muscle loss and improved cachexia compared to the placebo group. Reductions in circulating IL-1 concentrations over the study period correlated with increased survival times. These data suggest that anti-cytokine strategies with omega-3 fatty acids to help support a more normal inflammatory response may benefit patients with heart failure.

- Dogs have occasionally been used in experimentally induced conditions to study the effects of omega-3 fatty acids on ventricular and atrial arrhythmias. In a canine model of atrial tachpacing, orally administered long-chain omega-3 fatty acids prevented congestive heart failure-induced atrial structural remodeling and atrial fibrillation promotion.[23] In another canine cardiac pacing model of atrial cardiomyopathy, oral omega-3 supplementation reduced atrial fibrillation inducibility and maintenance, reduced conduction anisotropy in the left atrium and prevented pacing induced increase in collagen turnover and collagen deposition in atrial appendages.[24]

- Twenty-four Boxers with spontaneously-occurring arrhythmogenic right ventricular cardiomyopathy were administered fish oil, flax oil or sunflower oil for 6 weeks in a randomized, double-blinded study.[25] The number of ventricular premature contractions per 24 hours were reduced for the fish oil group but not the flax oil or sunflower oil groups. The results suggest the potential usefulness of omega-3 fatty acids in a fish oil form for ventricular premature contractions of dogs but more research is needed in other breeds and with larger populations.

- Based on the published evidence, Bauer concluded in his review article that "…many dogs with chronic valvular disease and dilated cardiomyopathy have arrhythmias. There often are no

outward signs of cardiac arrhythmias in dogs; however, they may result in sudden death. Thus, the use of omega-3 long-chain polyunsaturated fatty acids may be beneficial prior to the diagnosis of chronic heart failure."[2]

- In a retrospective study of 108 dogs with heart failure secondary to dilated cardiomyopathy or chronic valvular disease, there was a significantly ($P = 0.009$) longer survival time for dogs receiving omega-3 fatty acid supplementation in comparison to those that did not.[26]

- In her review article, Dr. Freeman concluded "…that there is adequate evidence to warrant the use of omega-3 fatty acids in dogs, and likely cats, with heart failure or certain arrhythmias for secondary prevention. In addition, omega-3 fatty acids may have benefits in earlier stages of cardiac disease (e.g. DCM, CVD, HCM) due to their numerous positive effects on the cardiovascular system but this requires further research."[21]

- Although more research is needed to establish an optimal dose of omega-3 fatty acids for cardiovascular support, the current recommendation based on the published evidence is 40 mg/kg EPA and 25 mg/kg DHA per day for both dogs and cats.[21] Furthermore, there is no optimal omega-6:omega-3 ratio as is often claimed. It is the total omega-3 dose that determines plasma omega-3 fatty acids, independent of the ratio.[27]

Renal Support

There is some evidence to support the potential beneficial effects of omega-3 fatty acids for renal health but less than for other organ systems mentioned in this review.

In dogs with experimental chronic kidney disease administered fish oil (omega-3), safflower oil (omega-6) or beef tallow (saturated fat) as their dietary fat sources, omega-3 fatty acids comparatively reduced proteinuria, prevented glomerular hypertension and decreased the production of pro-inflammatory eicosanoids.[28,29] Dogs in the fish oil group had the highest mean clearance of exogenous creatinine, lowest concentrations of cholesterol and triglyceride, and lowest urine protein-to-creatinine ratio. Dogs in the fish oil and beef tallow groups had similar survival rates but four of seven dogs in the safflower oil group were euthanized. The authors concluded that supplementation with omega-6's enhanced renal injury while supplementation with omega-3's was renoprotective. It should be noted that these dogs were administered very high dose levels of EPA/DHA, more than twice the NRC established safe level for dogs.

Results of a retrospective study of 146 cats fed seven different veterinary therapeutic foods or a control group (n=175) fed a standard feline diet revealed a median survival time of 16 months for the pooled population fed the therapeutic foods and 7 months for the control group.[30] The group of 24 cats with the longest median survival time of 23 months was fed a diet with the highest level of EPA. However, the diet was also relatively low in phosphorus and high in potassium so the result may be due to the combined effects of its constituent parts.

POTENTIAL ADVERSE EFFECTS

There are several potential adverse effects of high levels of dietary supplementation of long-chain omega-3 fatty acids as suggested in a review article.[31] Most of these would expect to be dose- and duration-dependent.

- GI upset, diarrhea, pancreatitis
- Altered platelet function
- Delayed wound healing
- Lipid peroxidation

- Weight gain
- Altered immune function
- Effects on glycemic control and insulin sensitivity
- Nutrient-drug interactions

Clinicians prescribing omega-3 fatty acids should be aware of these in light of a patient's medical history. However, clinically these are either extremely rare or have never actually been documented. This is likely explained by the relatively low doses recommended in relation to established safe levels. The National Research Council publication on Nutrient Requirements of Dogs and Cats indicates a safe upper limit of the combined amounts of EPA + DHA as 2,800 mg/1,000 kcal of diet, equivalent to 370 mg/kg$^{0.75}$ of combined EPA and DHA for dogs.[15] This is equivalent to the following for dogs:

- 10 kg: 2081 mg
- 20 kg: 3499 mg
- 30 kg: 4743 mg
- 40 kg: 5885 mg
- 50 kg: 6957 mg

Presently, not enough published data are available to set a safe upper limit for cats.

PRODUCT QUALITY AND FISH OIL OPTIONS

Sources of Fish Oil

- Wild salmon have historically been an important type of fish used for omega-3 fatty acids because of their high fat content. However, as they have been over-fished, quantities have declined.

- Farm-raised salmon and other fish species have become popular to address the diminishing wild population. The quality of fish-farming operations is variable. United States farming operations have more regulatory oversight than foreign operations. However, the US imports about 90% of its seafood, about half of which is from aquaculture and most is from Asia. Regulation of aquaculture operations varies widely by species, farming system and country.[32] Concerns include:
    - higher levels of PCB's due to diets fed to some farm-raised fish
    - variable levels of EPA and DHA in comparison to wild populations due to soy, canola and maize used as replacements in some diets
    - higher levels of parasites such as sea lice
    - bacterial contamination
    - chemicals to give the fish color
    - antibiotics to prevent infections in high-density operations
    - crowding into small areas
    - possible escapement leading to genetic modification or infection (e.g. Infectious Salmon Anemia) of wild populations
    - water pollution from farming operation runoff, etc.

- A more satisfactory option for source of fish oil may be the use of wild, smaller non-predatory and more easily renewable high fat content species such as anchovies and sardines.

- To address some of the above concerns, fish oils should be fully tested for heavy metals (e.g. mercury and lead), ocean pollutants (e.g. PCBs and dioxins), microbial contamination and other

contaminants. Some of these standards have been set by the Council for Responsible Nutrition (CRN), World Health Organization (WHO) and International Fish Oil Standards (IFOS). In the US, the FDA has set tolerable levels for many contaminants found in fish and fish oils, but only 1-2% of shipments of fish products entering the US are inspected and tested.

Chemical Forms of Fish Oil

- Triglycerides: most common, relatively low concentrations of EPA and DHA, well absorbed from the GI tract
    - Generally, about 25-30% of the total fish oil weight consists of EPA/DHA. For example, a 1,000 mg triglyceride fish oil softgel will contain approximately 250-300 mg of EPA/DHA.
    - This is the dietary form we ingest when we eat fish so companies have touted triglycerides as the "natural form" of fish oil. However, virtually all fish oil found in supplements (no mater the form) has been processed to increase stability and/or remove impurities.
    - Most OTC and veterinary products are triglycerides.
    - Re-esterified triglycerides are different than natural triglycerides. Processing is generally accomplished by chemically stripping the fatty acids off the glycerol backbone of the molecule, concentrating and purifying and then reattaching to glycerol. These may be more concentrated are absorbed well from the GI tract. However, they are rarely found in OTC or veterinary formulations because of their expense.
    - Examples of veterinary commercial triglycerides. These will vary in source and type of fish, purification procedures, testing standards, etc.
        - Derma-3 Softgels and Liquid, Ceva
        - EicosaDerm Liquid, Dechra
        - AllerG3 Capsules and Liquid, Vetoquinol
        - Allerderm EFA-Caps, Virbac
        - Omega-3 Pet, Nordic Naturals
        - Welactin, Nutramax
        - Canine Omega Benefits, VRN

- Ethyl esters: regularly found in human OTC products and some veterinary products, high concentrations of EPA and DHA, not absorbed well from the GI tract and more prone to oxidation
    - This form is processed by chemically stripping the fatty acids off the glycerol backbone but then reattaching them to an ethyl alcohol backbone allowing higher concentrations to be achieved.
    - Depending on the process, concentrations of EPA/DHA can vary from 40-90% but price becomes an issue at the higher levels.
    - However, bioavailability is significantly lower than triglycerides and free fatty acids and may be as low as only 20-30%.

- Free fatty acids: rarely found in veterinary products, high concentrations of EPA and DHA, well absorbed from the GI tract
    - In this form, the fatty acids are left free after stripping from the glycerol backbone. Therefore, they can be directly absorbed after ingestion without bile acid and enzymatic breakdown.
    - Concentrations of EPA/DHA can be as high as 75-80% with most cost-effective products at 55-60% or double what is found in triglycerides.
    - This concentrated form has resulted in the ability to use fewer softgels or less oil to get

comparable levels of EPA and DHA.
  - FreeForm Snip Tips and Oil, Bayer Animal Health
  - Eicosa 3FF SnipCaps, Dechra

- In addition to testing for the contaminants mentioned above, fish oil products (diet or supplement) should be tested and labeled for EPA and DHA levels in order to better calculate effective dosages. Simply reporting total amount of fish oil or total omega-3 fatty acids does not tell one about these critical components which help to support the normal inflammatory response. This is a real problem for interpreting food and supplement labels as there is no regulatory requirement to list individual omega-3 components.

- Fish oil is prone to oxidation and loss of activity which makes testing for peroxide and anisidine critical for assessing short- and long-term oxidation, especially for formulations more prone to oxidation such as diets, non-encapsulated oil, soft-chews and ethyl esters. Vitamin E or other antioxidants are added to fish oil formulations to help with stability. Other vitamins such as A or D_3 are unnecessary and should not be added since toxicity may occur if high volumes of oil are administered.

Labeling of Veterinary Omega-3 Supplements and Diets

- Label dosing recommendations for veterinary omega-3 fatty acid softgels are seldom found at levels consistent with the published evidence as described in this presentation. For some products, as much as 5-6 times the label dose would be required to reach what have been demonstrated to be effective! Therefore, it is important that EPA/DHA levels appear on the label and that one calculates a proper amount based on the patient's body weight.

- Label recommendations for oil formulations in pump or pour bottles generally are closer to the effective levels but, if triglycerides, require high volumes of oil to be administered in the diet.

- Very few diets actually list EPA/DHA content on their labels or are they tested for in the finished product after heat processing. Listing total fish oil or total omega-3 levels is not the same and makes dosage calculations difficult or impossible.

Ensuring Quality in Fatty Acid Products and other Veterinary Supplements

- The FDA regulates foods and drugs in the US so is ultimately responsible for the regulation of animal health supplements. For human supplements, there are codified regulations in the Dietary Supplement Health and Education Act. Unfortunately, the law does not apply to animal health supplements so quality of these products may be variable and unpredictable.

- In order to help address this issue, a non-profit trade association called the National Animal Supplement Council (NASC) (http://www.nasc.cc) was established in 2002. This organization is currently comprised of more than 100 member companies and works closely with FDA and AAFCO to establish fair and reasonable quality standards. If a product bears the NASC Quality Seal it indicates that the company:
  - follows written quality control standards established by NASC based on the Good Manufacturing Practices (GMP's) for human dietary supplements (21CFR111's).
  - reports adverse medical events to the NASC Adverse Event Reporting System (NAERS) to which the FDA has access.
  - follows established labeling guidelines developed with input from FDA and AAFCO,

including allowable claims, warnings and cautions.
- successfully passes a quality audit every 2 years based on the above requirements.
- participates in a random finished product testing program.

Why Not Human OTC Fish Oil?

- It is impossible for most owners to interpret labels and calculate effective dosages of EPA and DHA.
- Quality is variable amongst human OTC products just as it is for veterinary products.
- The form of the oil might not be indicated. Although most are triglycerides, there are now many ethyl esters sold with lower bioavailability.
- The fish source and husbandry practices are not commonly indicated.
- The gelatin source in the softgel is not known. Most are beef.
- There is no way to know what type of impurity testing is done and to what organizational standards.

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[1] For a complete review of fatty acids as summarized in this section please see: Gross KL, Jewell DE, Yamka RM, et al. Macronutrients (Lipids). In: Hand MS, Thatcher CD, Remillard RL, et al., eds. *Small Animal Clinical Nutrition*. 5th Ed. Mark Morris Institute, 2010;96-104 and Lenox CE. An overview of fatty acids in companion animal medicine. *JAVMA* 2015;246:1198-1202.

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Diagnosis and Medical Management of Canine Otitis

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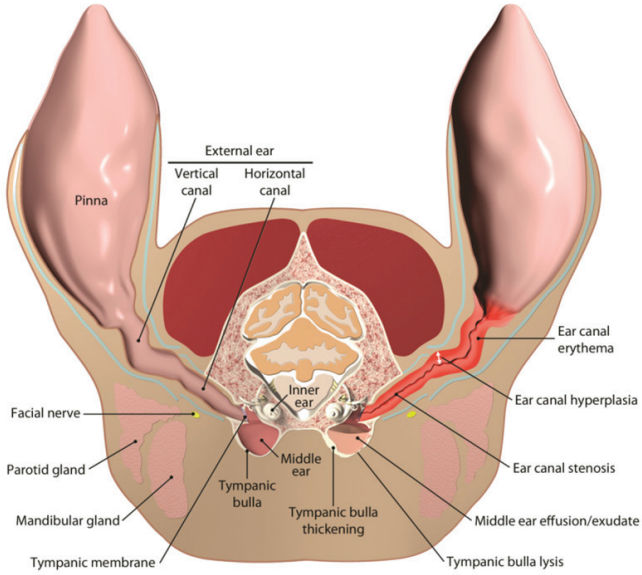
Canine otitis externa is defined as inflammation of the external ear canal which may also include the pinna. Otitis media is present when the middle ear is also involved, usually by extension of infection through the tympanic membrane.



From Logas D and Kwochka KW. *Illustrated Reference Guide of Basic Veterinary Dermatology*. American College of Veterinary Dermatology and Bayer Corporation

Canine otitis is one of the most common, challenging and frustrating conditions in veterinary medicine. The major reason for this is that it is not a single disease but a complex of interrelated etiologic components. Successful management requires: I) Identification and control of the various pathogenic factors which may be contributing to the otitis. This becomes especially important with recurrent and chronic otitis. II) Identification and treatment of the inflammation, pruritus, discomfort and infectious agent(s) present at the time of examination for a long enough period of time to control the infection and minimize the development of chronic changes. III) Establishment of a maintenance plan to control redevelopment of inflammation and secondary infections.

