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ABDOMINAL EXPLORE: EFFICIENT, THOROUGH, SAFE, & SECURE

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ENTERING THE ABDOMEN

- Clip & scrub the patient so you can incise from the *cranial* end of the xiphoid (where it attaches to the sternum) to the pubis if needed.
- Elevate the subcutaneous tissue (SQ) off the linea with Metzenbaum scissors (parallel to incision, open minimally and push); avoid lateral undermining.
- Tent the linea with Brown-Adson forceps and make a controlled stab incision with an inverted scalpel blade. Insert a finger and palpate for adhesions before extending the incision. The linea narrows as you go caudally. If incising alongside the xiphoid, stop before hitting the diaphragm.
- In male dog, clip the prepuce to the far side with a penetrating towel clamp. Starting 2-3cm cranial to the prepuce, deviate the skin and SQ incisions 2-3cms lateral to the prepuce on the near side. You'll also cut the preputial muscle and may need to ligate the preputial vessels and/or branches of the caudal superficial epigastric artery. Retract the prepuce and SQ to the far side so the linea can be incised along its entire length if needed. The linea narrows as you go caudally.
- Free the falciform ligament from one or both sides of the cranial part of the incision, ligating or cauterizing vessels as needed.

ABDOMINAL EXPLORE

There is no one right way to do an abdominal explore, but it is important to have a routine (Table 1). This ensures you do not miss anything and that you become very familiar with the normal so you can better recognize the abnormal. Develop a pattern that works for you and use it every time. A Balfour retractor will improve your access and visibility immensely.

Table 1. Example of Exploratory Laparotomy

Each of the following bolded structures should be assessed during your explore. The order here illustrates one logical way to move through the abdomen. 1. Falciform ligament 2. **Diaphragm** – retract the liver caudally (gently, with flat fingers) as needed to see the central tendon, muscular parts of the diaphragm, **hepatic veins**, and **esophageal hiatus** 3. Liver lobes a) From left to right: **left lateral, left medial, quadrate, right medial, right lateral, caudate process of the caudate lobe** (the latter two lobes may be seen better when using the mesoduodenum to expose the right gutter)

b) **Papillary process of the caudate lobe** – retract the stomach caudally and find this lobe cranial to the lesser curvature of the stomach and dorsal to the **lesser omentum**

4. Gallbladder, cystic duct, hepatic ducts, & common bile duct
   a) Gently squeeze the **gallbladder** (should be compressible; won't empty)
   b) Retract the gallbladder cranioventrally to see **cystic duct**
   c) Retract the duodenum caudally to better see the transition from the cystic duct to the **common bile duct**; the latter runs along the right edge of the lesser omentum before entering the duodenum. The **hepatic ducts**, the main tributaries from the liver lobes, join the common bile duct near its junction with the cystic duct.
5. **Stomach** - cardia, fundus, body, antrum, and pylorus; the **lesser omentum** attaches to the lesser curvature
6. **Duodenum**

(continued next page)

7. **RIGHT GUTTER:** The **mesoduodenum** is the most lateral mesentery on the right side. Retract the duodenum medially, and use the mesoduodenum to hold back all of the intestines from the right gutter (avoid fingers on the pancreas). Identify the following:
   a) Right lateral liver lobe
   b) **Caudate process of the caudate liver lobe** –cups the cranial pole of the right kidney
   c) **Right limb of pancreas** - in the mesoduodenum, dorsal and parallel to the duodenum
   d) **Portal vein** –in the mesoduodenum dorsal to the pancreas
   e) **Caudal vena cava** –at the dorsal attachment of the mesoduodenum, running parallel with the portal vein then disappearing dorsal to the liver
   f) **Right adrenal gland** –palpate it dorsal to the caudate process of caudate liver lobe
   g) **Epiploic foramen (EF) (**Figure 1**)** – hold the duodenum ventrally with your right hand, place your left forefinger on the mesoduodenum just dorsal to the portal vein, and slide your finger cranially. Bend your finger medially around the cranial edge of the mesoduodenum – you're now in the EF, entry into the omental bursa. The EF is bounded caudally by the mesoduodenum and celiac artery (feel pulse), ventrally by the portal vein and hepatic artery (pulse), and dorsally by the caudal vena cava. Here you can feel for enlarged lymph nodes in the omental bursa and perform the Pringle maneuver (hold off blood supply to liver by pinching off portal vein and hepatic artery on ventral border of EF).
   h) **Right kidney/a&v/ureter** – dorsal, often retroperitoneal; follow ureter to bladder
   i) Right reproductive tract
      i. Female: Ovary, uterine horn, broad ligament (mesovarium, mesometrium) with round ligament from ovary to inguinal canal
      ii. Male: testicular artery starts at aorta (just caudal to renal a.) and goes caudally to exit abdomen via inguinal canal; testicular vein travels with testicular a.
8. **Urinary bladder** – reflect the bladder ventrally, and identify:
   a) **Ureters** as they enter the dorsal trigone
   b) Female: the **uterine body/stump** between the bladder and descending colon
   c) Male: **ductus deferens** (DD) between the bladder and descending colon. Each DD enters the abdomen via the inguinal canal, wraps lateral to medial around the cranial side of the ipsilateral ureter, enters the prostate, and empties into the prostatic urethra. (The paired DDs look like a tiny uterus dorsal to the bladder). Locate a cryptorchid testicle by finding the DD dorsal to the bladder and following it to the testicle.
9. Palpate in the pelvic canal for the **urethra, vagina/prostate gland, rectum**, and **sublumbar lymph nodes** (latter are typically not palpable unless enlarged)
10. **Spleen** – elevate the spleen using flat fingers and assess

11. **Greater omentum** –superficial/ventral leaf attaches to greater curvature of the stomach, stretches caudally over the intestines with attachments to the spleen, and folds dorsally to form the deep/dorsal leaf, which stretches cranially to attach to left lobe of pancreas and dorsal body wall.
12. **Left limb of the pancreas** is in the craniodorsal aspect of the deep leaf of the greater omentum and can be seen in one of two ways:
    a) Reflect the spleen and greater omentum cranioventrally
    b) Open the **omental bursa** by gently tearing a window in an avascular area of the superficial leaf of the greater omentum between the stomach and spleen. The omental bursa is also a good place to look for enlarged **lymph nodes**.
13. **LEFT GUTTER:** The **mesocolon** is the most lateral mesentery on the left side. Retract the descending colon medially, and use the mesocolon to hold back all of the intestines from the left gutter. As on the right side, identify urinary and reproductive tracts. Unlike the right, the **left adrenal gland** is easily seen (phrenicoabdominal vein runs ventral to gland).
14. Run the **intestinal tract** from one end to the other, looking for and palpating for abnormalities. Look at the **mesenteric lymph nodes** in the root of the mesentery as well. The **duodenocolic ligament**, from distal duodenum to descending colon, limits exteriorization of the duodenal/jejunal junction, but can be cut if need be.

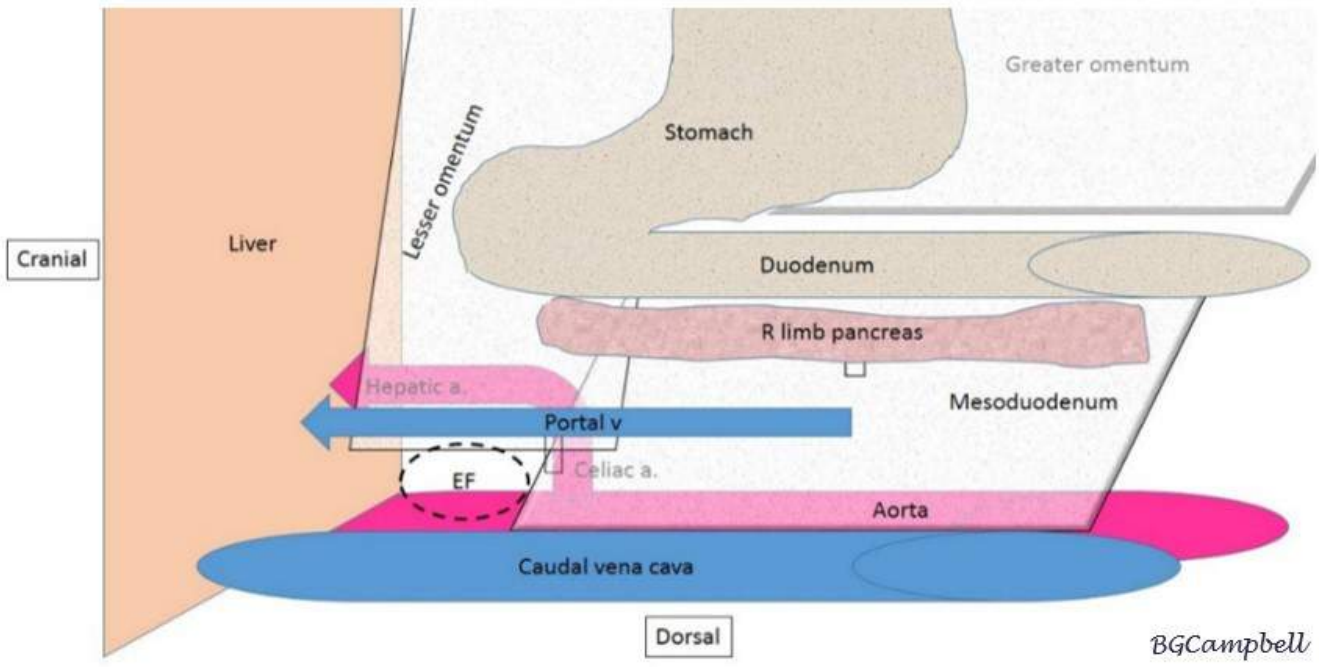

Figure 1. The position of the epiploic foramen (EF; dashed line) relative to other structures in the abdomen.

CLOSING THE ABDOMEN

- Change gloves & instruments if surgery involved sites with bacteria or tumor cells
- Lavage with warm sterile saline (no additives) to remove contaminants & blood clots (media for bacteria), warm patient, and find bleeders (see swirl of blood rising through saline). Suction out the lavage fluid (bacteria can swim, white blood cells can't, so bacteria can hide in fluid).
- Omentalize intra-abdominal surgery sites for pro-healing effects

- ***Close the linea***: Use an interrupted (4 throws/knot) or simple continuous pattern (6 throws/knot) of monofilament, absorbable suture such as polydioxanone – see Table for suture size

Patient weight	< 4.5 kg	4.5 – 17 kg	18 – 45 kg	> 45 kg
	< 10 lb	10-39 lb	40 – 100 lb	> 100 lb
Linea suture size	3-0	2-0	0	1

    - If the incision is off the linea, close the external rectus fascia. Do not include the rectus abdominus muscle, internal rectus sheath, or peritoneum.
- ***Close the SQ***: Typically use 2-0 or 3-0 absorbable suture in a modified Lembert or "quilting" pattern. Keeping bites small pushes SQ down to fill-in dead-space and allows skin edges to come together. Tacking to the external rectus fascia decreases seroma formation. Bury the knots on either end. May need two layers of SQ closure in thicker fat by prepuce or if obese.
- ***Close the skin***: Multiple options, typically with 3-0 or 4-0 suture. For intradermal, use monofilament, absorbable suture (avoid polydioxanone in the dermis as can cause suture reaction there). For the skin surface, use monofilament, nonabsorbable suture.

THE AMAZING OMENTUM: APPLICATIONS WITHIN THE ABDOMEN & BEYOND!

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Omental Anatomy, Physiology, and Superpowers

The omentum consists of a mesothelial membrane (2 cell layers thick) covering a connective tissue framework that contains scattered fibroblasts, fibrocytes, pericytes, and fat cells. Its rich vascular supply originates from the gastroepiploic and splenic arteries and drains into the portal system. It also has an extensive lymphatic system that drains into cranial abdominal lymph nodes. The mesothelial cells have a glycoprotein-polysaccharide coating that allows the omentum to easily slide over other abdominal organs. The superficial or ventral leaf of the greater omentum attaches to the greater curvature of the stomach and spleen. This leaf extends caudally and then folds dorsally on itself to become the deep or dorsal leaf, which attaches to the left lobe of the pancreas and dorsal body wall (see figure). The omental bursa is the potential space between the two leaves of the greater omentum. During an abdominal explore, a hole can be manually torn in an avascular area of the superficial leaf to allow assessment of the left lobe of the pancreas and cranial abdominal lymph nodes. The lesser omentum, a single sheet extending between the lesser curvature of the stomach and the liver, is much smaller and more anchored than the greater omentum.

Inflammation activates omental components in a number of ways. Lymphoreticular bodies are glomerular-like capillary structures in the omentum interconnected by lymphatic vessels. When exposed to inflammatory mediators, fenestrations open in the vasculature of the lymphoreticular bodies, allowing entry of fluid and particulate matter from the peritoneal cavity and stimulating the resident white blood cells into action. The extensive network of omental lymphatics provides a very large absorptive surface and effective peritoneal lymphatic drainage. Macrophages in the lymphoreticular bodies project microvilli into the peritoneal cavity, phagocytosing particulate matter and transferring antigens to omental lymphocytes for antibody production.

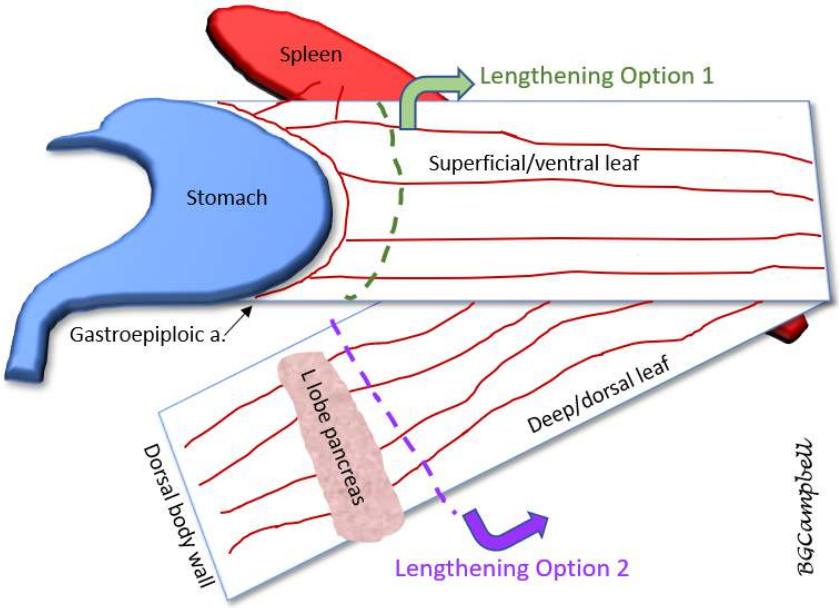
Omentum adheres to inflamed or ischemic tissues via activated fibrinogen. This adhesion seals off the diseased area from surrounding tissue and ensures direct access of omental healing factors to the inflamed region. The omentum aids in hemostasis by speeding the activation of prothrombin and by applying pressure via its adhesion. Angiogenic factors released by the omentum stimulate new vessels to cross from the omentum into the inflamed tissue within 6 hours of omental attachment, and omental neurotropic factors appear to stimulate reinnervation and may modulate pain.

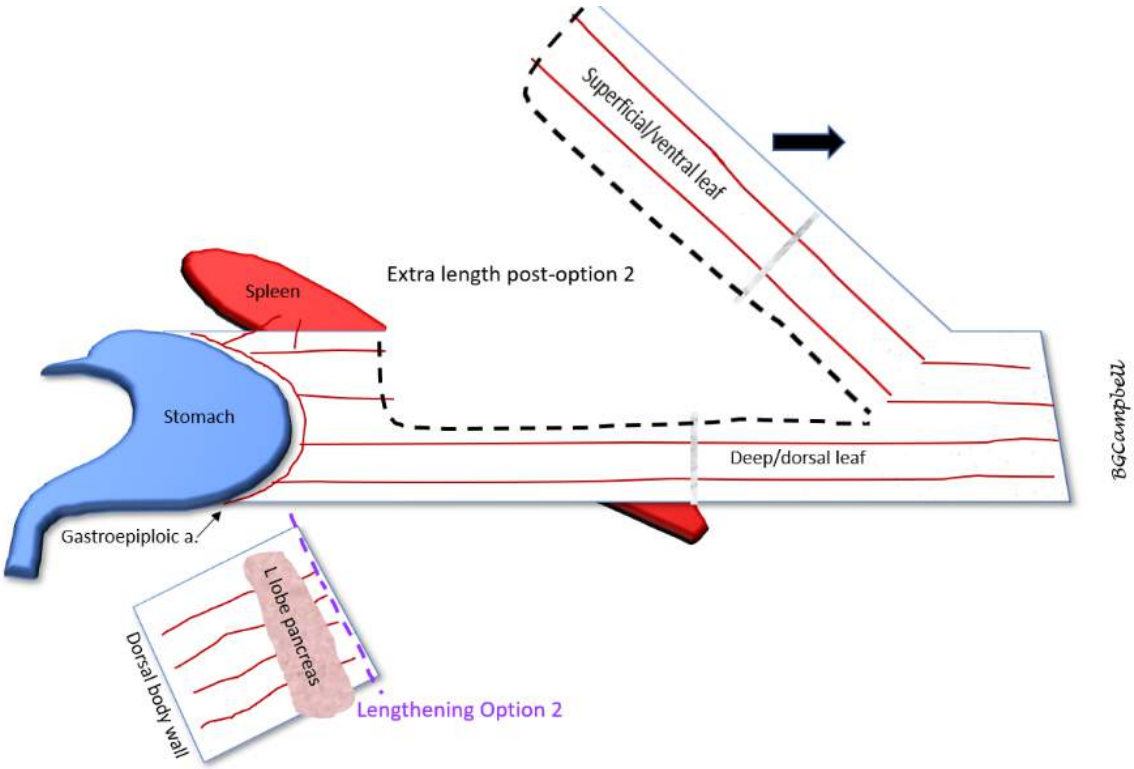
Omentalization and Omental Lengthening

Omentalization is the process by which the omentum is placed in a specific site by the surgeon. The omentum should always be kept moist and handled gently, with care taken to preserve its blood supply. The moldable nature of the omentum allows it to be placed in or around a variety of organs or defects, although it may be best to avoid 360 degree wrapping of a luminal organ out of concern for stricture. While the omentum readily adheres to sites of inflammation, it may also be sutured into place with 3-0 or 4-0 absorbable suture.

When needed, the omentum can be unfolded and extended to twice its normal length.

- **Option 1**: release superficial leaf from the greater omentum with electrocautery or vessel ligation/transection.
- **Option 2:** release deep leaf from left lobe of pancreas. If still more length is needed after option 2, an L-shaped incision is made in the extended omentum, with the short arm parallel to the greater curvature of the left side of the stomach and the long arm dividing the omentum in half for two-thirds of its extended length. When fully extended in this manner, the canine omentum can typically reach to the muzzle and to distal extremities.





Clinical Applications of the Omentum

The omentum should routinely be placed over sutured surgical sites in hollow organs such as the intestine or bladder. The omentum adheres to the incision site, which benefits from the omentum's hemostatic and angiogenic effects. The omentum also prevents leakage of luminal contents through small gaps in the incision and prevents peritonitis by dealing with local bacterial contamination. Overlay of omentum can also prevent adhesions from forming between the surgical site and other organs or the body wall. While the omentum often adheres to surgical sites with no help from the surgeon, deliberate omentalization ensures immediate and complete contact between the omentum and operated area.

When placed in an abscess, the omentum's extensive vascular and lymphatic networks absorb fluids (often precluding the need for drain placement) and actively fight infection. The abscess should first be debrided to the degree possible, lavaged, and then omentalized so that omentum is in good contact with the inner surface of the abscess. This technique has led to resolution of abscesses in the liver, prostate, uterine stump, and pancreas without the need for synthetic drains. Similarly, omentalization has been used to resolve various intra-abdominal cysts (liver, prostate, sublumbar lymph nodes, perinephric); the cyst is first deroofed and debulked to the degree possible, and then omentalized.

Omental use is not limited to the abdominal cavity. It can be passed through a hole in the diaphragm and spread out in the thorax or passed through a hole in the body wall and tunneled subcutaneously to the desired location. Care should be taken to make the hole large enough so omental vessels are not compressed, but small enough to prevent herniation of abdominal contents. For protection during subcutaneous tunneling to distant sites, the omentum can be temporarily placed in the lumen of a large, moistened Penrose drain. These extra-abdominal techniques have been used to treat chylothorax, reinforce sites of esophageal repair, support repaired thoracic wall defects, promote healing of difficult wounds, and support skin grafts. Free pieces of omentum placed around experimental nonunion fractures in dogs significantly enhanced fracture healing. In a prospective clinical study, radius and ulna fractures in small dogs healed faster (median 9 weeks with free pieces of omentum, 12 weeks with cancellous bone graft), with faster return to weight bearing and greater vascularity.

Pathology of the Omentum

Pathology of the omentum is uncommon. If a mass is found on abdominal ultrasound and does not seem to be connected to any organ, it may very well be in the omentum. Primary neoplasia of the omentum is rare. In dogs, hemangiosarcoma, as well as other metastatic tumors, may implant in the omentum. Gaps between omental mesothelial cells and lack of a basement membrane may make the omentum easier to infiltrate than other mesothelial surfaces in the abdomen, and the growth and angiogenic factors produced by macrophages in omental lymphoreticular bodies may stimulate tumor growth.

Omental infarction can cause acute abdominal pain and shock. In people, omental infarction is diagnosed with ultrasound or CT, and most cases resolve with medical management. Omental torsion is another cause acute abdominal pain. Be sure to examine the omentum in animals taken to surgery for acute abdomen; missing an omental infarction or torsion may explain some negative explores in these patients. If a concerning area of omentum is identified during surgery, it should be resected, cultured, and submitted for histopathology. Care should be taken to avoid damage to the left lobe of the pancreas in the deep leaf. The omentum can contain large abscesses; it has a remarkable ability to wall of the infection and protect the patient from sepsis. Surgical resection is the treatment of choice for omental abscess.

References available upon request

DIAPHRAGMATIC HERNIA: PERIOPERATIVE AND SURGICAL MANAGEMENT

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When abdominal organs move into the thorax through a diaphragmatic hernia (DH), they prevent full lung expansion and compress lung lobes, thus decreasing tidal volume and leading to ventilation-perfusion mismatch and hypoxia. Lungs become atelectic and pleural effusion may develop. Cardiac function is compromised by these hypoxic conditions as well as compression of the caudal vena cava and heart by the herniated organs. The most frequently herniated organs are small intestine, liver, stomach, and spleen, any of which can be compromised by compression of their blood supply due to herniation.

Clinical signs may include dyspnea, cyanosis, tachypnea, tachycardia, muffled heart and lung sounds, an 'empty' feeling abdomen, and abdominal or thoracic wall pain. Regurgitation or vomiting may occur secondary to entrapment of the stomach or intestines in the chest. Emergency care includes oxygen, analgesia, fluids, and, if pleural effusion or pneumothorax, thoracocentesis. Patients often find a body position (e.g., sitting upright) that decreases the pressure of abdominal organs on thoracic organs and should be allowed to stay in that position as much as possible.

Traumatic DH

The most common cause of traumatic DH are motor vehicle accidents (MVA). As the animal is hit, the combination of a sudden increase in intra-abdominal pressure and an open glottis increases the peritoneal-to-pleural pressure gradient, thus rupturing the diaphragm and propelling abdominal organs into the chest through the defect. Respiration can be further compromised by pulmonary contusions and a reluctance to fully expand the chest due to body wall. The pars costal muscles of the diaphragm (located ventrolaterally) are the most likely to tear. The tear may be radial (parallel to diaphragm muscle fibers, perpendicular to the body wall) or circumferential, with avulsion of the diaphragm off the body wall.

Thoracic radiographs are advised for any MVA victim, whether they are showing signs of DH or not. Approximately half of the patients with traumatic DH will also have other orthopedic and/or soft tissue injuries.

Chronic DH

Animals with lesser volume of herniated organs, or organs that readily slide in and out of the hernia, may not show clinical signs until weeks, months, or even years after injury, when adhesions and slow contraction of the hernia finally compromise organ function. Clinical signs of a chronic DH depend on the organs affected, but many present with only vague signs (e.g., anorexia, lethargy, weight loss). Thoracic radiographs may not show the DH; additional imaging modalities may be needed to get a diagnosis. A history of trauma, or old rib fractures seen on imaging, may increase suspicion for DH. The need for median sternotomy and resection of lung, liver, or intestine is higher for chronic than acute DH.

Congenital Pericardial Peritoneal Diaphragmatic Hernia (PPDH)

A congenital DH may involve herniation into the pleural space or directly into the pericardium (PPDH). Some PPDH patients are clearly compromised by the condition and require surgery. In others, PPDH is found

incidentally, often in an middle-aged to older animal being assessed for some other condition. Surgery is not typically done for non-clinical older animals as it is unlikely at that point in their life that the PPDH will become clinical. It is harder to know if surgery should be done in young non-clinical animals – they are good candidates for anesthesia and surgery at that time, there may be less adhesions to deal with, and repair now could prevent significant morbidity in the future. On the other hand, this could be an animal that would never become clinical, in which case surgery would be an unnecessary risk and expense. It is hard to gauge the percent who will stay non-clinical because we don't know how many animals have non-clinical PPDH. When surgery is done, survival rates are 90% or higher.

Imaging for DH

Thoracic radiograph may show loss of the diaphragmatic silhouette, visualization of abdominal organs such as gas-filled intestines, in the thorax, pulmonary contusions and rib fractures in trauma cases, and pleural effusion. If effusion interferes with interpretation, perform thoracocentesis, then repeat radiographs. PPDH often appears as a large globoid heart on radiographs. Abdominal radiographs may reveal cranial displacement of organs and absence of the diaphragmatic line. An experienced ultrasonographer can often diagnose a DH and obtain additional information about herniated organs. However, ultrasound can be misleading; e.g., pulmonary contusions can cause the lung to mimic the liver and suggest a DH that is not really there, or a DH may be missed if it is small without much going through it. Gastrointestinal contrast studies can be helpful if a part of the GI tract is in the chest. Positive contrast celiography is another option, but movement of contrast from abdomen to thorax may be blocked by herniated organs.

Timing of Surgery

While older papers suggested that dogs taken to surgery within 24 hours of trauma had significantly increased mortality, this has not been found in more recent studies. This is likely due to improved perioperative critical care and anesthetic management. Patients should be stabilized to the degree possible before surgery. DH patients are at risk of sudden decompensation, so they should be watched closely. Surgery is advised within 24 to 48 hrs of injury to decrease the risk of adhesions, permanent organ damage, and reexpansion pulmonary edema. Animals that have had prolonged, severe dyspnea can develop muscle fatigue and may need to be intubated and ventilated before they develop respiratory failure.

Emergency surgery is indicated when there is severe respiratory distress that does not respond to oxygen and thoracocentesis, gastrointestinal obstruction, or if the stomach is in the chest. Gas distension of the herniated stomach severely compromises ventilation. If possible, decompress the stomach with an orogastric tube or gastrocentesis to help the patient before surgery.

Anesthesia

Breathing is often easier for the dog in sternal than dorsal, so maintain this body position as long as possible during induction and surgical clip and scrub. Keep the dog's front end elevated throughout anesthesia and surgery to help decrease the pressure of herniated organs on the lungs. Pre-oxygenate before induction, then induce rapidly (e.g., propofol) so you can quickly gain control of ventilation. Avoid mask induction, which is stressful, takes longer, and is less predictable. As soon as the abdominal cavity is opened, air will move into the chest and create pneumothorax, so positive pressure ventilation must be started. Due to the risk of *reexpansion pulmonary edema* (see below), ventilation pressure should be no more than 20cmH_2O pressure and lungs should be allowed to reinflate on their own.

Start IV antibiotics at least 30 minutes before the incision and, if a time-dependent drug, repeated every 90 minutes during the procedure. Antibiotics can be stopped at the end of the procedure in most cases.

Surgical repair

Clip and scrub the patient to allow for ventral midline abdominal incision, median sternotomy, and paracostal incisions. Start with an incision from xiphoid to mid-way between the umbilicus and pubis. Place a Balfour retractor. Use flat fingers (avoid fingertip pressure points) to gently retract non-adhered organs back into the abdomen. Cotton-tipped applicators, right angle forceps, and electrocautery can be helpful. Make the hernial ring bigger if needed to improve visualization and access, taking care to not damage the caudal vena cava, hepatic veins, aorta, or esophagus that pass through it. Time your dissection with respirations to decrease the risk of damage to the lungs as they fill. Mature adhesions (more than 1-2 weeks old) may require resection of the tissue involved, such as liver, omentum, lung, or pericardium (watch for vagus and phrenic nerves). Extend the incision into a median sternotomy or paracostal approach if needed to safely reduce the herniated organs and repair the diaphragm.

Perform a full abdominal explore once organs are reduced. Carefully look for tissues that need to be resected because of damage from the initial trauma, or vascular compromise while herniated. Herniated liver lobes may be rotated 180^0 on their hilus, so that the normal caudal edge of the lobe is now cranial. With chronic hernias, the hepatic vessels may adapt to this position so much that replacing the liver lobe in its normal position compresses the blood supply. Liver lobectomy may be required in this case.

In most cases of traumatic hernia and PPDH, the sides of the defect can be sutured directly together with a simple continuous pattern of monofilament absorbable or nonabsorbable suture. The edges of the defect do not need to be trimmed not needed in acute cases; opinions vary as to whether to trim the edge of chronic hernias. Start the suture line at the dorsal-most aspect of the hernia, where it is hardest to reach. Suture the edges together so they are in good apposition, but do not overly tighten the suture as this can cause muscle necrosis and failure of the repair. If the defect is extensive or complex, place several simple interrupted sutures in key locations to properly line up the portions of the diaphragm before completing the remaining closure. If the diaphragm is avulsed off the thoracic wall, pass sutures around a rib to anchor it. If the diaphragm does not reach its normal location on the thoracic wall, it is okay to attached it to a more cranial site.

Patching techniques

If there is inadequate diaphragm to close the defect directly, patching options include:

- Greater omentum –make a scaffold of sutures spanning the defect, then suture omentum to the diaphragm and scaffold (see “The Amazing Omentum” talk for info on lengthening the omentum)
- Liver - suture liver lobe to diaphragmatic defect with mattress sutures
- Transverse abdominus muscle (TAM) flap – elevate a rectangle of TAM from the interior body wall, leaving it attached at the last rib, and suture the flap to the diaphragm. The peritoneum of the flap will be on the thoracic side. Make the flap 10% larger than the size of the defect. (Flaps have also been made from the latissimus dorsi and rectus abdominus muscles)
- Muscle fascia – close diaphragm with a piece of fascia lata from the hindlimb (requires extra surgery site that can be hard to access when abdomen is open)
- Synthetic mesh – strong, but can be a source of chronic inflammation and nidus for infection
- Multilaminate porcine small intestinal submucosa (good strength, contains growth factors, stimulates healing, replaced by host tissue within 90 days; omentalize after placing)

After closing the diaphragm, resolve the pneumothorax via by inserting an over the needle catheter though the diaphragm (remove needle after inserted), add a 3-way stopcock and syringe, and aspirate. Alternatively, place a red rubber catheter through the hernia just before it is fully closed, close the incision snugly around the catheter, add a 3-way stopcock and syringe, and aspirate. With either technique, do not apply more than ~2mL of force on the syringe, or you could damage lung. Some air may be left in the thorax to help prevent sudden re-expansion of the lungs.

Place the greater omentum over the diaphragm repair site to provide pro-healing, pro-angiogenic factors and decrease the risk of other organs adhering there.

Postop

Postop care includes IV fluids, analgesia, warming (patients can be very cold due to two body cavities being open during surgery), oxygen as needed, and close monitoring of vital signs. Residual pneumothorax is one of the most common complications. Be ready to perform thoracocentesis postop if the patient is dyspneic.

Reexpansion pulmonary edema (RPE) can occur when a collapsed lung (particularly if >72hrs) is reinflated. During the time of atelectasis, lung parenchyma becomes thicker and less flexible, resulting in damage to the microvasculature when reinflated. Fluid leaks into the interstitial space, causing pulmonary edema. Reinflation can also lead to air leaks and pneumothorax. Furthermore, the reintroduction of oxygen to the formerly hypoxic lung leads to the generation of superoxide radicals that can cause severe cell damage (reperfusion injury). The mainstay of RPE treatment is oxygen supplementation. Severely affected patients may need to be intubated and mechanically ventilated. RPE can be fatal. Decrease the risk of RPE by allowing lungs to slowly expand over time. It is common that the lungs will not be fully inflated at the end of surgery – do not suddenly force them open with aggressive ventilation.

Patients with chronic hernias may suffer from “loss of abdominal domain”, in which the volume of the abdominal cavity is smaller than normal because of the long-term absence of abdominal organs. If the abdominal organs don’t fit well, closure of the abdomen can cause a marked increase of intraabdominal pressure (IAP), compromising organ perfusion, decreasing venous return to the heart, and limiting ventilation. This condition can be fatal. IAP can be monitored via a urinary catheter in the bladder. Normal pressure is 5-10cm H2O. Treatment of high IAP may include good analgesia to relax the abdominal wall and evacuation of fluid or air from the abdominal cavity, bladder, or stomach. If the patient is not responding and IAP is over 20mmHg, surgery is indicated to first re-open the abdominal incision for immediate decompression, and then to increase the size of the abdominal cavity. Options include releasing incisions through the external rectus fascia on either side of midline and spanning the gap in the linea with mesh or porcine small intestinal mucosa (PSIS; preferred over mesh by author).

Prognosis

Survival rates for surgically treated DH patients are ~80-90%. Factors associated with a poorer prognosis include perioperative oxygen-dependence, concurrent soft tissue and orthopedic injuries, longer anesthesia and surgery times, postoperative pneumothorax, and pulmonary edema.

References available upon request

GASTRIC DILATATION AND VOLVULUS (GDV): PERIOPERATIVE & SURGICAL MANAGEMENT

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Pathophysiology of GDV

Gastric dilatation and volvulus (GDV) can adversely affect multiple body systems (Fig. 1). The large, dilated stomach restricts movement of the diaphragm, which limits lung expansion and results in generalized hypoxia. The dilated stomach also compresses the caudal vena cava and portal vein, decreasing venous return to the heart and causing an effective hypovolemia. The resulting decrease in cardiac output leads to systemic hypotension, poor tissue perfusion, and worsening of the generalized hypoxia. Hypoxia of the heart itself further compromises cardiac function, creating a viscous cycle of worsening cardiovascular status. Portal vein compression by the stomach leads to venous congestion in abdominal organs, making them more difficult to perfuse. The stomach wall is compromised both by the generalized hypoxia and because its local blood supply is compressed by the dilation. Gastric necrosis can lead to endotoxin absorption and bacterial translocation into the bloodstream, as well as gastric perforation. These accumulated effects on multiple body systems can cause multi-organ failure, disseminated intravascular coagulopathy, and systemic inflammatory response syndrome, and ultimately be fatal.