IDENTIFICATION AND CONTROL OF THE PATHOGENIC FACTORS WHICH MAY CONTRIBUTE TO OTITIS – PPSP – PREDISPOSING, PRIMARY, SECONDARY AND PERPETUATING FACTORS

This classification system or modifications of it have been used for many years. A detailed description is available.[1]

Predisposing Factors are pre-existent conditions that increase the risk of development of otitis when other factors are present. They include conformation (pendulous pinnae, narrow ear canals, high concentration of glandular tissue in the canal, etc.), previous treatments (aggressive use of cotton swabs for routine cleaning, irritant cleaning solutions, etc.) and excessive moisture. A fairly common example is a golden or Labrador retriever that swims

regularly with no problem unless the dog has some atopic inflammation in the canal. The moisture and inflammation together predispose to secondary infection and clinical otitis externa.

Primary Factors directly result in inflammation, hypersensitivity reactions, trauma or other damage to the ear canal either individually or in combination, usually resulting in secondary infections and chronic changes over time if left untreated. Primary factors are sometimes not diagnosed because changes are subtle, a proper diagnostic plan is not implemented or owners elect not to pursue the recommended plan. Factors include foreign bodies, ear mites and other parasites, trauma, atopic dermatitis, cutaneous adverse food reactions, endocrinopathies, epithelialization abnormalities and autoimmune diseases. Depending on history and clinical lesions, diagnostics include otoscopic examination, cytology, dietary changes, biopsy of the ear canal and/or pinna, therapeutic trials and serum or intradermal testing for reactions to environmental allergens.

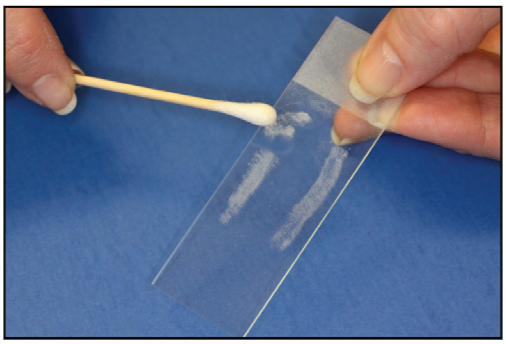
Secondary Factors, as the name implies, do not cause otitis by themselves but cause further pathology when present with primary causes and predisposing factors. Secondary factors are bacterial and yeast infections which are diagnosed by cytology and, when indicated, bacterial culture and susceptibility. These infections need to be treated aggressively until resolved and recurrence prevented by managing primary factors and/or instituting a long-term maintenance plan.

Staphylococcus pseudintermedius (*Sp*) and *Malassezia pachydermatis* (*Mp*) are the two most common otic pathogens associated with canine otitis. In a study of 100 clinical specimens from 50 dogs with bilateral otitis externa, *Sp* was isolated in 70 and *Mp* in 73 with *Proteus mirabilis* (*Pm*) in 7, *Pseudomonas aeruginosa* (*Pa*) in 3 and *Escherichia coli* (*Ec*) in 1.[2] Two microorganisms were isolated in 62% of the samples with *Sp* and *Mp* the most frequent association observed in 54.8%. In another study of bacterial isolates in 92 cultures from dogs with otitis externa, *Sp* was isolated from 73.9%, *Pa* from 10.9%, *Pm* from 3.3% and *Ec* from 1.1%.[3] In an 11-year study of lipophilic yeast of the external ear canals of 188 dogs with otitis externa, *Mp* was isolated from 62.2% of the dogs with 76.1% of the isolates showing heavy growth of the yeast.[4]

Perpetuating Factors are anatomic and physiologic changes which occur when inflammation and infection have been present with chronic otitis, generally over a long period of time. These factors include hyperplastic changes and fibroplasia of the ear canal tissue, disruption of normal epithelial migration, apocrine gland hyperplasia and rupture, furunculosis with a foreign body reaction to keratin in the dermis, false middle ear cavity, otitis media, ossification of cartilage and progressive hearing loss. Once these changes occur ears become more prone to recurrence of inflammation and infection. With time, these changes become irreversible leading to failure of medical therapy.

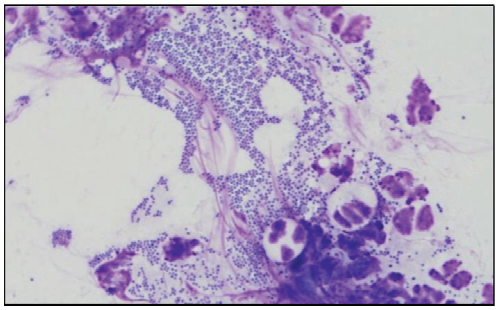
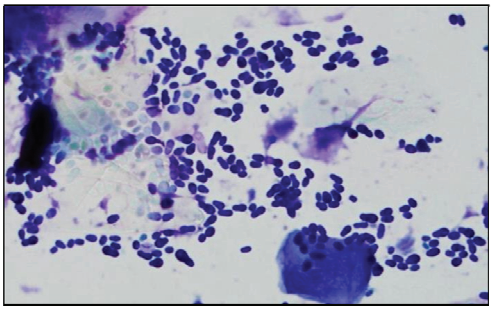
DIAGNOSIS

Ear Canal Cytology should be performed with a cotton-tipped applicator in all cases of otitis! Repeat cytology at recheck visits is the only way to monitor response to prescribed treatments and to be sure that pathogens have not changed in the ear canal. Samples should be taken from the entrance to the horizontal canal if possible, being careful not to rupture an intact tympanic membrane, or as deep in the vertical canal as possible. Gentle lateral traction of the pinna will facilitate passage of the applicator into the canal. Cytologic preps are then made by firmly rolling the swabs onto a clean microscope slide, heat fixing (personal preference), staining with modified Wright Giemsa (Diff-Quik) and examination at oil immersion 1000x.

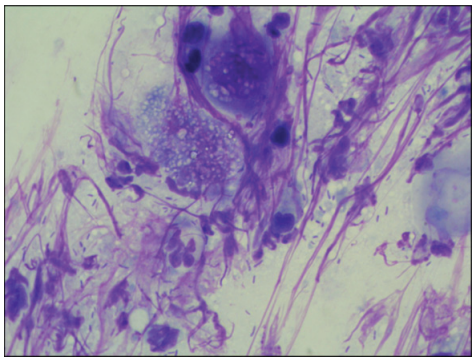
The value of the initial cytology is that the results will guide selection of an appropriate topical product to specifically treat the existing infection. The decision to treat and with what is based on the clinical condition of the ear canal, organisms identified, numbers of organisms and presence of inflammatory cells.

Staph. pseudintermedius *Malassezia pachydermatis*

Chronic gram-negative otic infections have a high prevalence of otitis media.[5] Patients with otitis media also need a cytology sample taken from the middle ear using swabs made for small body cavities such as 5.5 inch sterile calcium alginate swabs (Calgiswab®, Puritan Medical) or material from the tip of the catheter or needle used to perform a myringotomy. Cytology associated with gram-negative otitis is characterized by a predominant population of rods with neutrophils, phagocytized bacteria, red blood cells and proteinaceous debris.

Pseudomonas aeruginosa



Bacterial Culture and Susceptibility Testing (CS) is not needed for cases of acute otitis externa to be treated with ear cleaning, anti-inflammatory drugs and topical antimicrobials alone. It is indicated for severe chronic cases of otitis externa, when rods and inflammatory cells are found on cytology, when otitis media is present, when systemic antibiotics are deemed necessary and in cases not responding to empirical therapy. The sample should be taken from the middle ear (when otitis media is present) and/or within the horizontal canal using a sterile culturette passed through a sterile otoscope cone before cleaning or treatment. In a prospective study of 23 dogs

with chronic bilateral otitis externa of at least 6-months' duration, concurrent otitis media was present in at least one tympanic bulla in 22 of the dogs (38 of 46 ears).[5] Of the 38 ears evaluated, a difference in total number of isolates or susceptibility patterns between organisms from the horizontal ear canal and middle ear was found in 34 (89.5%) ears.

Even when CS is indicated, variable results may be obtained due to interference by concurrent antibiotic use, sample location, multiple strains of the same organism present in the ear canal, and variability among laboratories. CS results are not reproducible 100% of the time in samples taken from a badly infected ear canal or tympanic bulla.

BASIC TREATMENT PRINCIPLES

1) Identify and treat predisposing and primary factors. Especially consider the most common ones seen in practice: otic foreign bodies, ear mites, atopic dermatitis, cutaneous adverse food reactions, scaling/glandular abnormalities and swimming.

2) When needed, use topical and/or systemic corticosteroids to increase patency of a chronically affected stenotic ear canal to facilitate full examination, sample collection and flushing:

- Topical mometasone, betamethasone, triamcinolone, dexamethasone or fluocinolone/DMSO for 1-2 weeks. Most of these steroids are available in commercial otic formulations.
- Triamcinolone: 0.1 mg/kg total dose injected in a ring-like fashion with a 22-gauge spinal needle through an otoscope cone into proliferative tissue at various depths in the ear canal[6]
- Systemic dexamethasone: 0.1 mg/kg, IM or SQ
- Prednisone or prednisolone: 0.5-2.0 mg/kg/day for 1-2 weeks

3) Completely clean and flush the ear canal and tympanic bulla (if indicated) initially and keep the ear clean thereafter. In addition to physically removing debris and pathogens from the ear, cleaning the canal facilitates movement and penetration of topically-applied medications down the canal and removes organic material that may interfere with some topical antibiotics (aminoglycosides and polymyxin). The reader is directed to other references which describe in detail initial cleaning and flushing of the external ear and tympanic bulla.[1,7,8] Depending on the nature of the otic exudate, condition of the ear canal, and integrity of the tympanic membrane, various techniques and agents may be utilized for in-hospital or at-home cleaning.

- Mild to moderate cases may be adequately cleaned by filling the canal with the cleaner, massaging the canal for several minutes if possible, letting the patient shake debris out of the ears and drying with a cotton ball. With proper instruction, clients may be able to perform these cleanings at home if necessary.

- The goal is to start with a clean ear canal and then repeat as needed during the time that the infection is being treated if debris re-accumulates in the canal. When using the newer residual otic antibiotic/antifungal/corticosteroid treatment formulations (Claro™, Bayer; Osurnia®, Elanco), cleaning should not be repeated during the treatment duration. If cleaning is deemed necessary based on the condition of the ear at recheck then the medication may need to be re-applied.

- For moderate to severe cases, in-clinic deep flushing under general anesthesia is recommended. This may be accomplished with a bulb syringe, however, more directed flushing deep in the canal and middle ear may be done with a syringe (usually 12 mL) attached to a catheter or red rubber feeding tube passed through a hand-held otoscope. Fiberoptic video otoscopy (Karl Storz Otoscopy, https://www.karlstorz.com/ar/en/small-animals.htm) is very helpful when cleaning of the deep horizontal canal and tympanic bulla is necessary. This equipment allows superior visualization, magnification, a channel for diagnostic instruments and flushing tubes and the ability to capture digital images for clients

to enhance communication and compliance.

- Cleaning Agents
    - *Ceruminolytic Agents* purportedly act by emulsification of waxes and lipids to more readily flush ceruminous debris from the canal. Ingredients include calcium or sodium dioctyl sulfosuccinate, triethanolamine polypeptide oleate condensate, carbamide peroxide, sodium lauryl sulfate and squalene. Examples of commercial formulations include: Cerumene®, Vetoquinol; Cerulytic®, Virbac; Douxo® Micellar, Ceva; and OtiRinse®, Bayer. These have commonly been used in-clinic where they are applied 5-10 minutes before cleaning and then flushed out of the canal with water or saline after exerting their effect to avoid potential irritancy and ototoxicity. They may also be used for at-home maintenance flushing in dogs with intact tympanic membranes that accumulate ceruminous exudate in their canals regularly such as seborrheic cocker spaniels. There are no published studies in dogs or cats documenting the clinical efficacy of ceruminolytic agents.
    - *Mild Cleaning /Antiseptic/Drying Agents* are most often used for in-clinic flushing, at-home cleaning and long-term maintenance of chronic and recurrent otitis. Common ingredients include alcohol, chlorhexidine*, parachlorometaxylenol (PCMX), tris-ethylenediaminetetraacetic acid (tris-EDTA), ketoconazole, miconazole, propylene glycol, sulfur, aluminum acetate, enzyme combinations and various types of acids at low concentrations. Examples of commercial formulations include: Epi-Otic® and Epi-Otic Advanced®, Virbac; MalAcetic® Otic, Dechra; Mal-A-Ket Plus TrizEDTA® Flush, Dechra; Malaseb® Flush, Bayer; OtiRinse®, Bayer; OtiSoothe®, Ceva; T8 Keto® Flush, Bayer; TrizULTRA + Keto®, Dechra.
      (*Chlorhexidine acetate (0.2%) was applied twice a day for 3 weeks to the external ear canals of dogs with surgically perforated tympanic membranes. There were no observed abnormalities in vestibular or auditory function over the course of the study.[9] However, chlorhexidine may be ototoxic in some individuals and should be used with caution in dogs with confirmed or suspected ruptured tympanic membranes. Chlorhexidine is also a difficult molecule to formulate correctly and it is advised not to compound other ingredients into commercial formulations of chlorhexidine or risk it losing activity.[10])
    - For in-clinic flushing if there is concern that the tympanic membrane might be ruptured, the author has most commonly used warm isotonic saline and solutions containing trisEDTA. TrisEDTA also offers the advantage of destabilizing and increasing permeability of gram-negative bacterial cell walls thus potentially enhancing the activity of topically applied antibiotics.[11] It should be noted that there is no veterinary commercial product approved by the FDA for use in middle ears of dogs or cats.

4) If at all possible, eliminate swimming in dogs with a history of recurrent otitis. For dogs that cannot be completely kept out of the water and have problems with recurrent infections, regular use of the cleansing, antiseptic drying agents listed above may be helpful. Additionally, the combination of Burow's solution and 1% hydrocortisone (Cort/Astrin Solution, Vedco) is effective applied after swimming and as needed between swimming.

5) Use a sufficient volume of topical medication to adequately coat the ear canal. Most commercial veterinary products as labeled do not provide adequate volumes to achieve this.

- Depending on the size of the dog, 0.25-1.0 mL is needed, q12-24h (per product label).
- Use a dosing syringe.
- Claro, Easotic® (Virbac) and Osurnia deliver 1 mL of medication directly from their applicators and thus achieve adequate volumes for dogs of all sizes.[12]
- To facilitate more complete penetration into the canal, apply to the deep portion of the vertical canal and gently massage the ear for 30 seconds after instillation.

6) Continue antimicrobial treatments for 2 weeks after the infection is cytologically resolved.

7) Utilize a long-term maintenance program to prevent recurrence. This is generally accomplished by regular use of the cleansing, antiseptic drying agents listed above and topical steroids as needed to control inflammation (usually from allergies) which initiates the secondary infections. Ideally, the primary allergy should be diagnosed and treated to best eliminate recurrence of otitis.

8) Consider a surgical option for an ear that cannot be medically salvaged.[1]

TOPICAL THERAPY

Topical therapy alone is usually sufficient to successfully treat and control otitis externa. Systemic antibiotics, antifungals and corticosteroids may be needed with chronic proliferative otitis externa, otitis media, severe recurrent infectious otitis and when owner or patient compliance issues preclude the use of topical formulations that need to be administered once or twice a day for days or weeks. Clinical experience suggests that compliance is a major factor in treatment failures and recurrence of otitis. Recently approved products such as Claro and Osurnia address this issue with the former approved for single administration and the latter for 2 applications at a 7-day interval for *S. pseudintermedius* and *M. pachydermatis*.

The topical products approved by the FDA for otitis externa (see table below) contain combinations of ingredients including antibiotics, antifungals and corticosteroids. The appropriate product should be chosen based on clinical condition of the ear canal, cytologic findings of infectious agents (cocci, yeast, rods) and approved spectrum of activity. Culture and susceptibility results may also help guide selection of topical treatments. However, CS typically underestimates *in vivo* efficacy of topicals since topical antibiotics are used at concentrations many times those attainable in plasma and tissues and may be formulated with vehicles that enhance the efficacy of the antibiotic.

The staphylococcal and/or yeast infections most commonly seen in practice, as described above, generally do not require topical formulations with broad-spectrum aminoglycosides, fluoroquinolones or polymyxin. These are better reserved when needed for the less common gram-negative infections associated with *P. aeruginosa*, *E. coli* and *P. mirabilis*. Over usage when not indicated may lead to development of resistance to these important antibiotics for serious infections in animals and humans.[5]

Some commercial formulations (see table below) are in petrolatum, hydrocarbon oil or paraffin silicon suspension and ointment vehicles. While they may adhere well to the lining of the ear canal, they may occlude and further moisturize an already macerated epithelium, especially with once or twice daily application over several days. If the ointment or suspension does enter the middle ear with a ruptured tympanic membrane, it is uncertain how long it takes for normal metabolic processes to remove it. In most ears, commercial formulations with non-occlusive water-soluble and aqueous solution vehicles are more desirable.[12]

Compounded otic preparations for the treatment of ear infections in dogs have been utilized for many years. It should be noted that these are not FDA-approved so their use is considered extra-label and efficacy is based on anecdotal reports with lack of published scientific evidence. Over time, approval of new products has decreased the need for compounding. Compounding of active ingredients in lanolin and other occlusive vehicles was done to enhance residual activity and improve convenience and compliance. Residual activity has now been achieved in the FDA-approved topicals, Claro and Osurnia. There may still be occasions when commercial formulations are not clinically effective or tolerated by a patient. For these situations the reader is referred to a drug formulary for various compounding options.[13]

Combination Ear Treatment Products
(modified and updated from reference 1)

Brand, MFG	Active Ingredients	Vehicle	Indications*	Dosage and Duration
Baytril® Otic, Bayer	0.5% enrofloxacin, 1% silver sulfadiazine	Water-based emulsion	*CPS, Mp, Pa, E, Pm, S, Ah, A, Ca, Kp*	5-15 drops, Q12h, for 14 days
Claro™, Bayer	1.5% florfenicol, 1.33% terbinafine, 0.2% mometasone furoate	Clear, liquid solution	*Sp, Mp*	1 mL, single administration
Easotic®, Virbac	0.15% gentamicin, 1.51% miconazole, 0.11% hydrocortisone aceponate	Semi-liquid petrolatum jelly	*Sp, Mp*	1 mL, Q24h, for 5 days
GentaOtic™, Henry Schein	0.3% gentamicin, 0.1% betamethasone	Solution	Bacteria susceptible to gentamicin**	3-8 drops, q12h, for 7-14 days
Mometamax®, Merck	0.3% gentamicin, 1% clotrimazole, 0.1% mometasone furoate	Plasticized hydrocarbon oil suspension	*CPS, Mp, Pa, Ef, Pm, S*	4-8 drops, q24h, for 7 days
Osurnia®, Elanco	1% florfenicol, 1% terbinafine, 0.1% betamethasone acetate	Translucent gel	*Sp, Mp*	1 mL, repeat in 7 days
Otomax®, Merck; Tri-Otic®, Med-Pharmex	0.3% gentamicin, 1% clotrimazole, 0.1% betamethasone	Plasticized hydrocarbon oil suspension	*Mp* and bacteria susceptible to gentamicin**	4-8 drops, q12h, for 7 days
Panalog®, Zoetis; Anamax®, Dechra	0.25% neomycin, 2,500 IU/mL thiostrepton, 100,000 IU/mL nystatin, 0.1% triamcinolone	Cream or plasticized carbon polyethelene ointment	Bacterial and *Candida* infections**	No specific dosing recommendation for otitis
Posatex®, Merck	1.0% orbifloxacin, 0.1% posaconazole, 0.1% mometasone furoate	Plasticized hydrocarbon oil suspension	*CPS, Mp, Pa, Ef*	4-8 drops, q24h, for 7 days
Surolan®, Elanco	0.053% polymyxin B, 2.3% miconazole nitrate, 0.5% prednisolone acetate	Liquid paraffin silicon suspension	*Sp, Mp*	5 drops, q12h, for 7 days
Tresaderm®, Merial	0.32% neomycin, 9% alcohols, 4% thiabendazole, 0.1% dexamethasone	Propylene glycol solution	Acute and chronic otitis externa**	5-15 drops, q12h, for 7 days

**CPS* (coagulase-positive *Staphylococcus* spp.), *Mp* (*Malassezia pachydermatis*), *Pa* (*Pseudomonas aeruginosa*), *E* (*Enterobacter* spp.), *Pm* (*Proteus mirabilis*), *S* (*Streptococci* spp.), Ah (*Aeromonas hydrophila*), A (*Aspergillus* spp.), Ca (*Candida albicans*), Kp (*Klebsiella pneumoniae*), *Ef* (*Enterococcus faecalis*) **Older products with no specific organisms indicated

SYSTEMIC THERAPY

Systemic antimicrobials.[1,14] Routine systemic antimicrobial therapy for infectious otitis externa and otitis media is controversial. Some dermatologists have stated that there is not a difference in success rate managing otitis with or without systemic antibiotics. However, there are no credible data comparing efficacy using topical therapy alone, systemic therapy alone and topical and systemic treatments. Indications for use of systemic antibiotics include otitis media, a pure gram-negative infection, proliferative chronic otitis externa, purulent ulcerative otitis externa and when owners cannot treat their pet's ears with topical therapy. If at all possible, systemic antibiotics should be selected based on CS results. If an empirical choice is made, it should be based on cytologic findings and guided by a current antimicrobial reference.[15] Depending on the pathogen and the severity and chronicity of the infection, systemic antimicrobial treatment should be continued for 1-2 weeks after negative cytology followed by a topical maintenance program to prevent recurrence of infection.

For gram-positive infections associated with *Staphylococcus*, cephalosporins, clindamycin and amoxicillin trihydrate/clavulanate potassium are generally good initial choices. The only oral antibiotics that may be efficacious for gram-negatives such as *Pseudomonas* are the fluoroquinolones, enrofloxacin and marbofloxacin. They should be used at the high end of the approved dosage range to avoid the development of resistance. The human fluoroquinolone, ciprofloxacin, should only be used when CS indicates resistance to the veterinary-approved drugs but continued susceptibility to ciprofloxacin based on MIC's. Even in this situation, oral ciprofloxacin tablets may not achieve effective plasma and tissue concentrations because of extremely variable absorption after oral administration in dogs.[16]

When *Pseudomonas* has become multi-drug resistant and topical therapy alone does not resolve the infection, parenteral antibiotic treatment is required.[14] Options in dogs based on CS generally include ticarcillin disodium/clavulanate potassium (15-25 mg/kg, q8h, IV), meropenem (12 mg/kg, q8h, SQ; 24 mg/kg, q8h, IV), ceftazidime sodium (30 mg/kg, q6h, IV, IM; 30 mg/kg, q4h, SQ), amikacin (15-30 mg/kg, q24h, IM, SQ, IV), and gentamicin (10-14 mg/kg, q24h, IM, SQ, IV).[14] Patients on the aminoglycosides must be monitored for nephrotoxicity with urinalysis for protein and tubular casts and serum for BUN and creatinine every 1-2 weeks. Meropenem and ceftazidime should be used as a last resort due to implications for human health.

When *Malassezia* infections have failed to respond to topical therapy alone or if yeast otitis media is present, ketoconazole, fluconazole or itraconazole at 5-10 mg/kg, q24h or terbinafine at 30-40 mg/kg, q24h may be effective.

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Key Clinical Updates for General Practice from the 8th World Congress of Veterinary Dermatology and Recent Dermatology Publications

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Most of the abstracts included in these notes are edited with additional information added from the *Proceedings of the 8th World Congress of Veterinary Dermatology* held in Bordeaux, France May 31 – June 4, 2016 published in *Veterinary Dermatology* Volume 27 (Suppl. 1), May 2016.
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1. Repeated oral dose tolerance in dogs treated concomitantly with cyclosporine and oclacitinib for three weeks. Panteri A, et al. *Vet Dermatol* 2016;27:22.

Purpose: To evaluate the oral tolerance of oclacitinib (Apoquel) and cyclosporine (Atopica) given concurrently for 3 weeks.

Methods: Two groups of 8 beagles were randomized in an open parallel experiment to receive oclacitinib alone (0.4–0.6 mg/kg twice daily for 14 days then once daily for 7 days) or in combination with cyclosporine (5 mg/kg once daily) for 3 weeks. They were examined every day and adverse events were recorded. Blood samples were collected during the acclimatization phase, weekly during treatment and at the end of the study for hematology, clinical chemistry and coagulation evaluation.

Results: There were no abnormal clinical observations following treatment with oclacitinib given alone or concomitantly with cyclosporine, with the exception of diarrhea in 2 dogs receiving both drugs. Three dogs from each group experienced transient inappetence; 3 dogs treated with oclacitinib had mild weight loss. Clinical pathology parameters remained within the reference range for beagle dogs at that facility.

Conclusions and Clinical Relevance: The concomitant administration of cyclosporine and oclacitinib for 3 weeks to beagles was well tolerated and was not associated with an increase in the number of adverse events or laboratory abnormalities beyond those associated with oclacitinib given alone. The use of this combination short-term may be helpful in some atopic dogs where a more rapid clinical response is desired over 2-3 weeks (without the use of corticosteroids) followed by long-term administration of cyclosporine alone. It should be noted that precautions in the Apoquel package insert include: *The use of APOQUEL has not been evaluated in combination with glucocorticoids, cyclosporine, or other systemic immunosuppressive agents. Dogs receiving APOQUEL should be monitored for the development of infections, including demodicosis, and neoplasia.* Similar precautionary wording is also found in the Atopica package insert.

2. A better characterization of clinical signs of canine atopic dermatitis in a specialty practice: a prospective study of 300 cases. Bensignor E, Merven F. *Vet Dermatol* 2016;27 (Suppl. 1):65.

Purpose: To prospectively evaluate cases of atopic dermatitis (AD) diagnosed in a specialty practice to better define clinical signs.

Methods: Dogs (n = 620) presented for a pruritic disease were included. Among these, 300 were finally diagnosed

as having AD using ICADA recommendations for diagnosis (briefly a pruritic dermatosis after exclusion of parasitic and microbial causes of pruritus).

Results: Two hundred and twenty five (225) cases were considered 'classical' forms of AD as defined by Favrot's criteria (group A). Seventy-five (25%) cases did not 'fit into the box' (group B). Unusual forms recognized were peri-umbilical and/or mammary pruritus (12/75), relapsing otitis externa without any other clinical sign (24/75), recurrent hot spot (8/75), anal pruritus (10/75), urticaria (3/75), 'head and neck dermatitis' (2/75), dorsolumbar pruritus (10/75) and alesional pruritus (6/75). No statistical differences were noted regarding breed, sex or age for the two groups. Allergen testing was performed in 175/225 cases in group A and 75/75 cases in group B, without statistically significant differences in the sensitization results.

Conclusions and Clinical Relevance: Results of this study confirm that the clinical picture of AD is complex and that different clinical forms of the disease are recognized in dogs.

3. Effectiveness of regionally-specific immunotherapy (RESPIT) for the management of atopic dermatitis in 103 dogs. Plant J, Neradilek M. *Vet Dermatol* 2016;27 (Suppl. 1):73.

Purpose: To evaluate the effectiveness of a subcutaneously administered uniform allergenic extract mixture used for at least 9 months in 103 dogs with atopic dermatitis.

Methods: In this retrospective study, dogs in the author's practice were diagnosed with atopic dermatitis based upon identifying characteristic clinical features and ruling out alternative diagnoses. Each received a uniform mixture of 20 allergenic extracts (18 pollen and 2 dust mite allergens) selected based on the aerobiology of the region (RESPIT Injectable). The initial subcutaneous dose of 0.1 mL (10,000 protein nitrogen units/mL) was increased weekly by 0.1 mL up to a weekly maintenance dose (0.5–1.0 mL). The records for dogs that a) began therapy during a 3 year period, b) continued therapy for > 270 days, and c) included certain baseline and follow-up entries were evaluated retrospectively. Response to therapy was classified as excellent, good, fair or poor based on changes in pruritus (evaluated by owners using visual analog score (VAS)), lesion severity, and concomitant medications administered between Day 0 (D0) and the first post-therapy examination.

Score	Response	Description
4	Excellent	Complete remission with no other medications
3	Good	Greater than 50% improvement in clinical signs and reduction in medications
2	Fair	Improvement, but concurrent medications could not be substantially decreased
1	Poor	No clinical change or a deterioration

Results: 103/286 dogs (36%) returned for an examination after 270 days while still receiving treatment, meeting the inclusion criteria. The mean duration of therapy evaluated was 424 days (median 365, range 273-1,735 days). The overall response was excellent in 19.4%, good in 37.9%, fair in 25.2% and poor in 17.5% of dogs. Baseline (D0) age, weight, gender, pruritus severity and lesion severity did not correlate with response classification. No adverse reactions were reported in the 103 evaluable dogs meeting the inclusion criteria. Seven of 286 dogs initially screened (2.4%) were suspected by pet owners to have experienced adverse reactions including 3 with increased pruritus, and 1 each with vomiting, blepharitis, restlessness or urticaria.