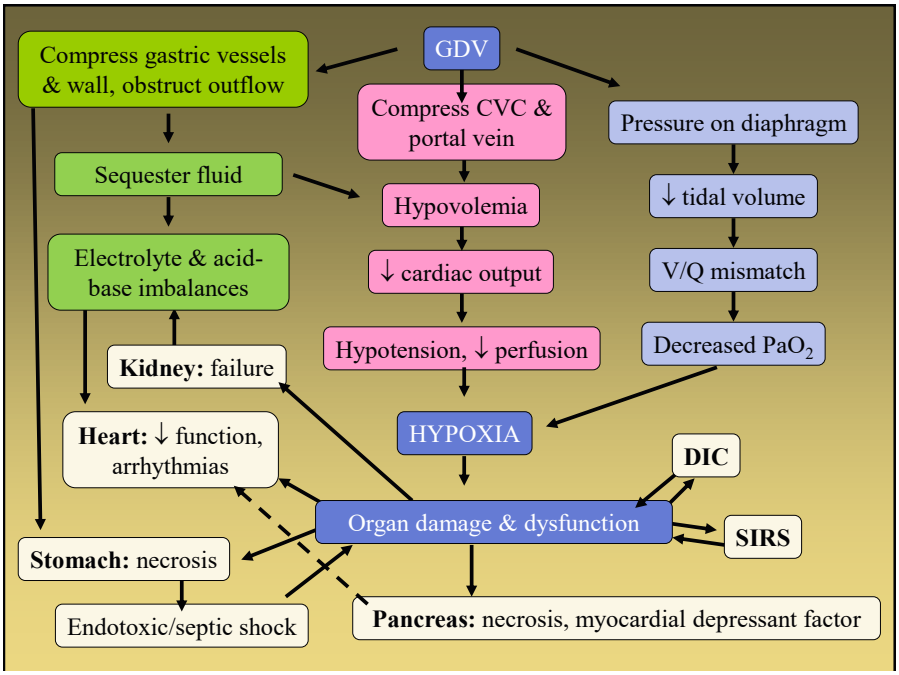

Figure 1: GDV pathophysiology flowchart. GDV sets off a series of events that lead to generalized hypoxia and subsequent organ damage and dysfunction. Abbreviations: CVC – caudal vena cava, DIC – disseminated intravascular coagulation, GDV - gastric dilatation and volvulus , PaO_2 – partial pressure of arterial oxygen, V/Q – ventilation/perfusion, SIRS – systemic inflammatory response syndrome.

History and Physical Examination

GDV most commonly occurs in middle-age to older, large or giant breed, deep-chested dogs. Most dogs present with a recent (within hours) onset of restlessness, depression, non-productive retching, hypersalivation, and/or abdominal distension. Abdominal discomfort ranges from mild to severe. Rapid, shallow breaths are an attempt to compensate for compression of the diaphragm, while elevated heart rate is an attempt to compensate for hypovolemia and hypoperfusion. Clinical signs can rapidly progress to shock.

Pre-Operative Treatment of the GDV Patient

The top two priorities for a patient suspected to have GDV are:

- #1: fluids – to correct hypovolemia and improve perfusion
- #1: gastric decompression – to relieve pressure on the diaphragm, caudal vena cava, portal vein, and stomach wall

Both are labeled #1 as both should be done as soon as possible (Fig. 3)! Coordinate your team so that someone is putting in a catheter and starting fluids while someone else is setting up and passing the orogastric tube. Keep the dog in sternal as much as possible to decrease compression of the caudal vena cava by the stomach.

Deliver fluids through one or two large (e.g., 18g) catheters in veins that are cranial to the heart (cephalic and/or jugular), since the dilated stomach blocks venous return from the caudal half of the dog. Start isotonic crystalloid fluids (e.g., lactated Ringer's solution) 22.5mL/kg IV (=1/4 shock dose), continuously reassessing the patient's response.

A large bore orogastric tube is the most effective way to decompress the stomach, which often contains thick frothy fluid and food as well as gas. Sedation (e.g., opioid +/-benzodiazepine) may be required. Mark a tube length equal to the distance from the dog's nose to last rib and lubricate it well. Place a roll of tape between the patient's incisors and pass the tube through the roll to prevent the dog from biting the tube. Gently pass the tube to the level of the mark; it will commonly enter the stomach even when it is torsed. If resistance is met, gently rotate the tube or change the patient's position to help it pass. Do not force the tube, as this can cause esophageal or gastric damage or perforation. If the tube cannot be passed, perform percutaneous gastrocentesis with a large (~14g) needle or over-the-needle IV catheter inserted at the most tympanic site. If stomach contents are not too frothy, this partially decompresses the stomach by releasing some air. Potential complications of gastrocentesis include bleeding from hitting the spleen (if you get blood, change needle location) and rupture of the stomach if the needle is inserted into an area of gastric necrosis. However, if an orogastric tube cannot be passed, the benefits of percutaneous gastrocentesis outweigh the risks.

The two #1 steps of fluids and gastric decompression take precedence over everything else, but with a well-trained team, you can also simultaneously perform the following steps (Fig. 3). Because hypoxia is a fundamental problem in GDV patients (Fig. 1), start flow-by oxygen right away. Collect blood from the IV catheter or another vein before attaching the fluid line so that blood results are not skewed by fluid administration. Attach an EKG and blood pressure cuff to monitor for arrhythmias and hypotension. Give opiates for pain and broad-spectrum IV antibiotics due to the risk of bacterial translocation and/or gastric perforation. Vasopressors (e.g., dobutamine, dopamine) may be required if hypotension is not responsive to fluids. Avoid steroidal and non-steroidal anti-inflammatory medications due to the patient's hypoperfusion and GI compromise. Avoid dexmedetomidine (decreases cardiac output) and acepromazine (decreases blood pressure, non-reversible).

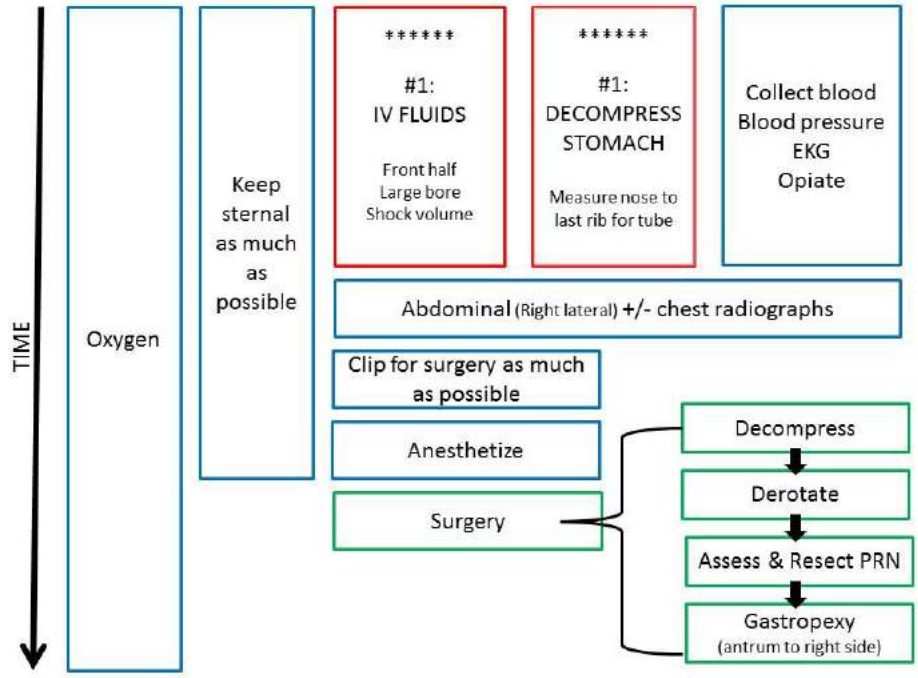

Figure 3. Timeline for managing GDV patient. The items labeled #1 should take priority when personnel numbers are limited. Fluids and decompression should be done before radiographs.

Diagnostics for the GDV Patient

Common blood abnormalities include elevated PCV and total protein due to hemoconcentration, leukopenia or leukocytosis (depending on stage of illness), decreased potassium, and increased alkaline transferase, alkaline phosphatase, lactate, BUN, and creatinine. Patients with DIC can have low platelet levels, elevated clotting times, and schistocytes.

Radiographs are not taken until AFTER doing two #1 priorities of fluids and decompression, since positioning a dog in lateral when the stomach is still compressing the diaphragm, caudal vena cava, and portal vein can worsen systemic compromise and predispose to aspiration pneumonia (Fig. 3). Even after decompression, volvulus and significant gastric distension commonly remain, so a radiographic diagnosis of GDV can still be made. A right lateral radiograph is preferred because air will collect in the pylorus, which has moved to the left side in GDV, showing the diagnostic image of a compartmentalized stomach.

Surgery of the GDV Patient

GDV patients require emergency surgery. Clip the surgical site as much as possible before anesthetizing the patient to decrease anesthetic time (Fig. 3). Once anesthetized, keep the patient in sternal or lateral recumbency as much as possible prior to the final surgical scrub, since dorsal recumbency increases the risk of regurgitation and increases pressure on the caudal vena cava by the dilated stomach. Anesthetize with drugs that have low impact on the cardiovascular system. Positive pressure ventilation may be needed until the GDV is resolved due to pressure on the diaphragm by the dilated stomach.

Make a ventral midline abdominal incision from the xiphoid to at least halfway between the umbilicus and the pubis. In most cases, the pylorus (which is normally on the right side) has moved ventrally and to the left side of the abdomen and then dorsally on the left side, ending up dorsal and cranial to the body of the stomach. From the surgeon's point of view, this is a clockwise rotation of the stomach, and it pulls the omentum over the stomach.

There are 4 main intra-operative steps:

(1) ***Intra-operative decompression*** must be performed before handling the stomach because the dilated stomach is fragile and at greater risk of perforation (Fig. 3). (Even with pre-operative decompression, the stomach is often markedly dilated again). In order of preference, decompression options are orogastric tube, gastrocentesis, and gastrotomy.

(2) ***Derorate the stomach*** by placing one hand between the stomach and body wall on each side. (Keep your fingers together and flat to avoid focal pressure that can lead to perforation). Gently lift the pylorus ventrally with the hand on the dog's left while pushing the body and fundus dorsally with the hand on the dog's right, thus moving the stomach counter-clockwise. Repeat for torsions greater than 180 degrees. After derotating, check the cardia & pylorus to make sure the stomach is back in its normal position. Derotation may precipitate reperfusion injury, so the patent should be closely monitored at this time.

(3) ***Perform an abdominal explore and treat any problems***, which may include gastric necrosis and/or a torsed or thrombosed spleen. If, after derotation, an area of the gastric wall does not look healthy, wait 5 or 10 minutes to see if it regains normal color and pulsations. If there is gastric necrosis, three options for partial gastrectomy are: (A) Cut necrotic areas back to healthy tissue (look for brisk bleeding from cut edges) and close with a simple continuous pattern oversewn by an inverting layer of 2-0 or 3-0 absorbable suture. This technique is effective but time consuming and increases the risk of contamination because the gastric lumen is opened. (B) Invaginate the necrotic tissue into the lumen of the stomach using two overlapping inverting suture patterns. The necrotic tissue will slough into the lumen of the stomach and be digested. This technique is faster than option A and does not require the lumen to be opened, but has the potential of obstructing the stomach. (C) Resect necrotic tissue with a thoraco-abominal (TA) stapler; this is the fastest. If the spleen is torsed around its pedicle, do not untwist it, as this can cause reperfusion injury (Fig. 2). Instead, remove the spleen by ligating its vessels in the twisted state.

(4) ***Perform a gastropexy*** by attaching the pyloric antrum to the RIGHT body wall caudal to the last rib. Gastropexy dramatically decreases the risk of GDV recurrence. I prefer an incisional gastropexy because it is fast, simple, and effective with low morbidity. Make a 5 cm seromuscular incision parallel to the long axis of the stomach on the ventral side of the pyloric antrum, leaving the submucosa and mucosal layers intact. Pull the antrum to the pexy site caudal to the last right rib and make a blood imprint of the incision. Use this imprint as a guide to make a matching incision through the peritoneum and transverse abdominis muscle. Suture the dorsal edges of the two incisions to each other with a simple continuous pattern of 2-0 monofilament absorbable or non-absorbable suture; repeat with the ventral edges. Start each suture line at the craniodorsal end of each incision, which is the hardest to see. Do NOT pexy the stomach to the celiotomy incision – this can results in the surgeon entering the stomach if abdominal surgery is needed in the future.

Reperfusion Injury

When the GDV is corrected and organs are once again perfused with oxygen-rich blood, there is a danger of reperfusion injury (Fig. 4). Oxygen interacts with the anaerobic metabolites that built-up in the tissues during hypoxia, creating reactive oxygen species (ROS). ROS set off chain reactions that damage proteins, nucleic acids, and membrane lipids, resulting in cell death. Most dogs that die from GDV do so within 96 hours of treatment, during the time of reperfusion

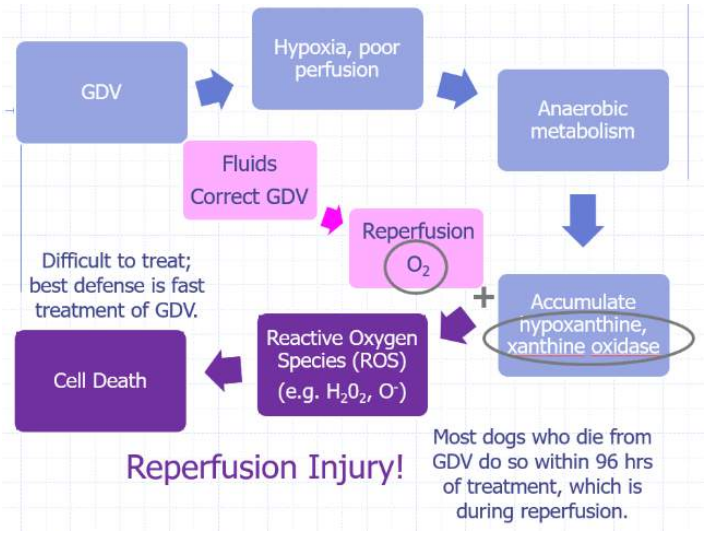

Figure 4. Reperfusion injury occurs when oxygen is reintroduced to hypoxic tissues

Postoperative Management of the GDV Patient

GDV patients can require intensive postoperative care, including IV fluids, potassium supplementation, analgesia, gastric protectants (H2 blocker, sucralfate), and oxygen. Continue antibiotics if there was gastric perforation or necrosis. In a stable, non-vomiting patient, offer small amounts of a low-fat diet every 4 to 6 hours. Healing is faster in patients that receive nutrition into the GI tract, so feed patients that are not eating via a nasogastric tube (this also allows aspiration of excess fluid and air out of the stomach).

Monitor ECG for ventricular arrhythmias, which may not start until 24-72 hours postop. Idioventricular rhythm (rate<120-160bpm) usually has a uniform QRS shape and typically alternates with sinus rhythm. If heart function is otherwise normal, this usually does not cause hemodynamic problems and will resolve on its own. Ventricular tachycardia (rate>150-160bpm) and ventricular premature contractions (VPCs) are more likely to cause hemodynamic issues. Correction of acid-base and electrolyte disturbances, hypoxia, and good pain management can reduce their frequency. Indications for treatment include signs of hypotension and poor perfusion (not related to hypovolemia), >20 VPCs/min, multiform VPCs, R-on-T, critically ill, heart failure, and/or breeds at risk of sudden death (Doberman, Boxer). Treatment starts with an IV lidocaine bolus (2-4 mg/kg) followed by a continuous rate infusion at 25-80 mcg/kg/min if needed.

Prognosis for GDV

The survival rate for GDV patients treated surgically in a timely manner is 85-90%. Causes of death include shock (hypovolemic, endotoxic, and/or cardiogenic), gastric necrosis and perforation, systemic inflammatory response syndrome (SIRS), DIC, and reperfusion injury. Factors that have been associated with a worse prognosis include >5-6 hours between onset of signs and admission to hospital; low body temperature, depression, or coma at presentation; initial serum lactate concentrations > 6 to 9 mmol/L; failure of serum lactate concentrations to decrease ~50% in the first 12 hours of care; arrhythmias (especially if present pre-op); cardiomegaly on pre-operative chest radiographs; gastric necrosis; and need for a splenectomy. Prompt and aggressive therapy, based on a solid understanding of the pathophysiology involved, will maximize the ability of the clinician to successfully treat GDV patients.

Predisposing Factors for GDV

Factors that appear to increase the risk of GDV include: large/giant deep-chested breed, having a relative with GDV, middle age, thin, fed 1 meal/day, rapid eating, elevated feeding, hospitalization/boarding, fearful temperament, and gastric motility issues. Some studies suggest a relation between the risk for GDV and postprandial exercise, IBD, GI foreign body, or previous splenectomy, while others do not. Prophylactic gastropexy is advised for large breed deep chested dogs.

References available upon request

PROPER PLANNING AND EXECUTION IN ONCOLOGIC SURGERY

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The most common mistake in oncologic surgery is failing to identify tumor type, grade, and stage so that the most appropriate surgery can be planned. Removing a mass without this information can result in tumor spread, the need for multiple and more major surgeries, and/or recurrence of a tumor that is more aggressive than the original. Good pre-operative assessment improves patient outcome.

Identify Tumor Type

Knowing the tumor type directs additional diagnostics (e.g., where to look for metastases), choice of treatment modality (e.g., surgery, chemotherapy, and/or radiation), and the client's interest in further treatment based on projected costs and prognosis. If surgery is indicated, tumor type guides surgical planning, including the imaging needed to assess the tumor's association with other tissues and the margins needed to best remove locally invading tumor cells.

A fine needle aspirate (FNA) is the first step to identifying tumor type – it is fast, easy, inexpensive, and can be diagnostic. A non-diagnostic FNA can be the result of poor exfoliation of cells, inflammation or necrosis obscuring tumor cells, or the needle not hitting a neoplastic area in a heterogeneous mass. Thus, the absence of tumor cells on FNA does not rule out neoplasia.

Biopsy and histopathology are indicated if the FNA does not provide adequate information. In most cases, this should be an INcisional biopsy, where small pieces of tissue are taken from representative areas of the mass (Fig 1). Avoid areas of high-inflammation or necrosis, and handle samples gently, to make histologic interpretation easier. Common biopsy techniques employ wedge incisions, dermal biopsy punch, or Tru-Cut needles. Bleeding from the biopsy site may be controlled with pressure, suture, and/or an absorbable, hemostatic, gelatin foam. Incisional biopsy can often be done under sedation with local anesthetic. It is important to plan the biopsy sites so the biopsy tracts can be removed with adequate margins along with the mass when the definitive excision surgery is performed. A properly performed incisional biopsy does not increase the risk for tumor spread.