Conclusions and Clinical Relevance: In this retrospective non-controlled study, the combined good-excellent effectiveness rate of RESPIT Injectable (57%) was similar to rates previously reported for allergen-specific immunotherapy in atopic dogs.

4. Inaccuracy of a hair and saliva test for allergies in dogs. Coyner K, Schick A. *Vet Dermatol* 2016;27 (Suppl. 1):68.

Purpose: To determine if the Immune IQ test (Vet DVM, Boulder, CO) could reliably differentiate between samples from a normal dog, an allergic dog and fake dog fur and tap water.

Methods: Ten fur/saliva samples were submitted from a known atopic/food allergic dog and a normal, non-allergic dog, as well as five samples of realistic appearing "fake" fur from a stuffed toy animal and tap water. To ensure appropriate sample blinding for laboratory analysis, samples were submitted under different pseudonyms. Laboratory testing was performed for 128 food and environmental allergens. Specific testing procedures were described as proprietary and are not detailed by the company. Results are reported by the company as RED (things to avoid), YELLOW (caution) and GREEN (not a problem). Statistical analyses were performed to determine if the response distribution differed significantly between dogs as well as to determine test-retest reliability.

Results: The distribution of Immune IQ test results among allergic dog, non-allergic dog and fake fur samples were not distinguishable from those expected from random chance, after correcting for multiple comparisons. Test-retest reliability was poor to slight.

Conclusions and Clinical Relevance: The Immune IQ test results could not differentiate between an allergic dog, a non-allergic dog and fake animal fur, and should not be recommended as an alternative to hypoallergenic diet trials or intradermal or serologic allergy testing in companion animals.

5. A randomized, double-blinded crossover trial testing the benefit of two hydrolyzed poultry-based commercial diets for dogs with spontaneous pruritic chicken allergy. Bizikova P, Olivry T. *Vet Dermatol* 2016;27:144.

Purpose: To determine the clinical allergenicity of an extensively hydrolyzed poultry feather diet (Royal Canin Ultamino/Anallergenic Formula Dry)(RCU) and a partially hydrolyzed chicken liver diet (Hill's Prescription Diet z/d Canine Dry)(HZD) in dogs with chicken-induced cutaneous adverse food reactions (CAFR).

Methods: A prospective, randomized, double-blinded crossover trial was conducted in 10 dogs with chicken-induced CAFR that were positive on oral challenge to chicken meat. The 10 dogs were client-owned, had non-seasonal pruritus, were managed with a non-chicken-based diet, had a positive challenge to chicken meat and negative challenge to corn, and had a pruritus visual analog scale (PVAS) $\leq$ 2.5/10 at the start of the challenge. Each diet was fed for 14 days separated by a 14 day wash-out period. Owners rated pruritus daily using a PVAS. The challenge was ended if the PVAS exceeded 5/10.

Results: The median PVAS values before feeding RCU and HZD were 0.9 (range: 0–2.5) and 1.7 (range: 0–2.5), respectively, which were not significantly different. Taken together in all 10 dogs, the PVAS values were not significantly different after feeding RCU compared to those at baseline. The pruritus scores were significantly higher after dogs were fed HZD. None of the dogs fed RCU were removed from the study due to pruritus flares of $\geq$ 5/10. Four dogs (40%) fed HZD were withdrawn for this reason. Additionally, maximal and average PVAS values were significantly higher after feeding HZD than RCU.

Conclusions and Clinical Relevance: The more favorable response to RCU in this population of chicken allergic dogs may be due to lower allergenicity associated with a different degree of protein hydrolysis. HZD has residual

peptides of larger sizes. Three percent (3%) of poultry-based peptides in this formulation were reported to be >10 kDa. Conversely, an extensively hydrolyzed diet contains the majority of the protein in the form of individual amino acids. The results of this study suggest that if a patient is allergic to the native protein in a partially hydrolyzed diet, that the diet may be effective in only 60% of dogs it is used on for diagnostic purposes.

6. Diagnostic value of home-cooked and an extensively hydrolyzed diet (Anallergenic, Royal Canin, France) in the diagnosis of canine adverse food reaction: a randomized prospective multicenter study in 72 dogs. Cadiergues MC, et al. *Vet Dermatol* 2016;27 (Suppl. 1):21.

Purpose: To compare the diagnostic value of a home cooked diet (HCD) and an extensively hydrolyzed diet (Anallergenic/Ultamino)(RCU) for the diagnosis of canine adverse food reactions (CAFR).

Methods: Dogs with suspected CAFR were randomized to be fed either a balanced HCD or RCU. Inclusion required that 5 out of 8 Favrot diagnostic criteria for chronic canine atopic dermatitis be met, a CADESI-04 score of $\geq$ 45 and a pruritus score of $\geq$1 on a 0-4 scale. Dogs that had at least a 50% reduction in pruritus over the elimination trial went through a dietary challenge. CADESI-04 and pruritus scores were recorded at days 0, 56, 70 and 154.

Results: Thirty-five (35) dogs were fed the HCD and 34 the RCU. There were no significant differences between the two groups at any time point for CADESI-04 or pruritus. After 8 weeks, 18 (52.9%) of the dogs in the RCU group and 19 (54.3%) of the dogs fed the HCD had at least 50% reduction in pruritus and significant reduction in CADESI-04 scores. 12/18 (66.7%) dogs in the RCU and 12/19 dogs (63.2%) in the HCD group relapsed after the dietary challenge. Therefore, CAFR was diagnosed in 35.3% of the RCU dogs and 34.3% of the HCD dogs.

Conclusions and Clinical Relevance: The extensively hydrolyzed diet, (Ultamino, Royal Canin) may be just as reliable as a home-cooked diet to diagnostically screen dogs for CAFR. The results also suggest that approximately 1/3 of dogs with non-parasitic allergic dermatitis have a significant ($\geq$ 50%) food reaction component to their dermatosis. Additionally, this study also underscores the need for a dietary challenge to fully confirm that an initial dietary response is indeed due to CAFR.

7. Subcutaneous administration of cyclosporine for feline allergic skin disease – An open label clinical trial. Koch SN, et al. *Vet Dermatol* 2016;27 (Suppl. 1):74.

Purpose: To evaluate the efficacy and tolerability of subcutaneous administration of cyclosporine in 11 client-owned cats with year round non-flea and non-food allergic skin disease.

Methods: All cats showed variable degrees of pruritus and lesions with or without hair loss, including erythema, crusts and/or excoriations (3 cats), miliary dermatitis (3), symmetrical alopecia (2), and lesions of the eosinophilic granuloma complex (3). Cyclosporine 50 mg/mL injection (Sandimmune, Novartis, NJ) was administered subcutaneously by the owners for 60 days with initial doses of 2.5–5.0 mg/kg every 24–48 h. If significant clinical improvement was seen after 30 days of therapy, the investigators attempted to reduce the dosage to 2.5-5.0 mg/kg every 36-72h. Clinical response was assessed using FeDESI (feline dermatitis extent and severity index) and PVAS (pruritus visual analog scale) between days 0 and 60.

Results: Six (6) of the 11 cats completed the study. Five (5) cats were withdrawn due to the following: injection site reactions (2 cats), owner's inability to give injections (2), behavior changes and lack of response after 30 days (1). Dosages at day 60 ranged from 2.5 to 5.0 mg/kg q36-72h. FeDESI scores decreased significantly from day 0 (median: 45.5, range: 10–77) to day 60 (2.5, 0–18). Similarly, PVAS scores decreased significantly from day 0 (median: 6.5, range: 3–9) to day 60 (2, 1–3). The most common adverse reaction was a focal lesion and/or alopecia at the injection site with no systemic signs reported. Cats had baseline and day 60 chemistry profiles, complete blood cell counts, urinalysis and urine cultures. There were no significant abnormalities reported for

any of the cats at any time point.

Conclusions and Clinical Relevance: Subcutaneous cyclosporine appears to be an efficacious and safe therapy for feline allergic skin diseases and may be a good treatment option for cats that cannot be treated orally.

8. Head and neck feline dermatitis: response to oclacitinib treatment. Pandolfi P, Beccati M. *Vet Dermatol* 2016;27 (Suppl. 1):58.

Purpose: To determine efficacy after oral administration of oclacitinib (Apoquel) in allergic cats where the major sign is head and neck dermatitis (HND) and where other therapies have failed.

Methods: Fifteen (15) cats had undergone previous treatment with systemic corticosteroids (11) or cyclosporine (4) at an adequate dosage. All cats received oclacitinib at 2.7 mg/cat twice daily (0.5–0.8 mg/kg). To facilitate administration of the drug, half of a 5.4 mg pill was administrated twice daily for 2 weeks, then cats received the same dosage once a day for an additional 14 days. Clinical lesions were evaluated with SCORFAD (SCORING Feline Allergic Dermatitis) system, which estimates the severity and extent of four lesions (excoriations, eosinophilic plaque, miliary dermatitis, self-induced alopecia) and the number of body regions involved. Owners monitored all cats weekly for pruritus using a Visual Analog Scale (VAS) with descriptors.

Results: There was a rapid decrease of pruritus in 10/15 cats; 3/15 dropped out, mainly for difficulty in administrating the pills; 2/15 showed no improvement in pruritus. SCORFAD and VAS were improved in 10/15 cats (66.6%).

Conclusions and Clinical Relevance: Oclacitinib treatment may provide relief for cats with HND. However, the drug is not approved for use in cats and long-term safety and efficacy studies have not been reported.

9. Evaluation of cytology collection techniques and prevalence of Malassezia yeast and bacteria in claw folds of normal and allergic dogs. Lo KL, Rosenkrantz WS. *Vet Dermatol* 2016;27:279.

Purpose: To compare three different sampling methods for claw fold cytology and to evaluate the numbers of bacteria, *Malassezia* yeast and inflammatory cells.

Methods: Sixty (60) client-owned dogs: a) normal, b) allergic dogs with no clinical signs of claw disease, c) allergic dogs with clinical paronychia. Claw fold samples were taken with a toothpick, acetate tape preparation and direct impression smear. Slides were evaluated by two investigators for inflammatory cells, nuclear streaming, debris, corneocytes, yeast, intracellular (IC) cocci, extracellular (EC) cocci, IC rods and EC rods. For each parameter, data were compared between groups and between methods. Inter-reader agreements were also calculated.

Results: Group c) allergic dogs with clinical paronychia had significantly higher numbers of EC cocci (36.62 over 9 fields) and corneocytes (30.55) than groups a) (3.5 and 24.33, respectively) or b) (0.82 and 24.74, respectively). Yeast counts were higher in allergic dogs (24.99 in group c) and 11.9 in group b)) but not significantly different than for normal dogs (6.83). There were significantly higher numbers of *Malassezia* organisms (27.13) and EC cocci (22.62) retrieved from samples collected with a toothpick compared to other methods. Tape preparations were associated with significantly more debris (8.66) and corneocytes (35.03) and impression smears with significantly more nuclear streaming (0.54).

Conclusions and Clinical Relevance: Based on these findings, the authors state that sample collection using a toothpick optimizes the value of cytological results when sampling allergic dogs with clinical paronychia. Additionally, yeast organisms are seen as part of the flora in the claw folds of normal dogs and allergic dogs with no clinical claw disease. These findings should be taken into account when a decision is made to treat with

systemic and/or topical antifungal therapy.

10. Evaluation of the squeeze tape impression for the diagnosis of canine demodicosis. Vogelnest L, Garibotto V. *Vet Dermatol* 2016;27 (Suppl. 1):38.

Purpose: To determine the sensitivity and specificity of this test for the diagnosis of demodicosis due to *Demodex canis* and to characterize this test.

Methods: Sixteen (16) affected and 30 control (15 normal skin, 15 with skin disease) dogs were evaluated. Squeeze tape impressions were collected from four sites, including one lesional site in affected dogs. A 5 cm strip of clear, 24 mm wide, adhesive tape was placed onto skin, and tape and underlying skin squeezed for 2–3 s, and repeated 2–4 times. Tapes were gently stretched and placed onto a glass slide. Deep scrapings were collected from control dogs with skin lesions (15 dogs).

Results: Tape samples revealed no mites in all control dogs (120 samples) and mites at lesional sites in all affected dogs. Deep scrapings were negative in control dogs with skin lesions and positive in 14/16 (87.5%) affected dogs. Two affected dogs with mites on tape samples had no mites on deep scrapings. The sensitivity and specificity of the squeeze tape impression were both 100%, with 90% sensitivity for the deep scraping.

Conclusions and Clinical Relevance: The squeeze tape impression has excellent sensitivity and specificity for the diagnosis of canine demodicosis associated with *D. canis* and is less invasive and more readily performed at multiple body sites in comparison to the deep skin scraping.

11. A blinded, randomized, placebo-controlled trial investigating three dose levels of lokivetmab (ZTS-00103289), a caninized anti-canine IL-31 monoclonal antibody, for the reduction of pruritus and associated skin lesions in dogs with atopic dermatitis. Michels GM, et al. *Vet Dermatol* 2016;27 (Suppl. 1):55.

Purpose: To identify a dose of lokivetmab for maximum relief of clinical signs of atopic dermatitis over 4–6 weeks in a randomized, double-blind, placebo-controlled trial.

Methods: Fifteen specialty clinics enrolled client owned dogs (n = 211) with chronic AD. Dogs were randomized to treatment with lokivetmab (0.125, 0.5 or 2.0 mg/kg) or placebo administered subcutaneously once on day 0. Dog owners assessed visual analog scale scores of pruritus and clinicians assessed Canine AD Extent and Severity Index (CADESI-03) scores periodically for 56 days.

Results: Treatment with lokivetmab (2 mg/kg) resulted in a significantly greater percentage reduction from baseline in pruritus (days 1–49) and CADESI scores (days 7–56) compared to placebo; significant differences were achieved in lower dose groups but at later time points and for shorter duration for pruritus (0.5 mg/kg, days 2–35; 0.125 mg/kg, days 7–21) and CADESI scores (0.5 mg/kg, 0.125 mg/kg; day 14). Treatment with lokivetmab (2 mg/kg) resulted in significantly lower mean pruritus and CADESI scores at day 28 compared to placebo (32.6 versus 58.0) and (73.7 versus 121.9), respectively; a significantly greater percentage of dogs achieved $\geq$ 50% improvement in pruritus and CADESI scores at day 28 compared to placebo (57% versus 14%) and (46% versus 9%), respectively.

Conclusions and Clinical Relevance: Lokivetmab provided dose-dependent improvement in owner assessed pruritus and clinician assessed CADESI-03 scores within as early as 1 day through $\leq$ 6 weeks and, in some dogs, $\leq$ 2 months following a single dose. Results of another paper presented at this congress revealed no differences in adverse events or clinical pathology values between treated and placebo groups after 2 monthly doses of this immunotherapy in 162 client-owned dogs.

12. Quality assessment of compounded fluconazole capsules and oral suspensions in the United States. Laporte C, et al. *Vet Dermatol* 2016;27 (Suppl. 1):35.