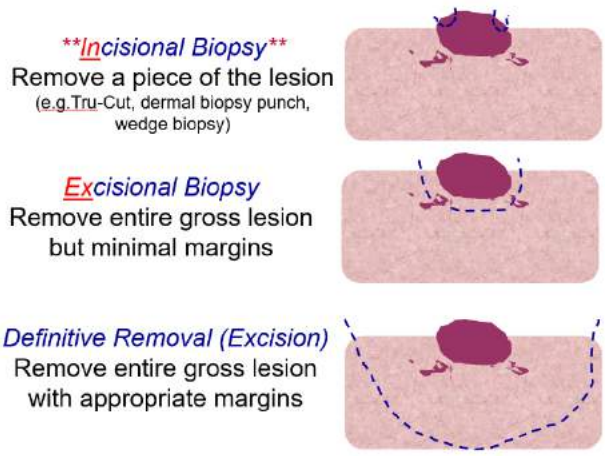

Figure 2. Biopsy types. Dark red = mass and invading tumor cells, dashed line = sample taken.

Indications for an excisional biopsy, in which the entire gross lesion is removed without knowing necessary margins (Fig.1), are limited, because this often results in residual tumor cells. The tumor then often returns in a more malignant form because it is growing from the more aggressive tumor cells that were invading tissue surrounding the mass. An excisional biopsy also alters local vascularity and immune function that can favor tumor growth. A second surgery to remove the residual tumor cells is made more difficult by adhesions and scarring caused by the initial excisional biopsy, and requires margins measured beyond the site of the first surgery, resulting in removing much more tissue then if adequate margins were taken during the first definitive removal. Situations that warrant excisional instead of incisional biopsy include a mass that is too small for incisional biopsy and when

knowing tumor type does not change the diagnostic or treatment protocol, including the surgical plan for definitive removal.

For both incisional and excisional biopsies, an accurate record of the surgical procedure, including the location, depth, and size of incisions, is important, so that margins for any subsequent surgery can be based on the parameters of the first procedure.

Grading, Staging, and Other Diagnostics

Tumor type and grade (degree of differentiation/anaplasia) are obtained from the histopathology report for the biopsy sample. This information is used to direct additional diagnostics. Staging is done to determine the extent of disease, and often includes FNAs of draining lymph nodes and imaging of areas where this tumor type tends to spread. Imaging may also be indicated to assess the tumor's association with other tissues for surgical or radiation planning. Bloodwork is done to look for paraneoplastic syndrome and assess the patient for comorbidities and suitability for anesthesia.

Definitive Surgical Removal of Tumor

The first time you do a definitive surgery (Fig. 1) to remove the whole tumor is the best chance for a surgical cure; this requires removing adequate margins around the mass to catch the locally invasive cells. Plan margins based on tumor type (see table). Ideally, remove tumors *en bloc*, without touching the tumor itself. Margin sizes refer to grossly normal tissue around the mass in *all* directions, including deep. An alternative for the deep margin is to remove one to two tissue layers beyond that touched by the mass (table, Fig. 2). This works because it is harder for tumor cells to move between tissue types than within the tissue layer of origin.

	Margins	Alternate deep margin
Mammary tumor	1 to 2 cm	Remove 1 tissue type beyond that contacted by tumor
Mast cell tumor	(2) to 3 cm	
Soft tissue sarcoma	3 cm	
Injection-site sarcoma	5 cm	Remove 2 tissue types beyond that contacted by tumor

With a sterile marker and ruler, draw the margins on the skin before incising. Once you start cutting, the tissue on the tumor side shrinks in, and the wound expands. As you go deeper, maintain the original margin size, removing a cylinder of tissue rather than coning down and compromising deep margins (Fig. 3).

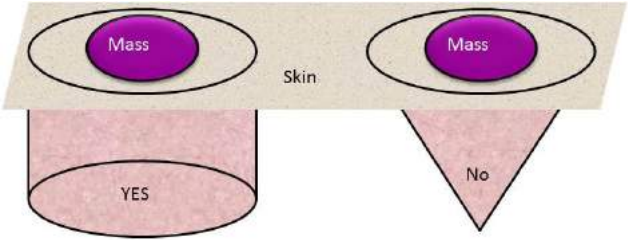

Figure 3. Maintain peripheral and deep margins by removing a cylinder of tissue instead of a cone.

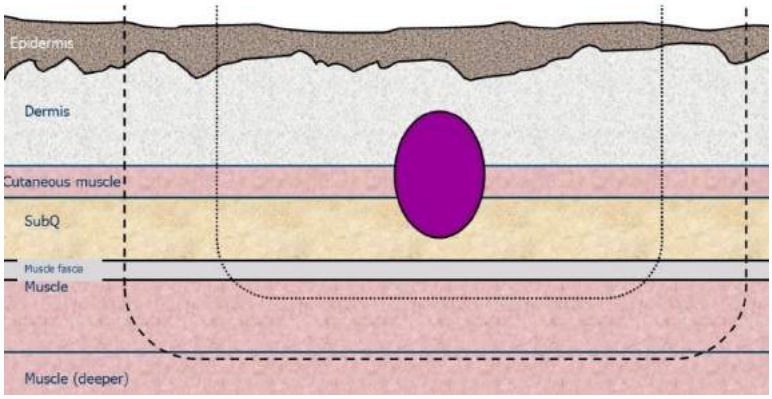

Figure 2. A cross-section of the tissue layers is shown. The subcutaneous tissue is the deepest layer contacted by the mass (purple oval). For a soft tissue sarcoma, excision follows the dotted line, removing 3cm peripherally and one tissue layer deep (muscle fascia in this case). For an injection-site sarcoma, excision follows the dashed line, removing 5cm peripherally and two tissue layers deep (muscle fascia + muscle in this case).

To help orient the pathologist, mark the sample with suture tags to denote specific sides of the mass, and/or paint the mass with special inks that stay on the tissue during processing and are visible microscopically. Most

samples can be placed in a volume of 10% buffered neutral formalin that is 10 to 20 times the sample volume for 12 to 24hrs, then be transferred to just enough formalin to keep them moist during shipment. Slice samples that are thicker than 0.5 cm to allow adequate fixation. Include a thorough description of the mass, history, and diagnostic findings.

Tumor Seeding

Tumor seeding is the release of tumor cells from the primary tumor that then go on to grow in a new location. Factors influencing seeding include surgical manipulation, tumor type, environment of the seeded site, and number of cells seeded. *Inflammatory oncotaxis* is the attraction of tumor cells to sites of inflammation; follow Halsted's principles of surgery to minimize the amount of inflammation. Meticulous hemostasis limits blood clots (a media for tumor cells). Tumor cells also grow along paths created by needle aspiration, surgical dissection, and drains. In human medicine, the most common location for tumor seeding during surgery is the primary incision.

To minimize the risk of seeding, treat oncologic surgery just like a surgery involving infected tissue or entry into the gastrointestinal tract; instead of bacteria, the potential contaminant is tumor cells. Protect non-tumor areas with moist laparotomy pads. Stick to your planned margins; what looks like a nice capsule isolating the tumor may actually be a compressed layer of tumor cells. Ligate the blood supply to the tumor early to prevent cells loosened by handling from escaping into the venous drainage. Lavage tissues and change instruments and gloves after the tumor has been removed and before closing.

Drains can create a path for tumor cells, but they can also eliminate dead space and prevent hematoma, seroma, and prolonged inflammation (which all favor growth of tumor cells. If a drain is placed, exit it near the incision at a site that can be readily resected (with appropriate margins) or included in the radiation field, if needed.

References available upon request

SPLENIC MASSES: PERIOPERATIVE AND SURGICAL MANAGEMENT

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In dogs, the most common benign splenic masses are hemangioma, nodular hyperplasia, and hematoma, while the most common malignant splenic mass is hemangiosarcoma (HSA). Other less common splenic malignancies include leiomyoma, a variety of sarcomas, plasma cell tumor, and mast cell tumor. Mast cell tumor is the most common splenic neoplasia in cats. This seminar will focus on dogs with splenic masses, although many aspects of management and surgery also apply to cats.

Splenic torsion is a condition that might be mistaken for a splenic mass on abdominal palpation or initial imaging. In splenic torsion, the spleen rotates on its vascular pedicle, obstructing the splenic vein and sometimes splenic artery, and leading to splenomegaly, congestion, and possible splenic thrombosis and necrosis. It occurs most commonly in large, deep chested dogs and while it is often associated with GDV (gastric dilatation and volvulus), it can occur as an isolated condition.

Diagnostic work-up

While researchers have looked at a number of variables, individually and in combination, including labwork, cytology, appearance on imaging, splenic mass size, splenic weight and volume, presence of hemoabdomen, and many others, none of these provide a definitive way to distinguish between hematoma, hemangioma, and hemangiosarcoma. Surgical biopsy is thus required for diagnosis. When a splenic mass is cavitated and highly vascular, percutaneous biopsy with a Tru-cut needle or similar device is not advisable due to the risk of bleeding and the relatively high chance of a non-diagnostic sample. Thus, the surgical biopsy is typically obtained via full splenectomy, which requires general anesthesia and surgery. While partial splenectomy can be done to remove just the part of the spleen containing the mass, full splenectomy is typically done because a second major surgery would be required to remove the rest of the spleen should the mass prove malignant, the risk of postoperative bleeding is higher with partial splenectomy than with full splenectomy, and the clinical consequences of not having a spleen seem to be minimal for dogs and cats.

News that their dog has a splenic mass can come as a surprise to clients, either because it was an incidental finding on a routine physical exam or because their dog became acutely ill due to a significant bleed from the mass. In these situations, the client is suddenly faced with the information that their seemingly healthy pet may have HSA, an aggressive tumor that will likely lead to death within 1-3 months if nothing is done. Furthermore, the client learns that a major surgery will be required to remove the spleen to prevent the risk of future bleeds and to get a diagnosis. If this mass is benign, this surgery can be curative; if it is HSA, median survival time is 1-3 months with surgery alone, and 6-9 months with follow-up chemotherapy (commonly doxorubicin).

The double two-thirds rule says that 2/3 of splenic masses are malignant, and 2/3 of these are HSA. Recent studies suggest that this rule should be modified by separating out patients with splenic masses into two populations: (1) if splenic mass + hemoabdomen secondary to a bleed from the mass, 63-73% are malignant (with up to 87% of these being HSA) and 27-34% are benign, and (2) if splenic mass and no hemoabdomen, approximately 30% are malignant and 70% are benign. While the client needs to be informed about the poor

prognosis if the mass is HSA, it is also important they know that non-negligible portion of patients will have benign disease or a non-HSA malignancy, and that those in this category may do very well long-term post-splenectomy.

The diagnostic work-up may identify co-morbidities and/or potential metastases that will further help the client decide about surgery and provide information on the patients suitability for anesthesia and surgery. Recommended pre-operative diagnostics include complete blood count (CBC), serum chemistry panel, coagulation tests (ACT, or PT & PTT), typing and cross-matching, imaging of the thorax, abdomen, and heart, and analysis of abdominal fluid, if present. Common bloodwork abnormalities in dogs with splenic masses, especially if the mass has bled significantly, include anemia, thrombocytopenia, stress leukogram, and hypoproteinemia. The likelihood of malignancy increases with anemia, nucleated red blood cells (rbc), abnormal rbc morphology, thrombocytopenia, coagulopathy, and disseminated intravascular coagulopathy (DIC), but none of these changes are diagnostic.

Thoracic radiographs (3-view) are taken to look for pulmonary metastasis and pleural effusion (the latter may occur in patients with DIC). Heart enlargement may be seen in dogs with right atrial HSA (which may occur concurrently with splenic HSA), but this is better assessed via echocardiography. Abdominal ultrasound or CT gives information on the splenic mass and potential pathology in other organs, but cannot distinguish benign from malignant disease. In some cases, imaging may identify a splenic mass that is not highly vascular and thus safer to aspirate. The differential diagnoses for liver nodules include nodular hyperplasia (most common), extramedullary hematopoiesis, and neoplasia; liver nodules are not a definitive indicator of metastasis. Abdominocentesis can confirm the presence of hemoabdomen, but, in cases of neoplasia, cytology rarely reveals any tumor cells.

Even if a number of factors in the work-up increase the level of concern for HSA, some clients opt for splenectomy to eliminate the risk of bleeding from the splenic mass and give them more quality time with their dog, and because there the mass could be benign and cured with surgery.

Pre-operative Management

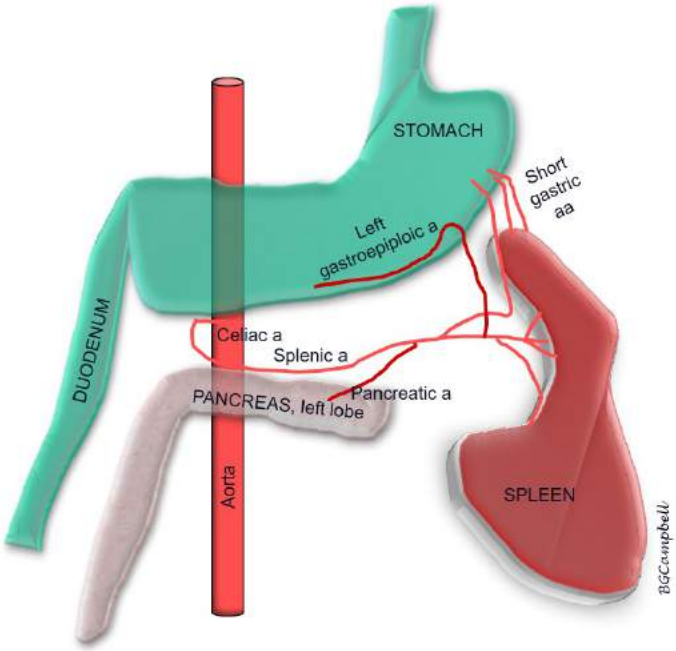
Patients with hemoabdomen should be stabilized prior to anesthesia if possible. Because the hemorrhage is often acute, the packed cell volume (PCV) may not reflect the full extent of blood loss until the patient is rehydrated. Treatment includes flow-by oxygen and fluids, commonly starting with ¼ shock dose of crystalloid fluids (90ml/kg shock dose/4 = 22.5ml/kg), continuously reassessing the patient, and repeating as needed. Some patients may need blood products (packed red blood cells or whole blood) as well. To avoid increasing blood pressure to the point where newly formed clots are dislodged, aim for low normal pressure (mean arterial pressure 70-80mmHg, which is still enough to perfuse vital organs. A wrap that starts at the hindlimb toes and extends over the abdomen may be helpful, but should be applied with caution – if too tight, it can restrict breathing and compromise blood flow to organs. If the bleed continues despite these measures, surgery may be the only way to stop it.

Keep patients with large splenic masses in sternal for as long as possible to decrease compression of the caudal vena cava by the weight of the splenic mass that occurs when in dorsal recumbency. Anesthetic induction and much of the clipping and initial scrub can be done with the dog in sternal or tipped to either side. The surgically prepped area should allow for a full-abdominal incision, from the cranial end of the xiphoid to the pubis. Give a prophylactic IV antibiotic such as cefazolin starting 30min before the incision and repeating every 90 minutes intraop.

Splenectomy

Surgery in patients with a splenic mass should include a full abdominal explore, biopsy of any additional masses, and splenectomy. Incise from the xiphoid to midway between the umbilicus and pubis to start, and extend if needed to accomplish all procedures with minimal splenic manipulation. While the abdominal explore is ideally performed first, start with the splenectomy if the mass is bleeding or if it is too big to allow for adequate explore. Pack off the spleen with moist laparotomy pads to decrease contamination of the rest of the abdomen with potential tumor cells.

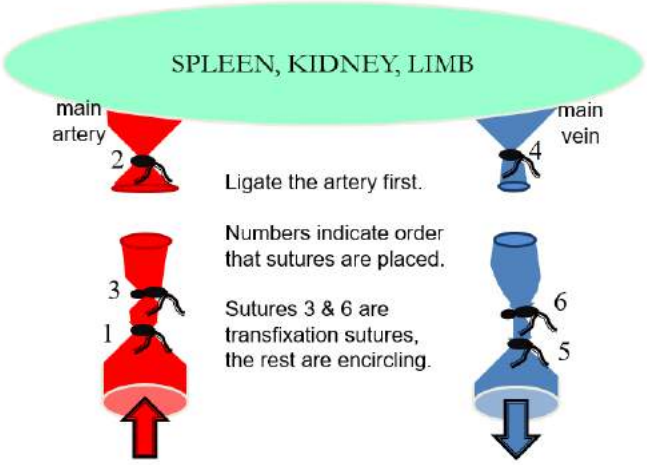
Surgical technique for splenectomy varies with the size of the mass, the amount of omental or other adhesions, and whether the mass is bleeding. Handle the spleen with flat fingers, avoiding fingertip pressure points that could penetrate the mass. Cover masses that are ulcerated or actively bleeding with a moist laparotomy pad to provide some local pressure and decrease further shed of potential tumor cells. Options for vessel ligation includes suture and electrocautery-based vessel sealing devices (e.g., Ligasure). Absorbable suture is fine for smaller vessels, while silk suture provides good long-term security for the main splenic artery and vein. Depending on the splenic lesion, the short gastric arteries and left gastroepiploic artery may need to be ligated; studies show that a healthy stomach has enough collateral circulation to compensate for the loss of these vessels.



If the splenic mass is well-contained within the splenic parenchyma and there are no omental adhesions, the small hilar vessels can be ligated and transected, moving from the tail to the head of the spleen. This technique avoids direction ligation of the large splenic artery and vein. Use a hemostat to bluntly separate out a bundle of vessels and surrounding omental/mesenteric tissue sized so it can be safely ligated with an encircling suture. Ligate the systemic side, then place a ligature or hemostat on the splenic side, and cut in between with Metzenbaum scissors.

When the branches of the splenic artery are easily accessed, another option is to ligate the short gastric vessels and the three to five main branches of the splenic artery that enter the spleen.

When the mass is large and bulging out of the hilar region of the spleen, and/or if there are a lot of omental adhesions, place the ligations several centimeters away from the spleen and mass to improve the margins obtained. Identify the left lobe of the pancreas (in the craniodorsal portion of the deep leaf of the greater omentum) and the pancreatic branch of the splenic artery as early as possible. These structures can be hidden in omental adhesions and accidentally cut.