Purpose: To evaluate the pharmaceutical characteristics (strength, accuracy, precision), physical properties and bacterial contamination of fluconazole compounded products (FCPs) (capsules and oral suspensions) from US compounding pharmacies.

Methods: FCPs (30 and 240 mg capsules; 30 and 100 mg/mL oral suspensions) were ordered from four pharmacies at three time points, 7 or 10 days apart. Generic FCZ (50 and 200 mg tablets; 10 and 40 mg/mL oral suspensions) was used as reference. Samples were evaluated upon receipt; suspensions were additionally evaluated at 3 and 6 months. Physical properties, bacterial contamination, accuracy (percentage predicted), and precision (reproducibility of results) were assessed for all CPs. High performance liquid chromatography was used to quantify FCZ.

Results: Aerobic bacterial cultures were negative. Physical properties differed between and within pharmacies. Capsules (30 and 240 mg) had acceptable accuracy (median 95.9%, range 87.2-135.2%) and precision (mean 7.4 +/- 5.9%). Suspensions (30 and 100 mg/mL) had poor accuracy (median 74.4%, range 53.9-95.2%) and precision (mean 14.9 +/- 6.9%). Capsules were statistically more accurate and precise than suspensions.

Conclusions and Clinical Relevance: Based on these findings, FCPs should be prescribed with caution. Further studies evaluating FCPs bioavailability or clinical efficacy are indicated but should be accompanied by data demonstrating the quality of the CP studied.

13. Triggers, risk factors and clinico-pathological features of urticaria, angioedema and anaphylaxis in dogs – a prospective observational study of 24 cases. Rostaher A, et al. *Vet Dermatol* 2016;27 (Suppl. 1):9.

Purpose: To improve knowledge of the triggers, risk factors and clinico-pathological features of urticaria, angioedema and anaphylaxis in dogs.

Methods: Dogs submitted to the Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, Zurich with signs of angioedema, urticaria or anaphylaxis were enrolled between 2014 and 2015. The immediate workup consisted of clinical examination and routine laboratory tests. The causes were determined according to the dogs' medical history and additional tests (Western blotting, IgE serology, intradermal testing, dermatographism, autologous serum and ice cube skin test), if appropriate. A causality algorithm for urticarial and anaphylaxis (ALUA) with a score range from 0 to 22 was designed, to objectively determine the probability of the identified triggers.

Results: Twenty-four cases were detected. The following clinical features were encountered: wheals (67%), angioedema (63%), pruritus (42%), vomiting (42%), atopic dermatitis (40%), diarrhea (25%) and collapse (12%). The predominant blood abnormalities were leukocytosis, and elevated lipase, creatinine kinase and alanine aminotransferase values. Venom, food and drug allergens were considered very likely (ALUA > 10) causes in six (29%), four (17%) and three (13%) cases, respectively. Venom or food allergens was considered likely (5 > ALUA < 10) causes in three (13%) cases. The cause was possible (ALUA < 5) in seven (29%) cases and consisted of reactions to food and venom allergens in six and one case, respectively.

Conclusions and Clinical Relevance: This is the first prospective study describing the triggering factors and clinico-pathological features of dogs with urticaria, angioedema and anaphylaxis in veterinary medicine. Food, insect venoms and drugs were the leading triggers, resembling what is described in human medicine.

14. Frequency of urinary tract infections in feline patients with dermatologic disease receiving long-term glucocorticoids and cyclosporine. Lockwood S, et al. *Vet Dermatol* 2016;27 (Suppl. 1):33.

Purpose: To investigate the frequency of UTIs in cats receiving long-term glucocorticoid and/or cyclosporine therapy for the treatment of dermatological disease compared to normal cats.

Methods: In this prospective study, 33 cats being treated with oral glucocorticoids and/or cyclosporine for more than 3 months or at least 2 injections of long-acting glucocorticoids within the preceding 6 months were included. Thirty-four (34) normal cats without abnormalities on physical examination and not receiving any medication were used as a control group. Ten (10) cats received glucocorticoids only; the mean dose was 0.71 mg/kg/day and the mean therapy duration was 10.4 months. Four (4) cats received cyclosporine only; the mean dose was 5.7 mg/kg/day and the mean therapy duration was 11.8 months. Nineteen (19) cats received a combination of both drugs, the mean dose for glucocorticoids was 0.41 mg/kg/day and the mean treatment duration was 19 months. The mean dose for cyclosporine was 5.6 mg/kg/day and the mean treatment duration was 15.4 months. All cats had a complete blood count, biochemistry profile, urinalysis (collected via cystocentesis) and urine culture performed.

Results: In the glucocorticoid/cyclosporine group, 0/33 cats had a positive urine culture. In the control group, 1/34 cats had a positive urine culture. For urinalysis, red blood cells were higher in the study group. For CBC, red blood cells, hematocrit, hemoglobin and lymphocytes were higher in the control group, and eosinophils and neutrophils were higher in the study group. For chemistry, the albumin/globulin was higher in the control group, and the globulins, glucose, and GGT were higher in the study group. The only values that were still within normal limits, yet statistically significant, were the albumin/globulin ratio and the GGT, all other abnormalities had values outside the normal reference range.

Conclusions and Clinical Relevance: There was no evidence in this study to suggest that receiving long-term glucocorticoids and/or cyclosporine was positively associated with UTIs in cats. The CBC and chemistry abnormalities were attributed to medications and/or diseases. Clinical and laboratory monitoring is warranted in cats on long-term immunosuppressive therapy.

The Unholy Trinity: Hookworm, Whipworm and Roundworm

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Dogs can become infected with many infectious agents, but the "unholy trinity" of roundworm, hookworm and whipworm, are among some of the most common and well-known. For many reasons, including persistence of infectious stages in the environment and zoonotic potential, it is advantageous to prevent these parasites. Excellent information about these parasites can be found at http://www.capcvet.org.

Roundworm

Roundworm is the common name for the canine ascarid, *Toxocara canis*. It is extremely common in puppies, and treatment is relatively straightforward. As with other parasites, by understanding the life cycle, we can understand how to treat and prevent transmission of the parasite. For an excellent summary of the life cycle, please refer to: http://www.cdc.gov/parasites/toxocariasis/biology.html.

As with all parasites, it is easiest to start our discussion with the adult worm. Adult *T. canis* can be easily seen, as they are 4 to 6 inches in length. It is important to be able to identify the adults, since clients will often bring the worm to you that they found in either their dog's vomit or feces. As a rule, *T. canis* is found primarily in puppies, although some studies have suggested that worms may be present in up to 33% of adult dogs. The reason for the predisposition in puppies is explained by the migration patterns (detailed below) in puppies versus adult dogd. The adults, which are separate sexes, will mate in the intestine. The female will then produce literally thousands of eggs per day, which are shed into the environment in the feces. These eggs are shed unembryonated, and are not immediately infective. Depending on temperature, eggs will be infective 2 to 4 weeks after being excreted into the environment. At this point, they contain the infective third-stage larvae (L3).

The egg is EXTREMELY resistant to disinfectants and environmental changes. What makes their presence even more insidious is that the eggs have a sticky outer coating, which makes them very difficult to remove from surfaces, including concrete. Eggs can survive for years, although extreme heat and prolonged exposure to sunlight will kill the larvae. Because of the resilience of eggs in the environment, humans, particularly children, can ingest these eggs. Once ingested by a suitable host, whether it is a definitive canid host or accidental human host, these eggs will "hatch" and the L3 will be released into the intestine.

Upon entering the intestine, the L3 will penetrate the intestine, and travel via the blood to the liver, after which the larvae will then travel to the lungs. Once in the lungs, the larvae will literally burst out of the alveoli. When this occurs in large numbers in puppies, the resulting condition is verminous pneumonitis. After entering the alveolus proper, the L3 can take one of two paths. It is important to understand both paths.

First, the larvae can travel up the trachea in what is known as "tracheal migration." After ascending the trachea, the larvae are swallowed, and travel to the intestine, where they will mature to adults. In the second pathway, the larvae will reenter the alveolar blood vessels and travel to the muscles or organs, where they will arrest. This is known as somatic migration, and it is the migration path that occurs in humans, and results in the condition known as larva migrans.

Larva migrans is typically associated with the eye (ocular larva migrans), or viscera (visceral larva migrans). As mentioned above, this disease occurs primarily in children, as a result of their propensity to eat dirt, which can potentially contain infectious eggs. The easiest way to prevent this horrible disease is to deworm puppies prior to the worms becoming adults. If the worms are not adults, then they cannot produce eggs. The other obvious way is to pick up the dog's feces upon defecation.

For the main reason as to why puppies are infected, we have to refer back to the life cycle. After somatic migration, worms will be encysted in tissues. In the pregnant bitch, these larvae will become reactivated and will

travel via the umbilical vein to the in utero puppies' liver and lungs. Upon birth, the lungs inflate; the larvae burst out and travel to the intestine via tracheal migration, where they mature. These worms will become mature in 3 weeks. Encysted larvae can also infect the puppies by the transmammary route, although the primary route is considered to be transplacental. By deworming the puppies every 2 weeks up to 12 weeks, you prevent any maturation of these transplacental or transmammary transmitted larvae. By preventing maturation, you prevent egg shedding, environmental contamination and reduce the risk of a child becoming infected.

Hookworm

While there are several hookworms, I will focus this discussion on the canine hookworm, *Ancylostoma caninum*. As with the roundworms, adults live in the intestines where they mate and produce eggs. They are roughly the diameter of a penny, and literally are shaped like a "hook." Like roundworms, they produce a large number of eggs. The eggs are shed into the environment where they will develop and hatch in a period of 2 or so days. At this point the larvae are L1s, and will molt to the infectious L3s during the next week (or in other words, up to 8 days after being shed). The L3s can then infect the host either through ingestion or skin penetration.

As with roundworms, some larvae will become arrested in the tissues. These larvae can become reactivated during partuition, and as a result can be transmitted to puppies through the bitch's milk. Transmammary transmission is a very important route of infection for puppies. Regardless of the means of infection, hookworms are going to attach to the small intestinal mucosa, after which they will suck blood, LOTS of blood. The loss of blood is the primary cause of pathology and clinical disease due to hookworm.

There are 4 types of clinical disease that I will briefly summarize:

1. Peracute: This involves dramatic anemia and is usually associated with newborn puppies (~1 week of age), secondary to transmammary transmission. This is a life-threatening situation. Eggs will not be detected on a fecal exam as the worms are not yet patent. Deworm the puppy and provide supportive care, including transfusions.
2. Acute: Acute disease is not as dramatic as peracute disease, but could be potentially life-threatening if untreated. This is observed in slightly older puppies. Eggs can be detected on fecal float. These puppies will be anemic.
3. Compensated: Adult dogs are more resistant to hookworm infection than puppies. Some adult dogs can still be infected with some level of hookworms, potentially due to a phenomenon known as "larval leak." These animals appear clinically normal.
4. Decompensated: Dogs that have compensated hookworm disease can become decompensated, which means they are showing signs consistent with hookworm disease, specifically anemia. This decompensation is typically secondary to a chronic disease (e.g. cancer, etc.)

As for prevention of hookworm, the same strategies that are used for roundworm apply to hookworm. That is deworming of puppies every two weeks, and prompt removal of feces.

Whipworms

Trichuris vulpis is the third member of the unholy trinity, but the one people seem to consider the least. Whipworm is important, and there is a very good chance you will diagnose it. Whipworms are named for their thin anterior end (esophagus) and thick posterior end (reproductive portion). Adults live in the large intestine, but especially the cecum. As with roundworms, adult whipworms produce environmentally resistant eggs, which are extremely difficult to destroy. Environmental contamination is the key to development of severe disease, since the eggs are resistant, they can accumulate in the environment and therefore be ingested in large numbers. After ingestion of the eggs containing the infective L1, the larvae will develop into patent adults after approximately 3 months. In comparison to roundworms, there is no migration outside of the intestinal tract. Therefore, there is no somatic migration into tissues, no migration of larvae to the pups in utero, and no transmammary transmission.

Because of the long prepatent time, whipworms are normally only diagnosed in dogs > 6 months of age.

Adult whipworms burrow their anterior end into the mucosa. This causes hemorrhage and irritation secondary to the subepithelial movement of adult worms during feeding. Also, chemical damage due to worm by-products can occur. The severity of disease is related to the number of worms—the larger number of worms, the more severe and debilitating the disease. If there are enough whipworms, death is possible.

The clinical signs of infection are those commonly seen with mild large bowel diarrhea. Diarrhea will be mucoid and/or bloody in nature. Also, tenesmus, and weight loss may be observed. Sometimes whipworm may be suspected on the basis of clinical signs, but no whipworm eggs are observed on a fecal float. This is because diagnosis by fecal flotation can be difficult. The eggs are shed in low numbers and do not float well.

Furthermore, because of the long prepatent period, disease may occur before worms are mature and shedding eggs.

In order to prevent whipworm, you may recommend deworming the dog 4 times a year or using a monthly heartworm preventive with efficacy against whipworms (i.e. one that contains milbemycin oxime or moxidectin). Finally, the point cannot be emphasized enough that one easy method for control of all 3 of these parasites is routine fecal pick-up. Practice it at your clinic, and convince your clients to do it at home.

Canine Heartworm: A Review of the Basics

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Dirofilaria immitis, also known as canine heartworm, is arguably the most important parasite of dogs in North America. Heartworm has a worldwide distribution, but as a general rule is most severe in tropical and warm/humid areas of the world. As of 2010, heartworm-positive dogs had been reported in every state in the continental United States. Due to the large number of dogs that are diagnosed every year, and the resulting expense of treatment, this disease is of huge economic importance. In fact, millions of dollars are spent on heartworm prevention, diagnosis and treatment each year. Because of the endemic nature of heartworm, and the expense of treatment, it is imperative that everyone, even those in historically non-endemic regions, be knowledgeable of the heartworm life cycle, which in turn allows one to understand treatment and prevention strategies.

As a note, the majority of the information referenced in these proceedings can be located at http://www.heartwormsociety.org.

The life cycle
Before we get to the nuts and bolts of the life cycle, there are a few important points:

1) Many animals can become infected with heartworm, including humans. While the heartworms may not develop to patent adults in many species, they can develop "part of the way." Domestic and wild canids are considered to be the definitive hosts.

2) There is no age-related immunity against heartworm. Any age animal can become infected, and previous infection does not impart immunity to future infections.