When the mass is actively bleeding, ligate the main splenic artery and vein as early in the procedure as possible. Unfortunately, extensive adhesions of the greater omentum can make it difficult to find these vessels (which are closer to the head of the spleen) until the tail of the spleen is freed up. The technique for ligating the splenic artery and vein (or similar large vessels) is different than for smaller vessels. Do not ligate the main artery and vein together, as this can lead to an arteriovenous fistula. Dissect the artery and vein away from attached mesentery. Ligate the artery first to prevent additional blood loss from the bleeding mass or from sequestration in the spleen. Each vessel gets two encircling and one transfixation suture (pass the needle directly through the artery, tie with 2 throws on one side, then 4 throws on the other side).

Ligate vessels in the order shown in the diagram & table.

Splenic artery	**Splenic vein**
(1) encircling suture 'upstream' (aorta side) (2) encircling ligature 'downstream' (spleen side) (3) transfixation suture in between (closer to encircling suture that is staying in patient) Cut artery between sutures (2) & (3)	4) encircling suture 'upstream' (spleen side) (5) encircling ligature 'downstream' (vena cava side) (6) transfixation suture in between (closer to encircling suture that is staying in patient) Cut vein between sutures (4) & (6)

If performing a splenectomy for splenic torsion, do NOT derotate the spleen. This can release emboli and vasoactive factors, and lead to reperfusion injury as oxygen returns to the spleen and interacts with the anaerobic metabolites that built up when the blood flow was occluded by the torsion. Use blunt dissection to separate the twisted splenic pedicle into sections small enough to safely ligate.

After splenectomy, double check that the left lobe of the pancreas is still its normal pink color. If its blood supply has been lost, perform a partial pancreatectomy by dissecting the avascular portion free from the greater omentum and ligating the lobe with a guillotine encircling suture of nonabsorbable, monofilament suture (not silk, which is multifilament). Since the splenic mass could be neoplastic, lavage the abdomen with warm sterile saline and change gloves and instruments before closing to reduce the risk of spreading tumor cells. Lavage also removes blood clots (a media for bacteria), rehydrates tissues, warms the patient, and helps find residual bleeding (look for swirl of blood moving up through the saline).

The evidence is mixed as to whether splenectomy increases the risk of gastric dilatation and volvulus (GDV). In large, deep-chested dogs at risk for GDV, consider prophylactic gastropexy if the patient is stable under anesthesia and all other procedures are done. Lavage and change gloves and instruments prior to the gastropexy to minimize the risk of potential tumor cells seeding the gastropexy incision.

Always submit the spleen for histopathology, which is required for definitive diagnosis. The results will inform what additional therapy, if any, is needed.

Post-op management and potential complications

Postoperative care includes IV fluids (with correction of electrolyte and acid-base imbalances) until the patient is eating consistently. Blood products may also be needed. Offer food once the dog is well-awake from anesthesia and not vomiting; start with small meals of a bland diet. Provide adequate analgesia (commonly opioids; avoid NSAIDs until hypotension and bleeding are resolved and the patient is eating). Antibiotics can usually be discontinued at the end of surgery.

Monitor the patient closely for signs of hemorrhage, such as tachycardia, pale mucous membranes, prolonged capillary refill time, weak femoral pulses, hypotension, and free abdominal fluid (compare PCV of abdominal fluid to peripheral PCV). Hemorrhage could be secondary to failure of ligations or DIC.

Continuous electrocardiogram is advised for 36 to 72 hours post-operatively to monitor for ventricular arrhythmias, which are often seen post-splenectomy. Idioventricular rhythm (rate<120-160bpm) usually has a uniform QRS shape and typically alternates with sinus rhythm. If heart function is otherwise normal, this usually does not cause hemodynamic problems and will resolve on its own. Ventricular tachycardia (rate>150-160bpm) and ventricular premature contractions (VPCs) are more likely to cause hemodynamic issues. Correction of acid-base and electrolyte disturbances, hypoxia, and good pain management can reduce their frequency. Indications for treatment include signs of hypotension and poor perfusion (not related to hypovolemia), >20 VPCs/min, multiform VPCs, R-on-T, critically ill, heart failure, and/or breeds at risk of sudden death (e.g., Doberman, Boxer). Treatment starts with an IV lidocaine bolus (2-4 mg/kg) followed by a continuous rate infusion at 25-80 mcg/kg/min if needed.

Pancreatitis may occur due to manipulation of the left lobe of the pancreas during the procedure. Signs include vomiting and abdominal pain; icterus may occur due to secondary bile duct obstruction. Treatment is supportive, with IV fluids, correction of electrolyte imbalances, antiemetics, analgesia, and nutritional support.

Take Home Message

You cannot definitively differentiate between splenic hematoma, hemangioma, and hemangiosarcoma without a surgical biopsy. Do not automatically assume that a splenic mass is malignant, and do not assume that liver nodules indicate metastasis. Educate clients about the benign and malignant possibilities for splenic masses so they can make an informed decision for their companion.

References available upon request

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Anesthesia & analgesia for emergency/critical care patients

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NOTE: Some drugs in this presentation may not be available in all countries.

Patients that are presented as emergencies are not necessarily also critical and the needs of critical patients are often different from those of emergency patients. However, both groups can be at increased risk for anesthetic death. Both increasing American Society of Anesthesiologists (ASA) scores and increasing urgency of the procedure increases risk of anesthetic death (Brodbelt 2009). Thus, **stabilizing both emergency and critical care patients prior to sedation and/or anesthesia is imperative**. **Analgesia should be part of stabilization**. Pain creates a tremendous stress and can contribute to **morbidity** and perhaps even **mortality**. Relief of pain can provide hemodynamic and respiratory stabilization and decrease catecholamine release and cachexia. Relief of pain can also be diagnostic. If relieving pain does not provide stabilization, continue diagnostics. Safe, reversible drugs like the opioids should be familiar and comfortable drug choices for the veterinarian treating emergency and critical care patients.

Anesthesia should be thought of as 4 distinct and equally important periods: 1) preparation /premedication; 2) induction; 3) maintenance and 4) recovery. We tend to diminish the importance of the phases of preparation/premedication and recovery and yet these phases contribute as much to successful anesthesia as the phases of induction and maintenance.

PREPARATION FOR ANESTHESIA & PREMEDICATIONS

Support and Monitoring: As evidenced by the fact that decreasing ASA status and decreasing urgency of the procedure increases the chance of patient survival, critical and emergency patients should be fully stabilized prior to anesthesia. Support includes restoring fluid and electrolyte balance and supporting oxygen delivery.

Sedatives / tranquilizers: Although not intuitive that critical patients need premedicants, the use of premedicants will decrease the dose of induction and maintenance anesthetic drugs. Since adverse effects are dose dependent, decreasing the dosages will improve anesthetic safety.

- *Opioids - morphine, hydromorphone, oxymorphone, fentanyl, methadone, butorphanol, buprenorphine:* Advantages: Provide moderate to profound analgesia, minimal to no cardiovascular effects, minimal respiratory effects, allow a decrease in dosage of injectable and maintenance drugs, reversible, most are inexpensive, provide sedation, versatile (can be administered PO, IM, IV, SQ, in the epidural space, in the intra-articular space, etc...). Disadvantages*:* May provide more sedation than desired in dogs or excitement in cats (both effects are reversible), relatively short duration of action when compared to the duration of most pain. **NOTE:** Opioid-induced respiratory changes are generally mild and related to degree of sedation.
- *Benzodiazepines - Diazepam (Valium®) and Midazolam (Versed®):* Advantages: minimal to no cardiovascular or respiratory effects, reversible. Disadvantages: won't provide adequate sedation when used alone in healthy, angry or excited dogs, no analgesia.
- *Acepromazine* – not commonly used in compromised patients; can contribute to hypotension and transient decrease in PCV, not reversible, no analgesia. But many emergency patients often benefit from a low dose of acepromazine, for example patients with upper airway compromise that need long-term

light sedation and some patients with cardiovascular disease that would benefit from a reduction in afterload.

- *Alpha-2 agonists* – not commonly used in compromised patients but definitely appropriate in stable emergency patients that need sedation and analgesia. Advantages: Provide both sedation and analgesia, effects are reversible. Disadvantages: Will cause an increase in cardiac work.
- *Alfaxalone* – a low dose of alfaxalone can be administered IM along with an opioid to provide sedation in critical patients. See more information in the induction section.

Other drugs: *Maropitant* is recommended as a premedicant, both for its anti-emetic effects and its potential for contributing to analgesia. Other support drugs (eg, anticholinergic, anti-arrhythmic, positive inotrope, etc.) would be patient-specific.

INDUCTION

REMINDER: All tranquilizers, induction drugs and inhalant drugs cause CNS depression and most cause some degree of **dose-dependent** negative respiratory and cardiovascular effects. In healthy patients, many of the physiologic effects of anesthetic drugs are well tolerated or can be counteracted by routine measures such as administration of oxygen or intravenous (IV) fluids. In compromised patients, these effects can be exacerbated, further contributing to the demise of the patient. Successful anesthesia in compromised patients is highly dependent on adequate patient stabilization, diligent patient support and monitoring, and the use of appropriate anesthetic drugs at appropriate **dosages. All drugs should be dosed 'to effect'**.
Preoxygenation should occur prior to induction.

- *Propofol:* Advantages: rapid induction and recovery, easy to titrate 'to effect', multiple routes of clearance from the body, good muscle relaxation. Disadvantages: Causes mild to moderate dose-dependent respiratory and cardiovascular depression
- *Alfaxalone:* Advantages: rapid induction and recovery, easy to titrate 'to effect'. Disadvantages: Causes mild to moderate dose-dependent respiratory and cardiovascular depression. Can cause excitement in recovery.
- *Ketamine:* Advantages: inexpensive, can be administered IM, mild to no negative cardiovascular or respiratory effects, especially in heart-healthy patients. In fact, mild sympathetic nervous system (SNS) stimulation from ketamine can often slightly increase heart rate and cardiac contractility. Disadvantages: can cause cardiovascular depression in patients in heart failure, SNS stimulation could exacerbate sympathetically-driven arrhythmias, can cause muscle rigidity if used without a muscle relaxant.
- *Etomidate:* Advantages: no cardiovascular effects. *Disadvantages:* expensive, poor muscle relaxation, vocalization, maybe not safe in septic patients due to adrenocortical suppression.
- *Tiletamine-Zolazepam:* Advantages/Disadvantages: Similar to ketamine/benzodiazepine. Very potent, titrate carefully.

Inhalant induction is NOT appropriate *for almost all patients.* The dose of the inhalant is entirely too high when used alone (side effects of inhalants are dose-dependent) and the induction will be stressful and will be prolonged. Furthermore, use of inhalants alone for induction and maintenance increases the risk of anesthesia-related death (Brodbelt 2009).

MAINTENANCE

Inhalant anesthesia is generally the safest and most effective way to maintain anesthesia that will last 30 minutes or more. However, inhalant anesthetic drugs should never be used as the sole anesthetic agent since this group of drugs causes significant hypotension, hypothermia, and hypoventilation. Our goal should always be to keep the vaporizer at the lowest possible setting and sometimes we must add *analgesia* to minimize *anesthesia*. *Advantages*: are eliminated with minimal metabolism, relatively easy to administer and inexpensive. *Disadvantages*: DOSE DEPENDENT contribution to hypoventilation, hypotension and hypothermia. MONITOR, MONITOR, MONITOR. **NOTE:** The advantages and disadvantages of the inhalant drugs are class effects and apply to all inhalants. However, sevoflurane has an advantage in critical patients since it is more easily dosed 'to effect' because of its lower solubility coefficient.

Analgesic Drugs & Techniques

Maintenance of anesthesia is much easier and safer if analgesia is provided prior to the painful stimulus. Most anesthetic drugs, including the anesthetic gases, block the brain's recognition that pain has occurred but

don't actually block pain. If the pain is severe enough, the brain can still respond and make the patient appear to be inadequately anesthetized. The result is that the vaporizer is turned up and the brain ceases to respond, but the patient is now too deeply anesthetized and can be at a very dangerous physiologic plane. A more appropriate response would be to block the pain and maintain anesthesia at a light, safe depth. An additional advantage of the drugs and techniques listed below is that they are anesthetic-sparing, meaning that they allow a decrease in the anesthetic dose necessary to maintain sleep.

- *Opioids:* Advantages and disadvantages are described above. Minor changes in respiratory or cardiovascular function that may occur are more than offset by the subsequent decrease in the dose of the inhalant anesthetic drug (ie, turn down your vaporizer after you give the opioid!).
- *Local anesthetic drugs & locoregional techniques:* Advantages: Inexpensive, easy to administer, very effective. Block input to the dorsal horn of the spinal cord and thus decrease the incidence of central sensitization. Disadvantages: Relatively short duration of action when compared to the duration of pain except for liposome-encapsulated bupivacaine, which has a duration of 72 hours.
  NOTE: This class of drugs is extremely underutilized yet they are easy to use, inexpensive and highly effective. **We should be using more local anesthetics**! And don't forget regional techniques like epidurals.

- *Constant rate infusions (CRIs):* Advantages: EASY, inexpensive, effective, many drug choices (opioids, lidocaine, ketamine, alpha-2 agonists and combinations of all of these drugs). Disadvantages: Almost none because of low dose delivered but side effects from any drug can occur. **NOTE:** Provide staff with training & dosage charts so that making CRIs is not cumbersome. If it is easy, it will get done!

Monitoring & Support

Monitoring: Anesthesia causes changes in all organ systems but the changes in the CNS, cardiovascular and respiratory systems are the most immediately life-threatening so we focus our monitoring and support on these systems. Also, support of these systems will provide support for other systems (eg, maintenance of adequate blood pressure supports renal function). Don't forget the basics: MM color, CRT, jaw tone, eye position, etc… Utilize SpO_2 (pulse oximeter) and end-tidal CO_2 to assess respiratory function. Utilize ECG and **BLOOD PRESSURE** to assess cardiovascular function. Measurement of blood pressure is IMPERATIVE in critical patients.

Cardiovascular support includes use of IV fluids & positive inotropic and antiarrhythmic drugs.

- *IV fluids* should be used, as needed, to rehydrate the patient and replace ongoing losses. Do not overhydrate – excessive administration of fluids can cause edema.
- Many critical patients would benefit from the use of *colloids* in addition to the crystalloids. Voluven (Vetstarch) is commonly used and the total dose in the dog is 50 ml/kg in a 24-hour period. Cats should generally receive 30-40 ml/kg in a 24-hour period. These dosages are extrapolated from human medicine and no veterinary dosages have been established.
- If patients have hemorrhaged, if severe hemorrhage is expected intraoperatively or if the patient is anemic (PCV < 18%), collect blood for a blood transfusion prior to anesthesia.
- Oxygen bound to hemoglobin is the main source of oxygen delivered to the tissues. If the patient is hypoproteinemic (albumin <2 g/dl), administer plasma prior to anesthesia.
- If the patient is hypotensive:
  1. If anesthetized, TURN DOWN THE VAPORIZER.
  2. Give boluses of fluids (5-10 ml/kg rapidly) or colloids (5 ml/kg rapidly).
  3. Consider positive inotropes like dopamine or dobutamine. Dose of each is 1-10 microg/kg/min. Positive inotropes should be used in place of fluid boluses in appropriately hydrated patients with decreased myocardial contractility from cardiovascular disease or conditions that secondarily cause decreased cardiac contractility (eg, sepsis, etc.).
  4. If these measures are not effective or if the patient is severely vasodilated, vasopressors (eg, norepinephrine, vasopressin) may be necessary.

Respiratory support includes oxygen delivery and maintenance of ventilation.

- Oxygen is cheap and profoundly beneficial in many critical patients. When in doubt, administer oxygen!
- If the patient is having any trouble ventilating (head trauma, thoracic trauma, profound CNS depression, impingement on thorax by GI contents, etc…) ADMINISTER OXYGEN.
- If the ventilatory depression is moderate, consider intubation. If severe, INTUBATE.

- Many compromised patients will require assisted ventilation because the respiratory drive response to hypoxemia and/or hypercarbia may be impaired and/or the patient may not be physically able to ventilate normally (muscle weakness, thoracic trauma, electrolyte imbalance, GI distension, etc…). Assisted ventilation: 2 breaths/min to 15-20 cmH_2O on the manometer. Controlled ventilation: 6-10 breaths/min to 15-20 cm H_2O on the manometer. If a ventilator is available, set tidal volume to 15-20 ml/kg. MONITOR End-tidal CO_2 – normal is 35-55 mmHg in the anesthetized patient (35-45 mmHg in conscious patients); Do not over ventilate.

RECOVERY

Unfortunately, most anesthetic deaths occur in recovery and the majority of those occur within the first 3 hours of extubation (Brodbelt 2009). This is a good indicator that patients recovering from anesthesia often need support and monitoring to be continued into the recovery phase, especially for emergency and critical patients. Analgesia should also be re-addressed. If appropriate analgesia was utilized pre- and intra-operatively, the analgesic needs of the patient may be minimal. Opioid boluses and constant rate infusions are excellent choices during the recovery period. NSAIDs? They are anti-inflammatory and treat pain at its source (inflammation) making them very powerful. Use them if they are not contra-indicated.

Sample protocols for critical patients

Premedication options - dogs

- 0.25-0.5 mg/kg morphine OR 0.1 mg/kg hydromorphone OR 0.3-0.5 mg/kg methadone.
    - Can substitute 0.02 mg/kg IM buprenorphine for opioid but may not achieve adequate sedation or pain relief for most patients.
- Can administer the opioids IV if a rapid sequence of events (ie, premedication followed immediately by induction) is required or desired. If IV is chosen, fentanyl (5-10 microg/kg; 10-20 microg/kg in healthy patients) is another option.
- No other sedative is required if the opioid alone is adequate; if inadequate, add 0.1-0.2 mg/kg midazolam IM (NOT A GOOD SEDATIVE IN EXCITED PATIENTS) or either midazolam or diazepam (0.1-0.2 mg/kg for either) IV (usually used as part of induction).
- MAY use low-dose ace in SOME PATIENTS - not routine.
- Alpha-2 agonists are not commonly needed in critically ill patients but are commonly needed in emergencies that are painful or agitated but not physiologically compromised.