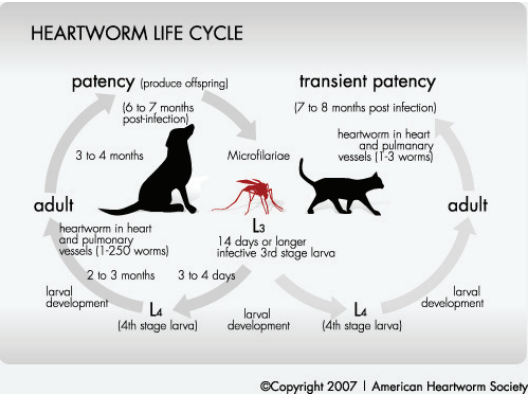
Also, before we delve into the details of the life cycle there are a few questions for one to consider:

True or False…

1. If you take microfilariae from one dog and put those into another dog (e.g. blood transfusion), adult heartworms will develop in that dog.

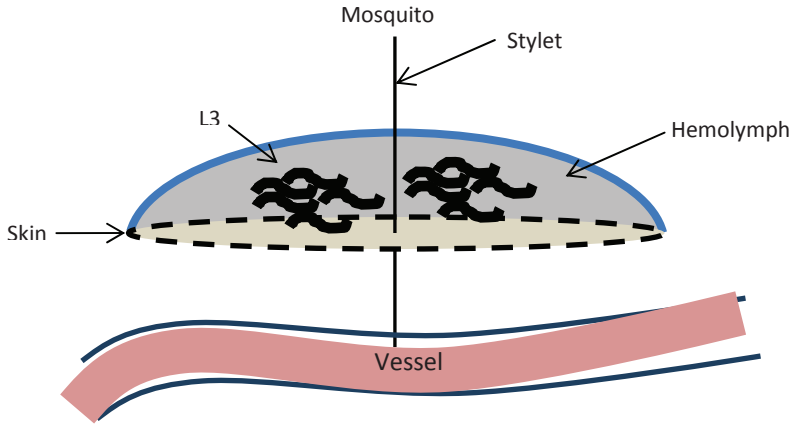
2. You should treat a 7-week old puppy that is microfilaremic for adult heartworm.

The life is depicted in graphic below (from the American Heartworm Society)



We will now consider the important stages of *D. immitis* in relation to the life cycle. The most logical place to start is with the adult worms. Female worms can grow to 10 –12 inches, where males can grow to a length of 4 – 6 inches. Adults can live up to 5 to 7 years in dogs. During this time, the adults will mate and produce microfilariae (>300 microns in length), which circulate in the blood. The microfilariae can then be ingested by a mosquito

intermediate host. The mosquito is ABSOLUTELY REQUIRED for heartworm to develop. Once inside the mosquito, the microfilaria migrate within the mosquito for an average period of approximately 14 days, during which time, the microfilaria develops to a first-stage larvae (L1.) Afterwards, the L1 molts twice to become an infectious third-stage larva (L3), which at this point is in the head of the mosquito. The L3 is approximately one mm in length. Upon landing on a host, the mosquito will then take a bloodmeal. At this point, the mosquito will "bust out" of the proboscis, which is essentially the mouthparts. The larvae will then "surround" the stylet (the piercing part of the mouthparts) in a pool of mosquito hemolymph, as shown in the schematic below:



When the stylet is removed, the larvae then enter the host through the hole made by the stylet. This is in contrast to the commonly-held belief that the larvae are "injected" into the host.

Once inside the definitive host, the L3s follow a complicated migration pathway. The L3 remains at the sight of entrance for approximately 3-4 days. Also during this time, L3 molt to fourth-stage larvae (L4). This is normally completed by 4 days, but may not occur until day 12 post-infection. It is generally agreed that the molt to the last stage, known as the juvenile adult occurs by day 58. By day 70 is when worms first arrive in their final location, the pulmonary artery. Most worms have reached this location by day 120. By day 180, worms are sexually mature and have begun to produce microfilariae, thus completing the life cycle. It is important to realize that while this is the generally accepted life cycle, there could be variations in these times.

The vector as part of the life cycle

A whole lecture could be given on the mosquito vector and its role in transmission of heartworm. Currently over 70 species of mosquitoes are thought to be potential vectors of heartworm, although 10 to 12 species are thought to be most important. While these are the documented species, it is important to remember that there could be yet unidentified species, or newly introduced species, such as the Asian Tiger mosquito, which could also serve as vectors.

An important concept in relation to the role of the mosquito is the concept of seasonal transmisson of heartworm. Maturation of parasites in mosquitoes requires higher temperatures. Practically what this means is that in most of US, the peak months of transmission are July & August. In the Northern US the transmission season is approximately 4 months, whereas in the southern US the transmission season is approximately 6-8 months. There is some speculation that "heat islands" in urban areas could extend the transmission season. In further southern climates, the transmission season would be extended even longer. In the Western United States, there is evidence of transmission, but at a much lower rate than the Southeast United States, where heartworm is endemic. However, with the current recommendation by the American Heartworm Society of administration of year-round heartworm prevention, tailoring prevention strategies for a specific locale has become moot.

Pathology of Heartworm Disease
Heartworm can be a deadly disease, especially when there are a large number of worms (caval syndrome.) While this acute presentation is spectacular, more often than not, we observe pathology secondary to the prolonged presence of worms. The severity of disease and extent of pathology can be the result of a myriad of factors, such as:

1. numbers of adult worms
2. duration of infection
3. individual host immune response
4. presence of dead worms

This last point is especially important as dead worms can "break up" and cause pulmonary thromboembolism, secondary to dying worms. One must remember that the heartworms are literally thrashing in the vessels multiple times a minute, like a bullwhip cracking the paint off of a wall. The trauma to the vessels results in thickening of the tunica intima and inflammation of the vessel wall, characterized by the pathognomonic roughened, stippled appearance. This prolonged damage can eventually lead to vessel inelasticity, which increases pressure on the main pulmonary artery, right heart and vena cava. This leads to chronic, passive congestion and pulmonary hypertension, resulting in right heart enlargement and eventually failure. The right-sided heart failure then leads to liver disease and ascites. Also, renal lesions, such as glomerulomephritis, can develop secondary to immune-mediated disease.

Wolbachia
While the worms themselves can cause damage, more recent data suggests that in fact it is bacteria that causes much of the inflammation associated with heartworm disease. By now, most people have heard of Wolbachia, which an endosymbiotic bacteria of many filarial worms. It seems to be transmitted vertically, and when in living a worm does not cause any overt pathology. The issue is when the worms die either of natural causes or due to drug treatment. When the surface proteins of Wolbachia are exposed to the host, the host immune system responds quite strongly. Because of the damage Wolbachia can do, it is important to eliminate it from the worms prior to treatment.

Clinical signs
Dogs infected with heartworm may present with severe clinical signs, be asymptomatic, or be somewhere in the middle of the spectrum. The severity of clinical signs, like the pathology of heartworm disease, is dependent of many factors. Ultimately, the presence or absence of clinical signs is an important component of staging heartworm disease. These are described briefly below. While these "classes" are presented as absolutes, it must be emphasized that there is a continuum. Full details are available at www.heartwormsociety.org.

With Class I heartworm disease, the animal can be asymptomatic or present with a mild cough. Otherwise, these animals are fine, and do not seem inhibited by the disease.

Animals with Class II heartworm disease will have a more moderate cough. Also, these animals could have difficulty breathing, and be somewhat exercise intolerant.

To be blunt, Class III is when things are going to "hell in a handbasket," so to speak. These animals are dyspneic, and can be severely exercise intolerant. Syncope and hemoptysis may be present. Signs of right-sided congestive heart failure, such as ascites, could be present.

'Caval Syndrome'
The first three classes of heartworm disease apply to signs associated with chronic heartworm disease. Class IV heartworm disease is associated with acute presentation of signs, normally associated with the presence of a large

numbers of worms obstructing blood flow through the tricuspid valve. Hemoglobinemia and pigmenturia are components of this syndrome. The onset is rapid and if not treated will result in death in 12-72 hours.

Animals presenting with caval syndrome are poor candidates for treatment by the traditional method. The treatment of choice is surgical removal. If possible, these animals should be referred to a specialist. If cost is an issue, which is very likely, you can perform the surgery yourself. Regardless of whether or these animals are referred, they will die without surgical intervention.

Diagnosis
Briefly, the method of choice is the antigen test, which tests for the presence of the heartworm female uterine antigen in the blood. This antigen can be detected as early as five months post-infection. There are a variety of tests on the market. Some recent tests claim to also detect antigen from male worms.

Prevention
Heartworm preventives, as a rule, are given monthly to kill the migrating stages of heartworm acquired during the previous month. They do not kill "forward." That is, the drugs do not work by killing infective L3s acquired after administration of the preventive. Most of these preventives, which are of the macrocyclic lactone drug class, either by themselves or when combined with another compound, are effective against certain intestinal parasites or flea life stages. One obvious exception to this is ProHeart 6, which is an injectable preventive that protects for six months.

Treatment
Immiticide is both the treatment of choice, and the only drug APPROVED for treatment of adult heartworm. The 3-injection protocol is recommended by the American Heartworm Society. This treatment will be detailed extensively in another lecture.

Heartworm treatment: making sense of it all
When Immiticide (melarsomine dihydrochloride) first came on the market in the mid-1990's, it was an immense improvement over the days of Carposolate. Caparsolate was injected intravenously, and while effective could have particularly nasty side effects, including skin sloughing. Early treatment protocols for Immiticide involved a 2-dose injection protocol that was quite straightforward. With advances in knowledge about heartworm, the treatment protocol for heartworm has become more complicated. In this lecture, we will cover the staging and treatment of heartworm in the context of these newer and continually evolving recommendations.

As a note, the majority of the information referenced in these proceedings can be located at www.heartwormsociety.org.

Diagnosis of heartworm
Obviously, one must diagnose heartworm before treating. While Immiticide is a safe drug, complications can result, and therefore no one should ever treat heartworm empirically. These diagnostics are absolutely essential to determining the class of heartworm disease. By determining the stage of heartworm disease, you will know whether the animal has improved after treatment, and more importantly, how much at risk the animal is for complications. The higher the class, the greater the risk. The classes are summarized below:

Class I (Mild)
These animals are normally asymptomatic or can have a mild cough. Otherwise, these animals are fine, and do not seem to be inhibited by the disease.

Class II (Moderate)
These animals will have a more moderate cough. Also, these animals could have difficulty breathing, and be somewhat exercise intolerant.

Class III (Severe)
These animals are dyspneic, and can be severely exercise intolerant. Syncope and hemoptysis may be present. Signs of right-sided congestive heart failure, such as ascites, will definitely be present.

Class IV (Caval Syndrome, life-threatening)
Class IV heartworm disease is associated with acute presentation of signs, normally associated with the presence of a large numbers of worms obstructing blood flow through tricuspid valve. Hemoglobinemia and pigmenturia are components of this syndrome. The onset is rapid and if not treated will result in death in 12-72 hours.

Tests and Procedures
The following is a list of tests and procedures for heartworm with a brief description of each:

1. History, physical exam: A history of exercise tolerance, and presentation with dyspnea or signs of congestive heart failure can be indicative of heartworm disease. Crackling or moist rales, and/or a split second heart sound may also be present.

2. Immunodiagnosis: The antigen test is considered the "gold standard" for heartworm diagnosis. There are many types available for in-clinic use. There are too many to cover everyone in detail.

There are some basics concerning antigen tests. As a rule, the tests are highly sensitive and specific for infections with adult female worms > 8 months of age, since older worms tend to produce more antigen. However, single sex infections of only males will not be detected. Also, it is extremely important to remember that tests DO NOT detect prepatent infections (< 5 mo. worms). A summary of the factors affecting the sensitivity of antigen tests is as follows:

1. Sex - only female worms are detected (by most tests)
2. Age of worms – more important than number in diagnosis
a. < 4 months old -- none detected
b. 5 months old -- some detected
c. 6 months old -- most detected
d. 7 months old -- practically all detected
e. > 8 months -- all are consistently detected
3. Number of worms (> 8 months)
    a. 1 female = 62 - 86%
    b. 2 females = 85 - 95%
    c. > 3 females = 93 - 99%

However, it is important to note that antigen tests are not "quantitative." The "color" of any test cannot be correlated to worm burden. Finally, antigen tests can be used to determine effectiveness of adulticidal treatment. If all the worms are killed, adult antigen should be cleared from the blood by 3 months after treatment.

3. Test for microfilaria (mf): Examination of the blood for mf was the definitive way to diagnose heartworm before the advent of the antigen test. Some practices still examine the blood for mf as the primary diagnostic method for heartworm. This is not a best practice, however.
When examining a drop of blood or "direct smear," one will only detect ~75% of patent infections. The ideal means to detect mf is to use a concentration technique, such as the Knott test or a filter test. One of these tests should be used after a positive antigen test, in order to determine the relative amount of mf.

Also, it is important to differentiate *D. immitis* from *Acanthocheilonema (Dipetalonema) reconditum*. This nonpathogenic worm lives in the subcutaneous tissue and is transmitted by fleas. Its mf are also in blood. The

major concern is that one would not want to treat an *A. reconditum*-positive dog for heartworm. This has become must less of a problem with the advent of antigen tests.

4. Radiography: This is an important part of staging the disease, as it allows one to assess the damage that has already occurred. Radiographic findings of heartworm will not be covered extensively in this lecture.

5. Echocardiography: Echocardiography is not a typical diagnostic method for heartworm. However, if one can visualize the heartworms via echocardiography, you may be able to infer their exact location and number.

6. CBC, Chemistry panel and Urinalysis: Liver and kidney function need to be assessed before administration of Immiticide. One needs to know what existing disease is present prior to treatment. Furthermore, the presence of heartworms in the vessels can cause hemolysis.

Treatment Considerations

Before we discuss the actual treatment regimen, it should be stated that pulmonary thromboembolism (PTE) and pulmonary damage are inevitable consequences of successful adulticide therapy. While no known tests are predictive for PTE, the severity can frequently be anticipated based on the stage of disease. Also, the more worms that are present, the more likely the risk of PTE.

The clinical signs of embolism include fever, cough, hemoptysis, and exacerbation of right heart failure. These are usually evident within 7-10 days, but may occur for up to 4 weeks post-treatment. For this reason, exercise restriction for four weeks post-treatment is essential. This part of treatment can be the most difficult to implement, but cage-rest (leash walk only) is as an important part of the regimen as the Immiticide injections.

The treatment protocol

The full treatment guidelines are available at http://www.heartwormsociety.org. What follows highlights some important components of heartworm treatment.

1. Melarsomine dihydrochloride (Immiticide)

The standard 2-dose regimen for Immiticide is 2 intramuscular injections give in the epaxial muscles, each at 2.5 mg/kg. This is still the labeled protocol; however, the alternate or 3-dose regimen is what is recommended by the American Heartworm Society. For the 3-dose protocol, 1 injection at 2.5 mg/kg is given, and then 1 month later, 2 more doses are administered 24 hr apart. The advantage of the 3-dose regimen is increased safety and efficacy. The obvious disadvantages are an additional month of exercise restriction, an increase in the total arsenical dose, and the additional cost of a third injection.

2. Macrocyclic lactones (ML)

It is now recommended that one should start a ML preventive (mainly ivermectin, which has been used in most studies) at the time of diagnosis, or up to 3 months prior to Immiticide treatment. The advantage of this is that further infection is prevented and developing larvae are damaged or eliminated. Furthermore, the administration of a ML, while delaying treatment also eliminates the "treatment/susceptibility" gap. By reducing the treatment gap, you eliminate worms <2 months of age, and allow maturation of 2-4 month old worms to the point to where they can be killed using Immiticide.

There is also evidence that ivermectin may reduce mass and health of existing heartworms. By reducing the mass of worms before killing them, you should be reducing the risk of PTE.

3. Steroids

Prednisone can be used. The dosage recommendations have been a bit "fluid." For the latest information, I would refer to the American Heartworm Society treatment guidelines.

4. Doxycycline

This antibiotic has become a very important drug in the treatment of heartworm, due to its activity against the bacterial endosymbiont, Wolbachia. There are some differing opinions as to when to administer it prior to adulticide treatment. What is agreed upon is the dose- 10 mg/kg BID PO, and the duration of administration- 4 weeks. Some people administer doxycycline the month prior to treatment, while others administer it immediately upon diagnosis (i.e. the first month of the 2 to 3 month treatment gap).

At the writing of these proceedings, doxycycline is in variable supply. Alternatives are being investigated.

Conclusion

Heartworm treatment recommendations are constantly changing. It is important to keep current on information, with the best source being the American Heartworm Society.

Heartworm preventives: a brave new world

Heartworm infection can be life threatening. As with many parasites, an ounce of prevention is worth a pound of cure. Due to the pathologic changes that occur due to heartworm infection, as well as the associated cost of treatment, prevention of heartworm is a necessity, not a luxury. Convincing clients of this necessity in the age of the internet, coupled with recent reports of lack of efficacy, has created challenges that were not present ten years ago. It truly has become a brave new world.

As a note, the majority of the information referenced in these proceedings can be located at http://www.heartwormsociety.org.

The life cycle:

Before we can discuss the challenges associated with heartworm prevention, we must first discuss how preventives function in relation to the life cycle.

The most logical place to start is with the adult worms, which live in the pulmonary arteries and heart. Adults can live up to 5-7 years in dogs. During this time, adults will mate and produce microfilariae, which circulate in the blood. The microfilariae are then ingested by a mosquito intermediate host. The mosquito is ABSOLUTELY REQUIRED for the heartworm to develop. Once inside the mosquito, the microfilaria migrate within the mosquito for an average period of approximately 14 days, during which time, the microfilariae develop to a first-stage larvae. After this, they molt twice to become an infectious third-stage larvae (L3), which at this point is in the head of the mosquito. The L3s are approximately one mm in length. Upon landing on a host, the mosquito will then take a bloodmeal. During feeding, the larvae will “bust out” of the proboscis. When the mosquito removes its stylet, the larvae then enters the host through the hole made by the stylet. This is in contrast to the commonly-held belief that the larvae are “injected” into the host.

Once inside the definitive host, the L3s follow a complicated migration pathway. The L3 remains in the vicinity of the sight of entrance for approximately 3-4 days. Also during this time, L3 undergoes a molt to the fourth-stage larvae (L4). This is normally completed by 4 days post-infection, but could not occur until day 12 post-infection. This is the most important part of the life cycle with regards to prevention. Heartworm preventives, as a rule, kill the migrating stages of heartworm acquired during the previous month. They do not kill “forward.” That is, the drugs do not work by killing infective L3s acquired after administration of the preventive.

It is generally agreed that the molt to the last stage, known as the juvenile adult, occurs by day 58. At day 70, the worms first arrive at their final location, the pulmonary artery. Most worms have reached this location by day 120. By day 180, worms are sexually mature and have begun to produce microfilariae, thus completing the life cycle. It is important to realize that while this is the generally accepted life cycle, there could be variations in these times.

A brief history of the evolution of heartworm preventives:
(Disclaimer: Mention or lack thereof of a particular product does not constitute bias on the author's part. At this point, it is almost impossible to mention every domestic small animal parasiticide on the market. Also, company names are mentioned as they are currently, not when the product was developed.)

Initially, heartworm preventives were administered daily and contained diethylcarbamazine (DEC). The most well-known of these was Filaribits®, which many of us still remember (although, there are more and more blank stares when I mention this drug to veterinary students). In the mid-1980's, preventives underwent a monumental change that has shifted the industry forever. This is when the first ivermectin-based monthly preventive was launched. A monthly preventive can kill migrating third and early fourth-stage larvae, thus giving it a distinct advantage over a daily dose of DEC, which is effective at a distinct point in the life cycle. With monthly prevention, owners had less "pills" to remember, and veterinarians no longer had to stock boxes and boxes of bottles containing daily preventives in their practice bathrooms and offices. The industry has not looked back, since the advent of the monthly preventive.

Ivermectin is in the macrocyclic lactone class of drugs. Macrocyclic lactone drugs contain all currently labeled heartworm preventives. These drugs are administered monthly with one exception discussed below. Ivermectin is normally combined with pyrantel. This combination of ivermectin and pyrantel was the start of another important shift in the industry: the combination product. Now with ivermectin and pyrantel, one could "prevent" heartworm, as well as treat and control certain intestinal parasites, specifically hookworm and roundworm.

Next on the market was milbemycin oxime. Milbemycin oxime had an advantage over the ivermectin/pyrantel-based drugs in that it was also labeled for whipworms. Milbemycin oxime would later be combined with the flea preventive lufenuron.

Next to market was selamectin in a topical formulation, which was unique at the time because it was a topical versus oral heartworm preventive. While anecdotally, most clients prefer to give their dog a pill, some do prefer administering drugs topically. Also, a topical formulation provided cat owners a much easier route to administer a heartworm/intestinal preventive to their pet.

Another topical, containing moxidectin would come to market, thereafter. Topical moxidectin was combined with the flea preventive, imidacloprid. This formulation like milbemycin will treat and control whipworm.

Finally, quite a few years ago, a combination of milbemycin oxime and spinosid, a flea adulticide, hit the market.

But wait, you forgot one…
The 6-month injectable moxidectin formulation is back on the market, and is deemed safe by the FDA. This formulation offers the non-compliant client a means to protect their pet from heartworm for 6 months. It also requires very little inventory space on your shelf when compared to its monthly competitors.

A brave new world…
There are many perceived problems surrounding monthly parasite prevention. I cannot begin to detail every one. However, I have listed the most important and pressing issues.

1. Internet Pharmacies: This debate could and has dominated hour-long roundtable discussions. As cost has become more of an issue in the eyes of the client, they have turned to these "cheaper" sources. Another problem, product diversion, allows these pharmacies to thrive. The "grey" market, which buys products from veterinarians, and then sells them to these pharmacies, is the central culprit.

2. "I read on the internet…": Clients increasingly turn to the internet in order to obtain veterinary advice. While some sites are reputable, many are not. Unfortunately, clients cannot always tell the difference. This could lead to use of internet pharmacies and unproven herbal remedies.

3. Cost: With more limited income, clients have to make tough choices between preventives and other necessities.

4. Lack of efficacy cases: Reports of suspected lack of efficacies, which cannot be attributed to non-compliance or a failure to administer preventives correctly, has raised doubts among both clients and veterinarians about these products.

5. Not communicating the value of prevention to the client: As veterinarians, we need to send a consistent message of compliance starting with the front desk, then the technician, and finally the veterinarian. We need to emphasize not only the importance of prevention, but the importance of the veterinarian's role in tailoring a parasite prevention program to the individual client. The internet will never be able to accomplish this task.

While there are many new challenges ahead of the profession with regards to parasite prevention, I believe that we can address these issues by emphasizing the value of these products to the client, and more importantly their pet.

Cats Get Worms, Too: Intestinal Parasites in Cats

Andrew R. Moorhead, DVM, MS, Ph.D., Dip. ACVM

In my experience, when people think about intestinal parasites in cats, they tend to think about protozoal diseases, specifically coccidiosis, or tapeworms. Now granted, tapeworms are intestinal parasites, but there are two other important parasites in cats that tend to be overlooked.

While in dogs, people commonly encounter the "unholy trinity" of roundworm, hookworm and whipworm, people forget about these three parasites in cats. Arguably, whipworm is rare in cats, and it is understandable as to why people forget about this parasite. Hookworm and roundworm are another story completely. We will focus on these two parasites. Excellent information about these 2 parasites can be found at the following website: http://www.capcvet.org/.

Roundworm

Roundworm is the common name for the feline ascarid, *Toxocara cati*. It is common in cats, and affects all ages of cats, as compared to *T. canis*, which primarily affects puppies. There is no documented evidence of age-related immunity. Treatment is relatively straightforward. As with other parasites, by understanding the life cycle, we can understand how to treat and prevent transmission of the parasite. As with all parasites, it is easiest to start our discussion with the adult worm. Adult *T. cati* can be easily seen, as they are 3 inches in length, and has prominent arrowhead-shaped cervical alae. It is important to be able to identify the adults, since clients will often bring the worm that they found in either their cat's vomit or feces. The adults, which are separate sexes, will mate in the intestine. The female will then produce literally thousands of eggs per day, which are shed into the environment in the feces. These eggs are shed unembryonated, and are not immediately infective. Depending on temperature, eggs will be infective 2 to 4 weeks after being excreted into the environment. At this point, they contain the infective third-stage larvae (L3).

The eggs are EXTREMELY resistant to disinfectants and environmental changes. What makes their presence even more insidious is that the eggs have a sticky outer coating, which makes them very difficult to remove from surfaces, including concrete. Eggs can survive for years, although extreme heat and prolonged exposure to sunlight will kill the larvae. Because of the resilience of eggs in the environment, humans, particularly children can ingest these eggs. Once ingested by a suitable host, whether it is a definitive felid host or accidental human host, these eggs will hatch and the larvae will be released into the intestine.

Upon entering the intestine, the larvae will penetrate the intestine, and travel via the blood to the liver, after which the larvae will travel to the lungs. Once in the lungs, the larvae will literally burst out of the alveoli. The larvae then ascends the trachea in what is known as "tracheal migration." After ascending the trachea, the larvae are swallowed, and travel to the intestine where they will mature to adults.

In paratenic hosts, including humans, the larvae will reenter the alveolar blood vessels and travel to the muscles or organs, where they will arrest. This is known as somatic migration, and is the migration path that occurs in humans, and results in the condition known as larva migrans.

Larva migrans is typically associated with the eye (ocular larva migrans), or viscera (visceral larva migrans). As mentioned above this disease occurs primarily in children, as a result of their propensity to eat dirt, which can potentially contain infectious eggs. The easiest way to prevent this horrible disease is to deworm cats regularly before the worms mature. If the worms are not adults then they cannot produce eggs.

One cannot pick up cat feces regularly, if the cat lives partially or completely outdoors. So to prevent contamination, attempt to keep cats out of gardens and sandboxes, even though this can be a difficult endeavor. For many years, it was taught that *T. cati* underwent transmammary transmission. However, recent data suggests

that this may not be the case. What we do know is that cats can become infected by ingesting infective eggs, or alternatively paratenic hosts. As a reminder, paratenic hosts are transport hosts, which is defined as a host in which larvae migrate, but no development occurs. Since adult cats hunt, they can become infected from ingesting *T. cati* larvae that are encysted in rodent paratenic hosts. With that being said, another way to prevent *T. cati* infection is to prevent cats from hunting. Prevention of transmission of *T. cati* to other cats and humans can be accomplished by periodic deworming of cats, or maintaining the cats on monthly heartworm preventive.

Hookworm

Cats can become infected with two hookworms of significance, *Ancylostoma tubaeforme*, and *A. braziliense*, which can also infect dogs. As with roundworms, adults live in the intestines where they mate and produce eggs. They are roughly the diameter of a penny, and literally are shaped like a "hook." Like roundworms, they produce a large number of eggs. The eggs are shed into the environment where they will develop and hatch in a period of 2 or so days. At this point the larvae are L1s, and will molt to the infectious L3s during the next week (or in other words, up to 8 days after being shed). The L3s can then infect the host either through ingestion or skin penetration.

Ancylostoma tubaeforme

Ancylostoma tubaeforme is uncommon as compared to *A. caninum* in dogs, and seems to be more common in young animals. Infection is by ingestion or skin penetration. No transplacental or transmammary infection occurs. It is also suspected that paratenic hosts play an important epidemiologic role in infection. *Ancylostoma tubaeforme* is considered less pathogenic than *A. caninum.* Cats infected with a low worm burden may be asymptomatic, however, heavy infections can result in clinical disease, especially in kittens.

Ancylostoma brazilense

Ancylostoma brazilense infects cats and dogs and is much less common than other hookworms. It is found in more tropical climates. Infection is primarily by skin penetration, whereas ingestion from the environment is much less common. *Ancylostoma brazilense* is not highly pathogenic. The reason it is important is it is considered to be the primary cause of cutaneous larva migrans in humans. With that being said, the other hookworms can also cause cutaneous larva migrans.

Prevention

With dogs, you can prevent transmission by picking up feces after defecation. This is obviously much more difficult with cats. Keeping cats indoors would prevent contamination of the environment, but this is not feasible for many pet owners. Depending on which recommendations you read, you can deworm kittens starting at 2 or 3 weeks. As with dogs, deworming cats every two weeks until 10 to 12 weeks of age is recommended. Finally, depending on the life style of the pet and owner, monthly administration of a heartworm preventive is recommended.

Fecal Diagnostic Testing: Why It Still Matters

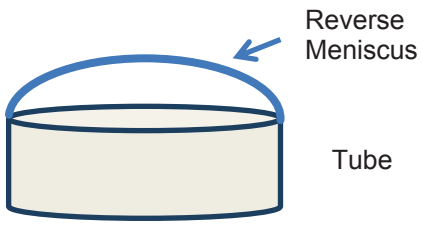
Andrew R. Moorhead, DVM, MS, Ph.D., Dip. ACVM

It is human nature to want to play with the newest and greatest "toys." As the science of veterinary medicine has advanced, we, as veterinarians, have tended to follow the trend of newer is better. However, there is one very basic, tried and true, diagnostic procedure that is in my opinion is still better than any new technology, and that is the fecal float. The float is the "bread and butter" diagnostic technique for diagnosis of intestinal parasites. For this reason it is important to understand how a float works, and in what situations it should be utilized.
As a disclaimer, these proceedings are not meant to be an all-inclusive summary of how to do a fecal, but rather to serve as an adjunct to previously published procedures that are detailed in Georgis' Parasitology for Veterinarians (9th ed.) by Dwight D. Bowman.

First, there are four main fecal diagnostic techniques: the fecal float, the direct, sedimentation and the Baermann. The fecal float is the most widely used of these techniques and therefore, is the technique on which we will focus our attention. Fecal floats are not all created equal. There are different solutions, as well as the debate as whether to perform a passive float or to use a centrifuge. However, there are some basics that should be common to all techniques, regardless of which method or solution that you choose.