Premedication options - cats

- Full mu/kappa opioids used alone in cats can cause excitement but this is unlikely to happen in sick and/or painful cats. Hydromorphone at low dose (0.1 mg/kg) generally won't cause excitement but concurrent sedation may be required. Buprenorphine at 0.02 mg/kg won't cause excitement but neither will it provide noticeable sedation – although it will provide calming and that might be adequate for compromised patients.
- As with dogs, the opioids can be administered IV and any of the opioids, including fentanyl (5-10 microg/kg; 10-20 microg/kg in healthy patients) are appropriate for IV use.
- If more sedation is required, consider butorphanol (0.2-0.4 mg/kg) instead of the other opioids but remember that duration of analgesia is short and you will need to supplement with longer lasting drugs.
- No other sedative required if opioid alone is adequate; if inadequate, add 0.1-0.2 mg/kg midazolam IM (NOT A GOOD SEDATIVE IN EXCITED PATIENTS) or 0.5 mg/kg alfaxalone.
- One of my favorite protocols in compromised cats is 0.2 mg/kg butorphanol + 0.2 mg/kg midazolam IM. As with dogs, can also administer either midazolam or diazepam IV.
- Alpha-2 agonists are not commonly needed in critically patients but are commonly needed in emergencies that are painful or agitated but not physiologically compromised.
- MAY use low-dose ace in SOME PATIENTS - not routine.

Induction options – dogs & cats

- 0.2 mg/kg diazepam or midazolam or 1-10 microg/kg fentanyl followed by 2-4 mg/kg propofol or 2-4 mg/kg alfaxalone IV or 1-3 mg/kg ketamine IV or 0.5-2.0 mg/kg etomidate IV.

- 1/2 normal dose of diazepam/ketamine combination (1 ml/20 kg).
- **DO NOT MASK.**

Maintenance options – dogs & cats

- LOW-DOSE sevoflurane or isoflurane. Use ANALGESICS and keep inhalant dosage low.
- ALWAYS use IV fluids, even if the patient is normovolemic since anesthetic-drug induced cardiovascular depression can generally be overcome by counteracting the decrease in cardiac output with an increase in circulating volume. Thus, the routine use of IV fluids should be considered as a beneficial countermeasure to the detrimental cardiovascular effects of the anesthetic drugs – HOWEVER, do not overhydrate. Fluid therapy may not mean crystalloids for all patients, consider use of colloids, whole blood, etc...
- Monitoring during maintenance and well into the recovery period is crucial. Monitoring during maintenance should include assessment of heart rate and rhythm, frequency and depth of ventilation, pulse quality and strength, color of mucous membranes, **blood pressure**, pulse oximetry and end-tidal CO2.

Recovery: Continue monitoring/support; readdress analgesia; assess need for sedation or sedation reversal

Post-op / Discharge options – dogs & cats: Depends on disease but DO NOT withhold treatment - pain is a bigger stressor in compromised patients than in healthy patients. Generally, opioids +/- NSAIDs or grapiprant +/- alternative drugs.

WHISKER OF TRUTH: Fact & Fiction Anesthesia & Analgesia IN CatS

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NOTE: Some drugs in this presentation may not be available in all countries.

Cats Facts

- Often nervous or fractious: Increased circulating catecholamines and increased Fear/Anxiety/Stress (FAS) = 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 sometimes)

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 and 1.33% vs 1.4%, respectively; Brodbelt 2009).

Preanesthesia

As with other species, patients should be stabilized prior to anesthesia and premedication should be utilized to improve the safety of anesthesia by allowing a decrease in the dosages of induction and maintenance drugs. Anxiolytics are often very helpful to decrease FAS.

Common Previsit Pharmaceuticals

Gabapentin	100-200 mg/cat 2 hours before leaving home +/- night before leaving home
Trazodone	50-100 mg/cat, same timing as gabapentin, can administer with gabapentin
Maropitant	1-2 mg/kg orally 2 hours before leaving home, nausea/vomiting can cause FAS

Preoperative drugs or drug classes and key cat points:

Opioids	Excellent choice for all cats. Moderate to profound analgesia, minimal adverse effects, reversible effects. Many drug and delivery options. Cat specific opioids: Simbadol® (24-hr duration) & Zorbium® (4-day duration, transdermal).
Alpha-2 Agonists	Excellent choice for many cats. Mild to profound sedation with analgesia. Effects are reversible. Contraindicated in some forms of cardiovascular disease but may be beneficial in left ventricular outflow tract obstruction because of decreased heart rate. Causes emesis, prevent with maropitant.
Acepromazine	Often a good choice. Provides 4-8 hours of light to moderate sedation, which is a benefit, especially for many hospitalized cats. No analgesia, effects not reversible.
Benzodiazepines	Minimal adverse effects, minimal sedation in young, active patients. Can be effective, especially when combined with an opioid, in very young/very old/sick cats. Midazolam would be the most likely benzo to be used as a premed since it can be administered IM. Anxiolytic☺.
Ketamine	Often administered IM as part of an anesthetic protocol – so not really a premed but administered concurrently with premeds (usually dexmedetomidine and an opioid).
Alfaxalone	Can be used at a low dose (0.5-2.0 mg/kg) IM for moderate sedation of 20-45 mins in very young/old or sick cats (in general, not enough sedation for healthy or excited cats). Better sedation when combined with an opioid.

Cat facts vs myths & misconceptions for the premedication phase of anesthesia

Opioids can cause hyperthermia in cats The hyperthermia is usually – but not always - mild and self-limiting. Body temperature should be monitored postoperatively and any cat that seems agitated in recovery should be checked for hyperthermia. There is evidence that the degree of hyperthermia may be related to the degree of HYPO-thermia during the maintenance phase of anesthesia.

- Full opioid agonists (bind to mu and kappa) receptors are slightly more likely to cause excitement in cats than in dogs. Combine with a sedative to decrease excitement.
- Buprenorphine and butorphanol are unlikely to cause excitement but are less potent (especially butorphanol) than full mu agonists.

- Butorphanol only lasts about 90 minutes in the cat (Lascelles BD, Roberston SA. AJVR 2004;65(8):1085-1089); buprenorphine lasts 4-6 (MAYBE 8 with mild pain) hours.
- Oral transmucosally (OTM) administered buprenorphine results in lower serum concentrations of the drug. Increase the dosing range to 0.01-0.05 mg/kg BID-TID.
- Simbadol® is buprenorphine in a higher concentration (1.8 mg/ml) 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).
- Zorbium® is buprenorphine that was just approved by the FDA for cats. It provides 4 days of analgesia following transdermal administration. DEA Class III.
- Dexmedetomidine is also FDA-approved for use in cats. Alpha-2 agonists provide analgesia and a range of sedation levels (depending on the dose), can be administered IM and the effects are reversible with atipamezole. If you aren't using alpha-2 agonists in cats, you are missing out on a great drug class.
- Alpha-2 agonist mediated vasoconstriction causes increased cardiac work, which is why these drugs are contraindicated in many types of cardiovascular disease. However, the slowed heart rate can be beneficial in relieving left ventricular outflow tract obstruction (Lamont et al. JAVMA 2002;221(9):1276-81).
- Alpha-2 agonist mediated bradycardia is a reflex that occurs secondary to vasoconstriction mediated hypertension. This allows decreased cardiac work and is a beneficial reflex. Don't increase the heart rate unless the patient is bradycardic AND hypotensive.
- Should NSAIDs be administered to cats as premedications? Cats have pain of inflammation. Both meloxicam and robenacoxib are approved for preoperative use in cats and NSAIDs are generally most effective if used preemptively. However, NAIDs block the prostaglandin effect of vasodilation that occurs in some organs (eg, kidneys) during states of low-flow. Cats seem to be more likely than dogs to suffer NSAID-related adverse renal effects so administration of NSAIDs postoperatively, after turning off the inhalant so hypotension is unlikely, is also a good option.

Induction drugs and key cat points

Propofol	Can easily be titrated 'to effect'. Cleared by multiple routes. Causes mild to moderate dose-dependent cardiovascular and respiratory depression. Can be administered with a benzodiazepine or ketamine ('ketafol') to decrease propofol dose. IV only.
Alfaxalone	Can easily be titrated 'to effect'. Causes mild to moderate dose-dependent cardiovascular and respiratory depression. Can be administered with a benzodiazepine to decrease alfaxalone dose. Can be administered IM or IV.
Ketamine	Can be administered IM or IV. Minimal to no respiratory changes, provides mild to moderate increase in heart rate and blood pressure (through stimulation of the sympathetic nervous system). Cleared in part unchanged in the urine. MIGHT contribute to sympathetically-driven arrhythmias? No muscle relaxation, administer with a benzodiazepine or alpha-2 agonist. CRI for analgesia.
Tiletamine/ Zolazepam	Physiologic effects similar to ketamine/benzodiazepine. Very potent, small volumes easy to dose – and to overdose if not careful.
Inhalants	Not the safest choice for induction. Dose is very high – increases risk for anesthesia-related death. Staff are exposed to gases so human health concerns as well as cat health concerns.

Cat facts vs myths & misconceptions for induction drugs

- 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 the 'newer' 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 an excellent option in cats for both sedation and induction. It causes dose-dependent cardiovascular and respiratory depression similar to that of propofol but absorption after IM administration is an advantage in cats and small dogs.
- KETAMINE IS NOT CONTRAINDICATED IN ANY CAT BREED (eg, Savannah or Maine Coons). The presence of cardiac disease, which these breeds may be more prone to, could maybe be a contraindication – but not the breed. Because of their traditionally high anxiety, these breeds often benefit from a 'ketamine stun' dose added to premeds. Ketamine infusions are extremely low-dose and not a concern even with cardiac disease.
- Inhalant induction (mask or chamber induction) is a risk factor for anesthesia-related death and should NOT be the routine method of induction to anesthesia in cats (Brodbelt 2009).

Cat specific information on intubation:

- Intubate carefully (not cat-specific but cats are more difficult to intubate than most dogs).
- Apply a drop of lidocaine on each arytenoid. Cats are more prone than dogs to laryngospasm. Lidocaine reduces the likelihood of laryngospasm. Lidocaine does not cause adverse effects – cetacaine does.
- If still difficult to intubate, administer more induction drug. Don't intubate an awake cat.
- Inserting an endotracheal tube was a risk factor for anesthesia-related death in cats (Brodbelt 2009) – but it isn't the tube that is a risk factor, it is poor intubation that is risky.
- Laryngeal mask airways are an excellent option for cats. They are easy to place, do not damage the airway and come in a variety of sizes.
- 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, some of which led to euthanasia (Stiles J, et al. Vet J 2012: 2012;193(2): 367-73).

Cat facts vs myths & misconceptions for the maintenance phase of anesthesia

- As with other species, inhalant anesthetic drugs are commonly used for procedures lasting > 30 mins. Nothing cat specific.
- 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
        - Common combination: 0.1-0.2 MLS per 4.5 kg of cat of the following 3 drugs: dexmedetomidine, ketamine, buprenorphine (or 10 mg/ml butorphanol). Combine all 3 drugs in same syringe and administer IM. Use low-end of dose for deep sedation and high-end for anesthesia. Increase or decrease the dose if cat is larger/smaller than roughly 4.5 kg. This combination ('kitty magic') takes effect in 5-10 mins and provides 20-30 mins of anesthesia.
    - Tiletamine/zolazepam alone (not ideal – no sedation or analgesia)
    - Tiletamine/zolazepam opioid + an alpha-2 agonist
        - Common combination: Reconstitute the Telazol with 2.5 mls butorphanol (10 mg/ml) and 2.5 mls ketamine (sometimes called 'TTDex'). Dose the combination at 0.005 mls/kg for mild sedation, 0.01 ml/kg for moderate sedation, 0.02 ml/kg for profound sedation and 0.035-0.04 ml/kg for surgical anesthesia (Ko and Berman. Top Comp Anim Med 2010;25(2):92-97.
- 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. Use opioids, local blocks and infusions. Lidocaine infusions are controversial in cats but lidocaine -or any other local anesthetic – used as a locoregional block is very effective.

Monitors/Monitoring & key cat points

ECG	Can be hard to detect the **small complexes**. Increase the tracing amplitude.
Blood pressure - oscillometric	Can be hard to get a reading. Blood pressure is the same as in the dog, but the **small vessels** can be hard to detect. Be sure that the cuff is not too large (cuff width should be approximately 40% of limb/tail circumference) and positioned over the largest artery possible. The cuff should fit snugly on the limb. Too big or too loose = falsely low BP. Same comment on MAP vs SAP as described for the Doppler.
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). Author note: **Assume it as systolic and carefully assess the cat.** Treat if necessary.
SpO_2	Great! But cats are very likely to get cold (small body size) and **vasoconstriction** decreases likelihood of getting a reading. Reposition the probe to an area of better blood flow (eg, base of tongue). But first check the patient and make sure it is breathing normally!
ET CO_2	**Sidestream may provide average CO_2 rather than true end-tidal** reading in patients with small tidal volumes and high respiratory. rate. Can use an adapter that extends down into the ET tube to increase accuracy.

- Support
  Be careful with fluids!
  - Administration of fluids was listed as a risk factor for anesthesia-related death (Brodbelt 2009). But it isn't the fluid – it is the amount of fluid - that kill cats.
  - Calculate – and administer – the volume of fluids very carefully. Best to draw up the desired amount in a syringe vs trying to deliver a small volume from a fluid bag. Can also use rate-limiting tools like syringe pump or burette.
- Cats are very likely to be hypothermic – be aggressive with warming - & monitor body temperature
  - Prevention is 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.**

Cat facts vs myths & misconceptions for the recovery phase of anesthesia
Most unexpected anesthetic deaths occur in recovery (Brodbelt D, Vet J 2009;182:152-161).

Timing of Death	**% of cats that died (number of cats)**
After Premedication	1% (14)
Induction	8% (53)
Maintenance	30% (30)
Recovery	61% (106)
0-3 hours after Recovery	66 total cats

- Continue monitoring and supporting the patients until they are safely awake. Make sure cats are warm – but not hyperthermic.
- Also need to address pain and dysphoria. A rough recovery is not acceptable as it can lead to injury, high FAS and can contribute to hyperthermia. Think pain first and re-dose the opioids. May need to include a sedative. Alpha-2 agonists are excellent because they provide both sedation AND analgesia.
- Of course, we can also reverse the effects of the reversible drugs if necessary – but be sure to address analgesia! There are numerous myths regarding atipamezole in cats. Atipamezole at ½-full

volume of dexmedetomidine (0.5 mg/ml) IM or very slowly IV. Readdress analgesia even when using a lower volume as a full reversal can still occur depending on how much of the drug has been metabolized.

- Discharge drugs: NSAIDs, buprenorphine, maybe gabapentin or other drugs. Long duration buprenorphine (24-hr injectable and 4-day transdermal) should be considered to decrease care-giver burden and ensure cat gets its medications.

Further Reading

Grubb T, Sager J, Gaynor JS, Montgomery E, Parker JA, Shafford H, Tearney C. 2020 AAHA Anesthesia and Monitoring Guidelines for Dogs and Cats. J Am Anim Hosp Assoc. 2020 Mar/Apr;56(2):59-82. Open access: https://www.aaha.org/aaha-guidelines/2020-aaha-anesthesia-and-monitoring-guidelines-for-dogs-and-cats/anesthesia-and-monitoring-home/

Robertson SA, Gogolski SM, Pascoe P, Shafford HL, Sager J, Griffenhagen GM. AAFP Feline Anesthesia Guidelines. J Feline Med Surg. 2018 Jul;20(7):602-634. Open access: http://www.aapma.com/resources/2018_FelineAnesthesiaGuidelines.compressed.pdf#:~:text=%20%20%20Title%20%20%20AAFP%20Feline,%20%20Created%20Date%20%20%20201806190920007Z%20

Simon BT, Steagall PV. Feline procedural sedation and analgesia: When, why and how. J Fel Med Surg 2020;22(11):1029-1045. Open access: https://journals.sagepub.com/doi/pdf/10.1177/1098612X20965830

Suffering SuffNot Allowed: Treatment Options FOR CHRONIC PAIN

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NOTE: Some drugs in this presentation may not be available in all countries.

Pain Identification/Assessment: The main 'update' that we should be making in the area of chronic pain is increased utilization of tools to identify – and to help pet owners identify – pain in animals. It is almost impossible that more patients with chronic pain are presented to the veterinary clinic for treatment than are left at home to suffer from unidentified – and thus untreated – chronic pain. Unfortunately, animals rarely exhibit pain in the veterinary clinic unless we are really looking for it through palpation and targeted questions for the client. Chronic pain is best assessed by the owner at home and is usually assessed by 'quality of life' (QOL) changes rather than pain scores. It is difficult for owners (and often veterinarians) to detect pain in their pets but easier to detect the impact of that pain on the pet's QOL. Since the main concern regarding untreated/ undertreated pain is affective changes and decreased QOL, this is not only the easiest but also the most appropriate way to assess pain. Various pain assessment forms are available for the owner to use at home. In addition, it is helpful if owners video the pain behavior at home and share the video during the pet's appointment at the clinic.

Analgesic drugs: According to the new AAHA Pain Management Guidelines for dogs and cats (Gruen et al. J Am Anim Hosp Assoc 2022 Mar 1;58(2):55-76; https://www.aaha.org/aaha-guidelines/2022-aaha-pain-management-guidelines-for-dogs-and-cats/home/), the most effective drugs for treatment of chronic pain in dogs and cats are non-steroidal anti-inflammatory drugs (NSAIDs) and anti-nerve growth factor monoclonal antibodies (antiNGF-mAbs).