1) More is better:
The basis of the fecal float is that we can isolate or concentrate the eggs in order to diagnose an infection. It would follow that the more material or feces with which you begin, the more likely that you will be able to detect eggs, or oocysts. Now, literally, insert the fecal loop. While this is an excellent device for obtaining feces from a dog or cat, it will rarely provide enough feces. The Companion Animal Parasite Council (CAPC) recommends that you obtain at least one gram (preferably 2-3) of feces to perform a fecal float. The easiest way is to ask the owner to bring the feces to the appointment with them. However, if that does not happen, obviously, you have to make do with what feces you can obtain.

2) Filter, Filter, Filter:
It is generally recommended that you mix the feces with ~10 ml of your solution of choice. This amount of fluid can be varied. The main point is that you mix and break up the feces, in order to try to equally distribute any parasite eggs or ova through the solution. After mixing, the solution is then poured into the appropriate container through cheesecloth, in order to remove any remaining large particle matter. The solution is then poured into a "cup" or centrifuge tube depending on whether you are performing a passive or centrifugal float. After you pour the solution into the tube, there should be a reverse meniscus as shown below:

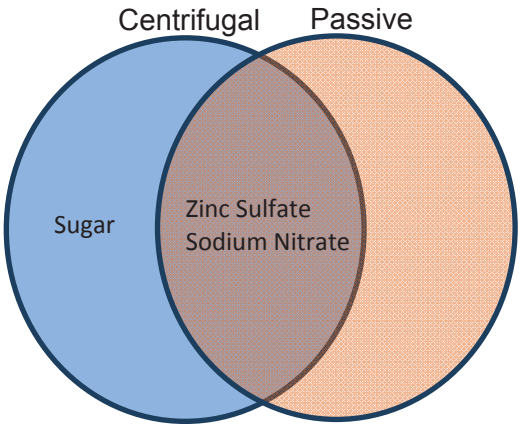


3) Quicker is not always better…
More often than not, flotations are much shorter than the desired time. You need time for the solution to do its job, so to speak. Passive floats should sit for 15 minutes, while centrifugal floats should spin for 10 minutes. If you take less time, you may have gotten clients out the door quicker, but could have made a diagnosis of "No parasites seen," when there were actually parasites present.

Is there only one right way?
CAPC, as well as most veterinary parasitologists, recommend that the best method for performing fecal flotation

is the centrifugal float, using a sucrose-based solution. This procedure is by far the most sensitive, and you will be much more likely to diagnose infections using this method. However, while this is the preferred method (the data supports this), there is more than one way to perform a fecal. The two big areas of debate are passive versus centrifugal float, and the type of solution to use. Not all solutions can be used with both methods:

This is summarized below in Figure 1:



Types of solutions:
Let's start our discussion with the different types of solutions that can be used for flotation. The float is based on the physical property of specific gravity, which we normally think about in terms of urine and an annoying concept in chemistry. Basically, if the specific gravity of an object, such as an egg, is less than that of the solution, the egg will 'float.' The higher the specific gravity or 'heavier' the solution, the 'heavier' an egg or ova that can be floated.

All solutions are not created equal. There are two basic types of solutions: salt and sugar. Each has its own pros and cons. Sugar is considered the best choice because of the relatively higher specific gravity, which means the solution can "float" the heaviest eggs. The three salt solutions that are used are: zinc sulfate, sodium nitrate, and sodium chloride. As zinc sulfate and sodium nitrate are used most commonly, we will focus our discussion on these.

Sugar or Sucrose (aka Sheather's sugar solution): Each solution has its pros and cons. Sugar is considered the best solution because it can float the "heaviest" eggs, including whipworm (*Trichuris vulpis*) eggs, which can be difficult to diagnose. In other words, sugar provides the most sensitivity. If the sugar solution has a high enough specific gravity then sometimes heavier eggs, such as spirurid, fluke, and tapeworm eggs can be floated. If not using a sugar solution, then one would have to use the sedimentation technique, in order to diagnose these eggs.

Another pro of sugar solution is that it is relatively easy and cheap to make. Finally, sugar does not crystallize quickly, thus allowing you some time to read the slides. The cons of sugar include that *Giardia* cysts will become distorted in sugar solution, and, of course, that it is 'sticky.'

To make a sugar solution use the following steps:
Materials:
454 g granulated sugar (1 1b)
355 ml tap water (12 oz or 1 ½ cups)
6 ml full-strength (37%) formaldehyde (this is added to prevent mold growth).

Procedure:
1. Heat water to near boiling.
2. Add the granulated sugar, and stir until the sugar is dissolved.

3. Allow the mixture to cool to room temperature, and then add the formaldehyde.
4. Check the solution's specific gravity, and adjust it to 1.27 by adding water or sugar.

As a note, if you do not wish to add the formaldehyde, which prevents mold growth, you can store the solution in the refrigerator.

Salt solutions: There are a number of advantages with salt solutions. One is that they are significantly less 'messy,' than sugar solutions, and as indicated above, they can be used for both passive and centrifugal floats. Also, salt solutions are less likely to distort *Giardia* cysts. In the case of zinc sulfate, the solution can be easily made by dissolving 350 grams of zinc sulfate in 1000 ml of water, and then adjusting the specific gravity to 1.18. Also, Sodium Nitrate (aka Fecasol) can be purchased, and can have a range of specific gravities (1.18 to 1.30). The con of both of these solutions is that they are relatively more expensive than sugar. Also, they will both crystallize quicker than sugar, with zinc sulfate crystallizing quicker than sodium nitrate. You will need to check the specific gravity of salt solutions regularly, especially zinc sulfate. What you will notice is that over time crystals will form in the bottom of the plastic jug. Since the salt is no longer in solution, this means that you are basically performing fecal floats with water. You will get a lot of "negative" results, but not because you have great compliance from your clients. The final, and in my opinion the most important, 'con' is that due to the lower specific gravity of solutions, you will not be able to detect heavier eggs.

For your reference, listed below are the specific gravities of some common eggs and solutions:

Solution	specific gravity		Parasite	specific gravity
Sodium nitrate	1.18-1.20		*Toxocara canis*	1.09
Zinc sulfate	1.18-1.20		*Toxocara cati*	1.1
Sucrose	1.25-1.27		*Ancylostoma* spp.	1.06
Sodium chloride	1.18-1.20		*Trichuris vulpis*	1.15
			Taeniid-type ova	1.23
			Physaloptera spp.	1.24

Passive (or simple) versus centrifugation:
The debate about passive versus centrifugal floats is directly related to the debate about solutions. As stated above, sugar floats can only be performed with centrifuges. Thus, the same criticisms of sugar floats apply to centrifugal floats. Additionally, I hear from both current veterinarians and veterinary students that centrifugal floats take too much 'time.' Where one can set up multiple passive floats in an almost assembly line manner, you have to wait the required 10 minutes for the centrifuge to finish spinning another sample. You can, however, spin 6 samples at once. This inconvenience is more than outweighed by the increased sensitivity of the centrifugal float method. Remember, with the centrifuge you are not only floating "lighter" eggs in a "heavier" solution, but you are also applying centrifugal force. If you do not want to use sugar, remember you can still use zinc sulfate or sodium nitrate for a centrifugal float.

For centrifugation, there are 2 types of centrifuges that may have to use: the swinging bucket and the fixed-angle. The procedures for both are listed below:

Swinging bucket method:
1. Mix the feces and solution of choice.
2. Pour through cheesecloth or strainer into a centrifuge tube.
3. Place tube into a holder.
4. Add enough solution to form a reverse meniscus. Place into centrifuge.
5. Place a cover slip on top of the tube. Make sure that the coverslip is firmly "seated" on top of the tube.

6. Spin at 1,200 to 1,500 rpm for 10 minutes.
7. Place the coverslip on a slide and examine at x100 magnification (the x10 objective).

Fixed-angle centrifuge method:
1. Mix the feces and solution of choice.
2. Pour through cheesecloth or strainer into a centrifuge tube to within ½ to 1 inch from the top.
3. Place into centrifuge.
4. Spin at 1,200 to 1,500 rpm for 5 minutes.
5. Place tube into a holder.
6. Add enough solution to form a reverse meniscus.
7. Place a cover slip on top of the tube. Make sure that the coverslip is firmly "seated" on top of the tube.
8. Let stand for 10 minutes.
9. Place the coverslip on a slide and examine at x100 magnification (the x10 objective).

Both these methods work quite well, and I would encourage people to adopt the centrifugal float in their practice.

A few final notes on other fecal diagnostic procedures:
1) Direct smears: These should be the exception, not the rule, unless the other procedures are cost-prohibitive. The preferred method for identification of *Giardia* spp. trophozoites.
2) Sedimentation: This procedure should be done when you suspect a parasite infection (i.e. fluke eggs), where the eggs could be difficult to float using normal methods.
3) Baermann: In small animal practice, this method is used to diagnose the feline lungworm, *Aelurostrongylus abstrusus*.

In conclusion, the fecal float has stood the test of time as a diagnostic technique. It will most likely be used in veterinary practices for decades to come, which is exactly why everyone should learn to perform the technique correctly.

The Small Animal Parasites That You Want to Forget, But Should Not

Andrew R. Moorhead, DVM, MS, Ph.D., Dip. ACVM

Many people remember the common small animal parasites: heartworm, roundworm, flea tapeworm, and *Giardia* spp., just to name a few. However, there are other important parasites that are not as common. We learned about them in order to pass a test and then thought, "I can forget these, because I will not see them in practice." You may not diagnose the following parasites frequently, but you will encounter them often enough that you should keep them in the back of your mind. Treatment regimens for these parasites are based on what has been attempted and what worked. The list below is not all inclusive, and has been compiled from multiple years of lecture notes, and interaction with clinicians.

Physaloptera spp. aka "Stomach worm"

This parasite has a sporadic distribution and prevalence, and as its name implies, lives in the stomach of the definitive host. Transmission is via ingestion of arthropod intermediate host or a mammalian paratenic host. The worms have a "spiky" cuticular collar that when attached to gastric mucosa can cause local gastric irritation and bleeding. Secondary to the gastric irritation, acute or chronic vomiting can occur. Also, the worms may cause anorexia, melena, and anemia, secondary to the bleeding.

Diagnosis is normally made when a worm (normally an adult) is found in the vomit. *Physaloptera* spp. are the diameter of *Toxocara* spp., but shorter in length. As stated above, there is a collar on the anterior end of the worm, and caudal alae on posterior end of male. While not ideal, diagnosis of infection is sometimes made on endoscopy. Diagnosis by fecal flotation is possible, however, eggs can be difficult to detect, since they are 'heavier.' Alternatively, one can use a sedimentation technique.

The following regimens have been used for treatment:

-Fenbendazole (Panacur) - 50 mg/kg PO x 3d
-Pyrantel (Strongid) - 5-10 mg/kg PO
-Ivermectin - 0.2 mg/kg PO or SC

Capillarids

This is the class of parasites that people remember as "the other eggs that look like whipworm eggs." They live in the urinary or respiratory tract of the definitive host.

Pearsonema spp.- the Urinary Capillarids

Pearsonema plica can infect dogs and cats, whereas *P. feliscati* seems to be specific to cats. Adults embed in the urinary bladder mucosa, and shed unembryonated eggs. The life cycle most likely involves an earthworm intermediate host (IH). Infection is usually asymptomatic, although cystitis can occur due to a large number of worms embedded in the bladder mucosa. These animals will present with hematuria, and will attempt to urinate frequently. Observing eggs upon examination of urine sediment is definitively diagnostic.

Eucoleus spp.- the Respiratory Capillarids

Adult worms are embedded in the nasal or respiratory mucosa, and depending on the species can be found in both dogs and cats.

Eucoleus aerophilus is found in foxes, dogs, and cats. Adult nematodes live in the mucosa of the trachea, bronchi, and bronchioles. Eggs are produced, coughed up in sputum, swallowed and excreted in the feces. Infection results upon ingestion of infective eggs or potentially an earthworm paratenic/intermediate host. Larvae hatch in the small intestine and then migrate via blood to the lungs, where they penetrate the alveoli and migrate into the air passages. The prepatent time is 3 to 5 wks. As with the urinary capillarids, infection is normally asymptomatic. An occasional to chronic cough and wheezing may be noted. In severe cases, the animal may

present with tracheobronchitis, dyspnea, and pneumonia. Definitive diagnosis is made by detecting eggs in fecal flotation, sputum, or a trans-tracheal wash. Eggs are greenish brown, rather asymmetrical, with a granular shell, bipolar plugs and single-cell embryo.

The following regimens have been used for treatment:

-Fenbendazole 50-100 mg/kg PO x 10d
-IVM 200ug/kg, may have to repeat

Eucoleus boehmi is the nasal capillarid of dogs. Adults live in the mucosa of the nasal turbinates and sinuses. The life cycle is unknown, but is hypothesized to be direct. Although, as with *E. aerophilus*, an earthworm may be involved with the life cycle. Eggs are passed in feces or in excess nasal mucous. Infection is usually asymptomatic. The presence of worms and eggs can result in inflammation, which can then cause sneezing and mucopurulent nasal discharge. Definitive diagnosis is made by observing eggs on a smear of nasal discharge or on fecal flotation. The eggs can be difficult to recover by nasal swabs. The eggs are symmetrical and golden with bipolar plugs. The surface of the egg is pitted, and has a "thimble" pattern. The eggs are passed in partial stage of embryonation. Fenbendazole and ivermectin are used for treatment.

Aelurostrongylus abstrusus

Never forget about *A. abstrusus* as a differential diagnosis in a coughing cat, at least in the southeast US. Adult worms live in the terminal bronchioles, and alveolar ducts. The lifespan of the worms is about 9 months. Eggs are deposited in clusters in the lung. The larvae inside the eggs will hatch and travel up the trachea, after which they will be swallowed and enter the GI tract. First-stage larvae (L1) are shed in feces. A snail or slug will become infected with the L1, which will then develop to an infectious L3. The slug can then be consumed by a paratenic host. When a slug or paratenic host is ingested by a cat, the definitive host, the larvae will migrate from the GI tract to the lungs. In 5 to 6 weeks, the worms will develop to adults, thus completing the life cycle. Radiographic changes may be evident. In order to obtain a definitive diagnosis you may perform the Baermann technique, which is the most reliable diagnostic method, a sedimentation, or a centrifugal flotation. If the animal is infected with *A. abstrusus*, you will observe larvae with an S-shape kinked tail and sub-terminal dorsal spine. Larvae may also be detected in the sputum. Treatment includes fenbendazole at 50 mg/kg PO for 3d or 15d, or IVM at 0.2 mg/kg PO for 5d. Prednisone may also be used for symptomatic treatment.