AntiNGF-mAbs: Nerve growth factor (NGF) is a potent pain generator and propagator, perhaps even more potent than prostaglandin. Nerve growth factor (NGF) binds to tropomyosin receptor kinase A (Trk-A) receptors on peripheral nerve endings, resulting in nociceptor depolarization and the potential for peripheral sensitization. NGF also binds to Trk-A receptors on pro-inflammatory cells like mast cells, resulting in the release of more inflammatory mediators which contribute to the development of peripheral sensitization. In addition, the NGF-TrkA complex is transported to the cell body in the dorsal root ganglia (DRG), where it modulates or increases expression of other receptors and ion channels involved in pain production (eg, transient receptor potential vanilloid 1, acid-sensing ion channels, bradykinin receptors, voltage-gated sodium channels, voltage gated calcium channels and mechano-transducers; Enomoto et al. 2018). This causes phenotypic alterations in primary afferent fibers, which leads to an increase in their excitability and a further contribution to peripheral sensitization. In addition, NGF/TrkA-mediated transcriptional changes occur, resulting in increased expression of pronociceptive neurotransmitters (eg, substance P, calcitonin gene-related peptide (CGRP) and brain-derived neurotrophic factor). With the increased nociceptive input to the dorsal horn neurons in the spinal cord, central sensitization is highly likely to develop. With the development of peripheral and central sensitization, pain becomes intense – perhaps even intolerable – to the patient.

Monoclonal antibody drugs are a leading platform for drug development because they have several advantages over most traditional pharmaceuticals including, injection rather than oral route of administration, long duration of action (4+ weeks) and elimination of the drug through protein catabolism and recycling rather than hepatic and/or renal clearance. One mAb drug, Cytopoint®, is already available in veterinary medicine. The new anti-nerve growth factor monoclonal antibodies are species specific for dogs (bedinvetmab, Librela®) and cats (frunevetmab, Solensia®) and have proven highly efficacious with minimal adverse effects for the treatment of osteoarthritis pain. Frunevetmab is now the first FDA-approved chronic pain drug for cats in the US. For a good review of the anti-NGF mAb and more information on its use for OA in veterinary medicine see Enomoto et al. 2018 (OPEN ACCESS, available at https://www.zoetisus.com/oa-pain/canine-oa-pain.aspx Nerve growth factor is a potent pain generator and propagator, perhaps even more potent than prostaglandins.

NSAIDs: Non-steroidal anti-inflammatory drugs (NSAIDs) are effective since most forms of chronic pain have an inflammatory component. NSAIDs provide analgesia AND treat pain at its source (inflammation). Multiple NSAIDs are approved for treatment of chronic pain in dogs. In some countries, there are no approved NSAIDs for treatment of chronic pain in cats, but there are guidelines and clinical reports demonstrating safety & efficacy of NSAIDs when administered at the correct dose to cats. **Both meloxicam and robenacoxib are approved in some countries for treatment of both acute and chronic pain in cats.** The meloxicam dose most commonly used for chronic pain in cats is 0.03-0.05 mg/kg PO SID. Dosages as low as 0.01 mg/kg/SID may be effective (Gunew, et al. 2008) and perhaps even beneficial – or at least not harmful - in some cats with chronic kidney disease (Gowan, et al. 2012; Gowan, et al. 2011). Robenacoxib is approved at 1-2.4 mg/kg (which is also the dose range for acute pain) for a duration 'decided on an individual basis' (robenacoxib European product label). The author commonly uses 1 mg/kg SID, or less frequency if effective, for treatment of chronic pain in cats.

Grapiprant is **not yet available** in all countries. It is a 'piprant', or prostaglandin receptor antagonist anti-inflammatory drug. 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) may be decreased. At the time this manuscript was written, grapiprant was not approved in cats but a published safety study indicated a wide safety margin in cats (Rausch-Derra & Rhodes, 2016).

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. There are few published research studies on the analgesic effects of gabapentin in dogs and cats but many practitioners are using the drug for control of various pain syndromes. In one of the few published studies a dose of 10 mg/kg gabapentin BID improved owner-identified impaired activities in osteoarthritic cats (Guedes et al 2018). And in dogs with neuropathic pain secondary to Chiari malformation, the addition of gabapentin was more effective in improving quality of life than carprofen alone (Plessas et al 2015). The dosage generally ranges from 3-10 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.

This is a 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.

Gabapentin can be compounded as a liquid, which may be easier to administer to cats. Gabapentin in a lipid formulation is absorbed when applied to the ears of cats (Slovak JE, Costa AP. JVIM 2021;35(4):1981-1987).

Pregabalin: The mechanism of action of pregabalin is the same as that for gabapentin but the drug undergoes linear pharmacokinetics, making dosing easier. Pregabalin is widely used in human medicine for treatment of a variety of chronic pain conditions. Research in animals is limited but has, for example, been shown to alleviate central pain from syringomyelia in Cavalier King Charles Spaniels (Thoefner et al. 2019; Sanchiz-Mora et al. 2019).

Other Anxiolytics/Antidepressants: Antidepressants are a common addition to pain management in humans. Their role in the pain pathway is in the descending inhibitory limb, which is a feed-back mechanism from central centers to the spinal cord. The tricyclic antidepressant amitriptyline at 3–4 mg/kg PO BID may be an effective component of a multimodal protocol in some patients (Moore 2016). In human medicine, serotonin and norepinephrine reuptake inhibitors (SNRIs; duloxetine, venlafaxine, desvenlafaxine, and milnacipran) are used for pain relief but no data are available for veterinary patients.

Tramadol may have some efficacy via this mechanism. Cats may also have an opioid effect but dogs produce very little of the intermediate (M-1) metabolite that is likely responsible for a good deal of tramadol-mediated analgesia. Tramadol used alone in dogs is unlikely to provide analgesia for OA pain (Budsberg et al 2018) Tramadol was effective at controlling osteoarthritis pain in cats (Monteiro et al 2017) but the margin between the effective dose and the dysphoric dose is very narrow. Cats really dislike the taste of tramadol.

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; Cohen et al. 2018), 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 following a loading bolus of 0.2-0.3 mg/kg is a common protocol. 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', which could be anything from never again to weekly. 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.

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 should be added to the treatment protocol anytime pain of 'wind-up' could be an issue. Scenarios include: NSAIDs suddenly 'not working' after controlling pain long-term, long standing untreated pain, moderate to severe cancer pain. Amantadine should be dosed at 2-7 mg/kg SID-BID (**BID is recommended**) for at least 3 weeks. It can be made as a compounded liquid, which may be easier to administer to cats.

Opioids: Opioids are not traditionally used – and are not the most effective drug class – for treatment of chronic pain but may be necessary for profound pain. Opioids to consider include transdermal fentanyl and oral formulations of codeine, codeine + acetaminophen (DOGS ONLY), morphine, oxycodone, hydrocodone and methadone. These opioids are DEA scheduled (fentanyl, codeine and morphine are Class II, codeine with acetaminophen is Class III) and have a high potential to cause adverse effects (primarily sedation, nausea and, eventually, constipation). 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. Fentanyl patches can be used in times of severe break-through pain or for 'end-stage' pain when a few days of pain relief prior to euthanasia are needed.

Buprenorphine (Class III) can be administered on the oral mucosa 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. Occasionally, very low dosages are surprisingly effective.

For all patients with chronic opioid use, consider that constipation may occur and increase dietary fiber.

Lidocaine infusions: In human medicine, perioperative lidocaine infusions have been shown to prevent the development of chronic pain (Bailey et al. 2018). Lidocaine infusions have also been shown to play a role in treatment of chronic pain and reduction of opioid need (Kandil et al. 2017). The dose is the low-end of the dose used for treatment of acute pain or arrhythmias. Remember that lidocaine infusions may be dangerous for cats.

Maropitant?: Although there are no studies on the use of maropitant to treat chronic pain, maropitant likely provides analgesia through antagonism of neurokinin-1 (NK-1) receptors in the pain pathway. Since maropitant can be administered orally, it is an option for owners to use at home and is anecdotally dosed at 2 mg/kg PO SID for conditions like chronic pancreatitis. Administration would be for as long as needed.

Steroids: Perhaps systemically, but better – targeted pain therapy like steroid epidurals (methylprednisolone acetate [eg, DepoMedrol] 0.1 mg/kg) or joint injections (methylprednisolone acetate – 'dose' is generally by volume which is limited by joint size but should not exceed 0.1 mg/kg).

Other compounds:

Cannabinoids (CBD): Efficacy is controversial in human medicine, where more studies on the products are available. In veterinary medicine, numerous studies are underway but only one has been published to date (Gamble et al. 2018). A good review on the topic from human medicine is: VanDolah HJ, Bauer BA, Mauck KF. Clinicians' Guide to Cannabidiol and Hemp Oils. Mayo Clin Proc. 2019 Sep;94(9):1840-1851 (OPEN ACCESS). Because cannabinoid receptors are present in the pain pathway, the compounds are likely to have efficacy – albeit potentially mild since the main site of action appears to be the descending inhibitory limb of the pain pathway. However, currently studies are limited by legal issues and product ingredients and purity are not regulated.

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. Here is a list of proposed modalities with references to utilize if you are interested:

Acupuncture: Strong evidence of efficacy (Petty MC, Huntingford JL. Evidence-Based Application of Acupuncture for Pain Management in Companion Animal Medicine Vet Sci 2022 May 26;9(6):252;

Silva et al. Effect of acupuncture on pain and quality of life in canine neurological and musculoskeletal diseases. Can Vet J. 2017 Sep;58(9):941-951; Fry et al. Acupuncture for analgesia in veterinary medicine. Topics in Companion Animal Medicine 29;2014:35–42).

Physical therapy/rehabilitation: Strong evidence of efficacy of various physical therapy/rehabilitation modalities for treatment of chronic pain (Lamoreaux Hesbach A. Manual therapy in veterinary rehabilitation. Topics in Companion Animal Medicine 29;2014:20-23).

Massage: Corti L. Massage therapy for dogs and cats. Topics in Companion Animal Med 29;2014:54-57.

Laser: Gross DM. Introduction to therapeutic lasers in a rehabilitation setting. Topics in Companion Animal Medicine 29;2014:49-53.

Myofascial trigger point release: Wall R. Introduction to myofascial trigger points in dogs. Topics in Companion Animal Medicine 29;2014:43-48.

Stem cells: There is moderate evidence in both humans and animals (examples: Kim et al. 2019; Sasaki et al. 2019; Shah et al. 2018) that stem cell administration can decrease pain from osteoarthritis. The limitations are cost (several thousand dollars per treatment) and need for anesthesia/sedation. There are several types of stem cells (eg, umbilical cord, mesenchymal) supplied from a variety of sources (autologous [patient's own cells], allogeneic [cells from a donor of the same species], xenographic [cells from another species, generally human umbilicus]).

Pulsed electromagnetic field therapy (PEMF): Gaynor JS, et al. Veterinary applications of pulsed electromagnetic field therapy. Res Vet Sci. 2018;119:1-8.

Platelet rich plasma (PRP):?

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 compounds may modify the progression of OA, especially diets rich in eicosapentaenoic acid (EPA) and potentially all omega-3 fatty acids, and some evidence for green-lipped mussels (Fox 2009). For the chondroprotective compounds, there is one injectable polysulfated glycosaminoglycan (PSGAG) available that is FDA-approved for the treatment of OA in dogs (Adequan®) in the US and pentosan polysulfate (Cartrophen) is used in Canada. The evidence for efficacy is moderate, with some patients not responding and some having a profound response. 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.

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. Listed in alphabetical order – not necessarily by order of preference.*

Drug	DOG Dosage mg/kg unless otherwise stated	CAT Dosage mg/kg unless otherwise stated	Comments
Amantadine (Various capsules, liquid)	2-7 PO SID-**BID** for at least 21 days	2-7 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.
Amitriptyline	3-4 PO BID	3-4 mg/kg PO BID	Serotonin-reuptake inhibition may provide analgesia through the

			descending inhibitory limb of the pain pathway. Some proof of this in humans. Tastes bad and $$.
Anti-NGFmAb	Minimum 0.5-1.0 mg/kg	Minimum 1 mg/kg LABEL: 1 **mL** cats 2.5-7.0 kg; 2 **mL** 7.1-14 kg	Cat approved in US, dog in other countries. SQ administration provides 4+ weeks of analgesia.
CBD oil	2 PO BID	Unknown	Gamble LJ, et al. Front Vet Sci. 2018 Jul 23;5:165.
Gabapentin (multiple tablet or capsule sizes; liquid)	3-20 PO BID-QID; up to 50; usually start with 5-10	3-20 PO BID-QID; up to 50; usually start with 5-10	Effective for treatment of neuropathic pain. Best used as part of a multimodal protocol. Increase the dose by about 25% every 5-14 days (depending on pain severity) until the patient is more comfortable or sedate. If sedate, go back to previous dose.
Ketamine (100 mg/ml) infusion	5-15 microg/kg/ min for minimum of several hours. Optimal duration unknown.	5-15 microg/kg/ min for minimum of several hours. Optimal duration 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. Use in multimodal protocol.
Ketamine (100 mg/ml) SC	0.5 mg/kg	0.5 mg/kg	At least weekly to start. Up to every day or every other day for severe pain, monthly may provide maintenance analgesia
Lidocaine infusion	25-50 microg/kg/min	CONTROVERSIAL 10-25micg/kg/min	Combine with ketamine. Optimal infusion duration unknown.
Maropitant	1-2 PO SID	1-2 PO SID	Perhaps best for visceral pain?
Pentosan polysulfate (eg, Cartrophen [CA])	Use label dose	Use dog dose	Not scheduled for cats. Clinically most effective for mild pain or as part of a multimodal protocol.
Polysulfated Glycosamino-glycan (eg, Adequan)	4 IM twice a week for up to 4 weeks, max 8 injections (label dose)	4 IM or SQ twice a week for up to 4 weeks, max 8 injections (dog dose)	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. Uptake following SQ injection proven in cats.
Pregabalin	4 PO BID	1-2 PO BID	No analgesic studies. Can cause sedation.
Tramadol (50 mg tablets)	2-5 PO BID -QID. Low bioavailability, needs frequent dosing. Up to 10 mg/kg?	2-5 mg/kg PO BID-TID. Start with 2 mg/kg BID. High bioavailability,	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

		likely to cause dysphoria.	or other analgesic drugs. **DEA CONTROLLED.**
Opioids			Chronic use may cause constipation. **DEA CONTROLLED. Maybe used for break-through pain.**
Oral morphine (10,15,30 mg tablets)	0.5-2 PO TID - QID (can be dosed as often as q2-4hrs)	0.25-0.5 mg/kg PO TID-QID (can dose as up to q 3-4 hrs)	Higher doses may induce sedation or dysphoria. Nausea & vomiting may also occur but tolerance to these effects generally develops within 1 week.
Sustained release oral morphine	2-5 PO BID - QID	Difficult to dose due to size of tablets (don't cut tablets)	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 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.
Codeine30-60 mg + acetaminophen (300 mg)	1-2 (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	3-5 ug/kg/hr	3-5 ug/kg/hr	May induce sedation or dysphoria. Adding NSAID may improve analgesia.
Methadone (various)	0.6 q 4-8 hrs OTM	0.6 mg/kg q4-8 hrs OTM	Absorbed transmucosally in cats – not yet proven in dogs but used anecdotally.
Buprenorphine (0.3mg/ml)	0.01-0.03 SC, IM, IV; 0.03-0.05 OTM	0.01-0.03 SC, IM, IV; 0.03-0.05 OTM	May cause mild opioid side effects.

FULL REFERENCES AVAILABLE BY THE AUTHOR ON REQUEST or at VetAACE.com/come learn with me

STOP pain: Local/Regional Blocks PARTS 1 & 2

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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 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.
- And blocks are very cost effective!!

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 IV
  - Lethal dose in dogs: 5-11 mg/kg IV
  - Data is mostly anecdotal in the cat but the general feeling is that 3 mg/kg IV is the toxic dose
  - **NOCITA**®: (not available in all countries) liposome-encapsulated bupivacaine that **provides analgesia for 72-hours**.
    - FDA-approved in both the dog (5.3 mg/kg) and cat (10.6 mg/kg)
    - FDA-approved for tissue infiltration (dog) and peripheral nerve block (cat) but used for both tissue infiltration and nerve blocks in both species.
    - Injection technique important – put the liposomes where you want them – ie, deliberate, thorough injection into the tissues/around the nerves.
- **Ropivacaine**
  - Onset of action: approximately 5-10 minutes (up to 20 minutes)

  - Duration of action: 4 to 6 hours
  - **IMPORTANT POINT:** Much less cardiotoxic than bupivacaine
  - **DOSE:** 1-3 mg/kg in the dog and 1-2 mg/kg in the cat
  - Convulsive dose in dogs: 20 mg/kg IV
  - Lethal dose in dogs: 42 mg/kg IV
  - No data in cats but predicted to have same wider safety range than bupivacaine
- **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

Additions to local blocks to prolong duration of action (potentially up to 24 hrs)

- **Buprenorphine:** 0.003–0.004 mg/kg (Snyder & Snyder, 2016; Grubb & Lobprise 2020)
- **Dexmedetomidine:** 0.0001 mg/kg (Bartel et al., 2016; Grubb & Lobprise 2020)

Adverse effects of 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)
- 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, especially of bupivacaine (but not NOCITA – high safety margin) can result in cardiovascular collapse. ONLY LIDOCAINE CAN BE ADMINISTERED IV.
- Anaphylaxis – rare, more common with esters (but still rare).
- 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.

- *Advanced techniques:* All of the blocks in this manuscript can be completed appropriate knowledge of anatomy, good palpation skills, a needle and syringe. However, more advanced techniques (nerve locators, ultrasound guidance) can also be used and may be an option for some practices. Desensitization for some blocks (eg, brachial plexus) may be more consistent with these techniques, whereas for some blocks (eg, intraperitoneal lavage) these techniques are not useful.

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.
  - NOCITA is a good choice for long duration 'field' block in both dogs and cats. Duration = 72 hrs.
- *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

- *Maxillo-facial ('dental' or '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).
    - 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
    - The caudal maxillary approach is often preferred over the infraorbital approach because the field of desensitization is much larger. This block will desensitize all ipsilateral tissue from the caudal molars rostrally and from the skin to midline. Use this approach if working on the caudal molars or doing surgeries on the nares, nasal passages, sinuses, soft palate or any other structures of the maxilla. In cats and brachycephalic dogs, the distance from the infraorbital foramen to the pterygopalatine fossa (where the maxillary nerve and its branches enter the skull) is very short and caudal diffusion of drug injected at the infraorbital foramen may be adequate for blocking the caudal structures of the skull.
    - **Extraoral approach 1** (extraoral, from zygomatic arch): 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.
    - **Extraoral approach 2** (extraoral, from bony orbit): Approach the pterygopalatine fossa from the bony orbit. The needle is placed at the midpoint of the ventral rim of the bony orbit and inserted straight down between the globe and the bone.
    - **Intraoral approach**: Open the mouth as wide as possible. From inside the mouth, insert a short needle no more than 2-4 mm (to avoid being close to the globe) inside the mouth just caudal and medial to the last molar.
    - 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 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 to ensure maximum caudal/distal diffusion of the drug into mandibular canal.

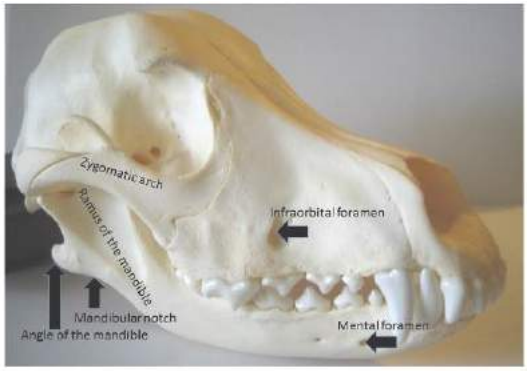


Figure 1: Diagram of a dog's skull showing the landmarks for a variety of local anesthetic blocks. Landmarks in the cat are the same as the dog. *Diagram from:* **Anesthesia and Pain Management for Veterinary Nurses and Technicians. Grubb T, et al. Teton New Media. 2020. Amazon.com**

- *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

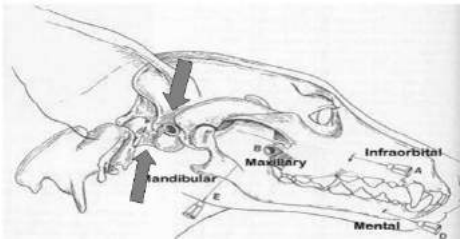
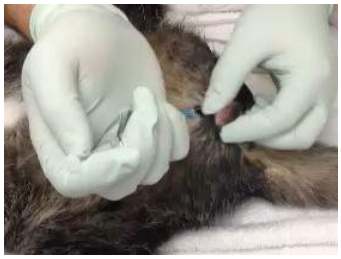


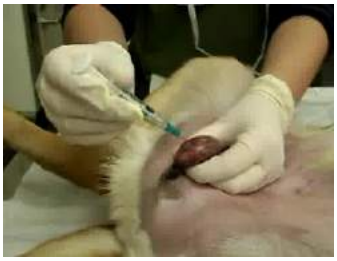
Figure 2: Landmarks for auriculotemporal and greater auricular nerve block. *Diagram From*: **Lumb & Jones Veterinary Anesthesia & Analgesia; 4th edition; 2009**

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) *Photos from:* **Anesthesia and Pain Management for Veterinary Nurses and Technicians. Grubb T, et al. Teton New Media. 2020. Amazon.com**





- *Mesovarium block or **peritoneal lavage (**Figure 4**)***
  - 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.
    - Elevate either 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' or 'lavaged' with local anesthetic.
    - After opening the linea (preferred) OR after completing the OHE, draw up 2-4 (cat) – 4-6 (dog) mg/kg lidocaine OR 1-2 (cat) – 2-4 (dog) mg/kg bupivacaine and, if necessary, dilute the drug with saline – the total volume needs to be 0.4-0.6 ml/kg to 'lavage' or 'bathe' the entire abdominal cavity. 'Bathe' the peritoneal cavity with the mixture by instilling it into the abdomen through the incision. Complete the OHE and close the incision as usual.
    - This technique may be more effective than mesovarium block since analgesia will be provided at both the ovarian and uterine surgical sites.
    - Publications are available in both dogs and cats for the efficacy of this block for OHE. In humans, the block is also used for abdominal exploratory surgeries and cesarean sections. These uses are also common in veterinary medicine, but there are no research studies.

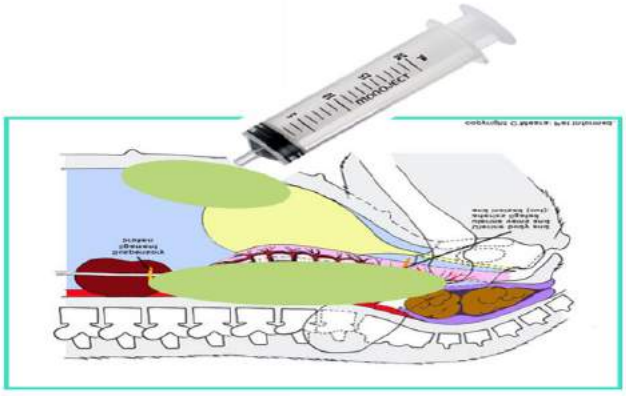


Figure 4: Diagram of local anesthetic spread following intraperitoneal 'lavage' in a dorsally recumbent dog or cat.

Adapted from:
Petinformedveterinaryadviceonline.com

- *Lumbosacral epidural analgesia (Figure 5)*
  - **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 the drug has been injected, remove the 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 incomplete 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.

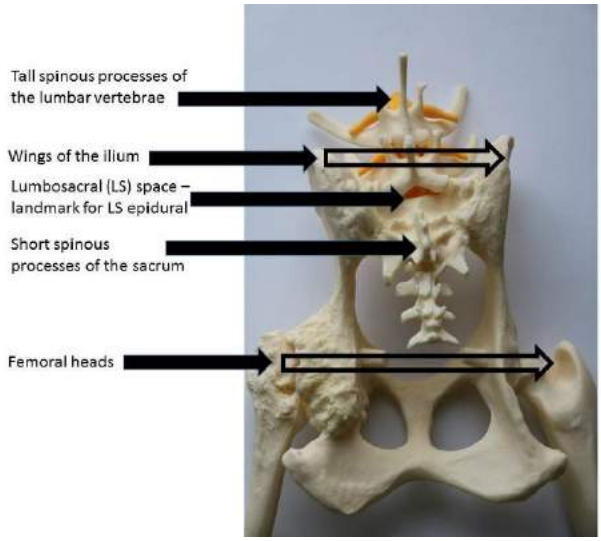


Figure 5: Diagram of the landmarks for an epidural injection into the lumbosacral space. *Diagram from:* **Anesthesia and Pain Management for Veterinary Nurses and Technicians. Grubb T, et al. Teton New Media. 2020. Amazon.com**

- *Sacrococcygeal or intercoccygeal epidural (Figure 6)*
  - 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.

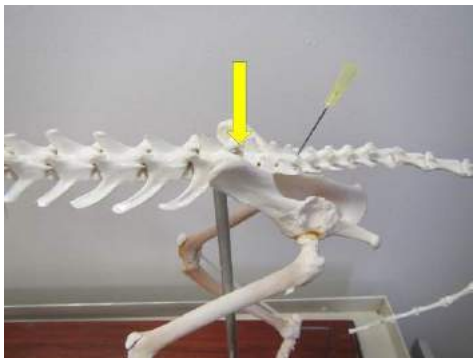


Figure 6: Landmarks for lumbosacral epidural (dark yellow arrow) and sacrococcygeal epidural (needle). *Diagram from:* **Anesthesia and Pain Management for Veterinary Nurses and Technicians. Grubb T, et al. Teton New Media. 2020. Amazon.com**

- *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 7)*
  - 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).
- NOCITA FDA-approval in cats is for a similar (4-point) block.
- 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

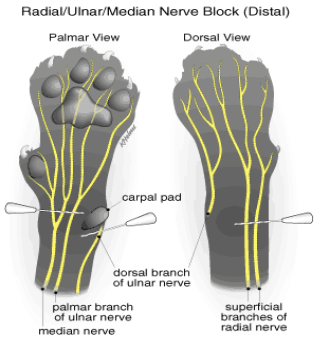


Figure 7: Diagram of a cat's distal forelimb showing the locations for placement of local anesthesia for desensitization of the meta-carpals/tarsals & digits. Diagram used with permission from Tranquilli WJ, Grimm, KA, Lamont LA. Pain Management for the Small Animal Practitioner. Teton New Media Jackson, 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.

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- **GREAT RESOURCE:** WSAVA.org; go to tab 'committees', click on 'global pain council', scroll down to 'Pain Management Guidelines' (manuscript) and 'Educational Videos' (local block videos!). https://wsava.org/committees/global-pain-council/

What Are They Hiding? Pain Assessment in Dogs and Cats

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The main barrier to treating pain in animals: We can scientifically prove that animals feel pain since the pain pathway is very similar across mammalian species – thus, if a stimulus is painful to a human, it is painful to a dog or cat. But due to an evolutionary need for survival, **animals hide pain from humans** (and other animals). This instinct may be even stronger in cats and this, along with their more sedentary lifestyle when compared to dogs, results in pain being diagnosed less frequently in cats than in dogs. Difficulty in diagnosing/recognizing pain in both species is true for both acute and chronic pain and for in-hospital and at-home pain. Untreated pain causes a myriad of adverse effects that impact health, behavior, quality of life and welfare. Thus, it is imperative that the veterinary team and animal caregivers learn to identify pain in our patients and pets so that pain can be effectively treated. For an in-depth discussion of both acute and chronic pain and a list of validated pain scoring systems, see the 2022 WSAVA Global Pain Council Guidelines (https://wsava.org/Global-Guidelines/Global-Pain-Council-Guidelines/). In addition to the Global Pain Council Guidelines, an excellent review of assessment of acute pain in cats is available: Steagall PV, Monteiro BP. Acute pain in cats: Recent advances in clinical assessment. J Feline Med Surg. 2019;21(1):25-34.

ACUTE PAIN

Instead of relying on the patient to exhibit pain signs, pain should be **anticipated** and analgesic plans made based on the presumed level of pain from the surgical procedure, traumatic injury or disease/condition that the patient is experiencing. This can be accomplished using knowledge of the pain level in humans for that stimulus and by understanding that the degree of pain in an animal would be very similar in an animal (for examples of expected pain levels see: Mathews KA, Vet Clinics of North America, Small Animal Practice 2000;30:729-755.). However, pain is a very **individual sensation** and the analgesic protocol, even one that is very robust, may not be adequate for all individual patients. Thus, the pain level should be assessed in all patients.

Assessment

A brief pain exam should be a routine part of the postoperative physical exam. A few quick pain assessments can be added to the post-operative physical exam that can provide a normal/abnormal 'diagnosis'. The patient should be examined more in-depth if abnormalities are identified during the pain exam, just as the patient would be examined more in-depth if any abnormalities were identified during any other part of the physical exam.

What is assessed in a pain exam?

For a 'quick look' (these can all be assessed from outside the cage):

1. CATS: Facial expressions or 'grimace': 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 pain-related changes in facial expressions has been described and validated in a number of species. The Feline Facial Grimace Scale is a validated, easy to use scale (Evangelista et al. 2018) that can be used first as a screening

tool as part of a 'quick' look and second as the actual pain scoring tool to assign a pain level to the cat. The scale and a training manual for the scale are available as open access (see links in list of scoring systems). **You need this!** The same facial pain indicators can be used in dogs but have not yet been validated by research. In part, this is because there is more variability in dog skull/facial anatomy, thus potentially more variability in exhibition of facial expressions. The grimace scale is difficult to use in both dog and cat brachycephalic breeds.

2. **Body posture**: Changes in posture like 'tucked' abdomen or 'hunched' back, head down, neck stretched, ears rotated outward (cat) or flat (dog) and tail down/tucked are all signs that could indicate pain. Body posture while lying down is also important. For instance, cats generally sleep 'curled up' in cold environments, like most veterinary hospitals, and cats that are laying stretched out in this environment may be experiencing pain. Dogs laying in awkward or not normal positions may also be experiencing pain.
3. **Behavior**: Has the patient's behavior changed? There may be some residual effects of drugs in the immediate postoperative period (especially for the first 30 minutes in most patients) but a major behavior change should be obvious and subsequent assessments will be less impacted by anesthetic drugs. Common behaviors to watch for: defensive/aggressive (growling/hissing in a previously non-vocal cat; growling, excessive barking in a previously quiet dog, etc.), hiding or not interacting in a previously friendly cat or dog, etc. Although this is first assessed from **outside the cage**, the cage door should be opened so that the person assessing pain can **interac**t with the patient.
4. Vital signs are **not pain specific** and not included in many pain scoring systems but abnormalities detected in a routine physical exam should be investigated and may be attributed to pain. Since pain is a stressor, physiologic signs of stress can occur and include tachycardia, tachypnea, hypertension, arrhythmias, etc… However, a change in physiologic parameters without any other change may not indicate pain and pain can be present without changes in physiologic parameters. Also, physiologic parameters can be altered by any stress, including hospitalization, loud environment (eg, barking dogs!), etc… so they must be assessed in conjunction with other signs of pain.

A little deeper look:

1. If abnormalities are detected on any parameter above, do a more focused pain exam. GENTLY **palpate the areas around the wound or incision** to assess for both localized and expanding pain areas. Watch the patient **move** around the room and/or use other manipulations specific for the source of pain (eg, flex/extend joints).
2. Obviously the patient will receive analgesia if pain is detected. If unsure, assume pain is present, **administer analgesics and evaluate the response**. We call it 'asking' the animal if it is in pain and this is often the most useful way to determine the presence or absence of pain. For acute pain, an opioid is often the best option because of the rapid onset and potency of the drug class. If the patient's behavior returns to normal after treatment, then the diagnosis has been made – PAIN, and now a treatment plan that will address the patient's analgesic needs can be made. 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/or 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 to determine the cause of the behavior change are begun.

Scoring Systems: Acute Pain

All of the information from the pain assessment should be put into a pain score in the patient's record (and on the cage card if your practice uses them). No pain scoring system is perfect, especially since we 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) AND before and after pain relieving treatment. Using the same person to score the patient improves the consistency of results from the scoring system. Systems are available for both acute and chronic pain. The previously mentioned Feline Grimace is the most commonly used scale in cats. The Colorado State

University pain scale, an easy-to-use descriptive scale, is available for both dogs and cats but has not yet been validated by research. The Glasgow Composite Short Form has been at least partially validated to identify pain in both dogs and cats. Another validated pain scale for cats is the UNESP-Botucatu scale from Brazil. The website includes a series of videos of painful cats for scoring practice. Whether you use this scale or not, the practice section is very useful for the entire veterinary team.

The Feline Grimace, CSU, Glasgow and Botucatu scales can be downloaded at the following sites:

Feline Grimace: https://www.felinegrimacescale.com/

CSU Canine: https://vetmedbiosci.colostate.edu/vth/wp-content/uploads/sites/7/2020/12/canine-pain-scale.pdf

CSU Feline: https://vetmedbiosci.colostate.edu/vth/wp-content/uploads/sites/7/2020/12/feline-pain-scale.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: https://animalpain.org/en/home-en/

CHRONIC PAIN

As is the case in human medicine, osteoarthritis (OA) is the main cause of chronic pain in dogs and cats. Experts estimate that the overall incidence of OA in all ages of cats and dogs is 40% of the total cat or dog population. Based on radiographic evidence, 90% of cats over 12 years old (Hardie EM, et al. J Am Vet Med Assoc. 2002;220(5):628-32) may have OA. This does not mean that all of these cats have pain, but it is likely that more have pain than are being treated. Other causes of chronic pain include orofacial/dental disease, gastrointestinal disease like pancreatitis and inflammatory bowel disease, cystitis, otitis, cancer and nonhealing wounds or surgical sites. As with acute pain, instead of solely relying on the patient to exhibit easily recognizable signs of pain, analgesic plans should be made based on the presumed level of pain from the chronically painful disease/condition that it presents with.

Assessment

Although the expected prevalence of OA is similar between dogs and cats, cat owners are less likely than dog owners to identify pain in their pet (AVMA Sourcebook 2017-2018). Identifying chronic pain can be very difficult for a number of reasons. 1) Owners often mistake signs of pain for 'just getting old'; 2) Evolutionarily, animals hide pain, especially cats – who can be both predators and prey. As prey, their natural instinct is to hide any vulnerability that could increase predation, including pain. However, the impact of pain on the cat's lifestyle and quality of life can be discerned if cat owners are educated on pain manifestation. As with acute pain, change in behavior is the most common sign that the dog or cat might have chronic pain. Examples include: previously friendly, gregarious animals that are now spending all of their time hiding; previously fastidious animals that have stopped grooming; and animals that suddenly start urinating and defecating right outside the litter box (cats) or in the house (dogs). Of course, these can all be signs of other medical issues so a full medical assessment is necessary to rule in (or rule out) pain as the cause. 3) Cats (and some dogs) are largely sedentary, making pain-related mobility changes more challenging to observe, and are often at least semi-nocturnal, so the owner may be sleeping when the cat is exhibiting mobility changes. Mechanistically, feline OA is often idiopathic and bilateral as compared with canine OA, which is primarily secondary and unilateral. Thus, classic limping as exhibited by dogs is unlikely to be exhibited by cats. Finally, cats also spend more time moving vertically (eg, jumping, climbing). Vertical mobility changes, which most owners do not know how to identify, are important indicators of cat OA pain. Owners should be educated that cats with a favorite high-up perch that they no longer jump to might be painful.

The successful identification and treatment of chronic pain lies largely on the pet caregiver. To educate caregivers on signs of both dog and cat pain, we need to reach them. Placing information on chronic pain assessment on clinic websites, Facebook pages, in-clinic media (eg, TV screens), etc… is critical. Some

excellent owner (and veterinary professional and staff!) resources are available at: https://www.zoetispetcare.com/checklist/osteoarthritis-checklist-cat and for dogs, https://www.zoetispetcare.com/checklist/osteoarthritis-checklist

As with acute pain, if unsure, assume pain is present, **administer analgesics and evaluate the response**. We call it 'asking' the animal if it is in pain and this is the most useful way to determine whether or not an animal is in pain. For chronic pain, an NSAID is often the best choice, but a dose of an opioid can be used to make a rapid decision. As with acute pain, 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 address the patient's analgesic needs. Again, as with acute pain, relief of severe pain often requires multimodal therapy and may require higher than expected drug dosages so provide more aggressive therapy if pain is suspected but not relieved by one drug alone.

Scoring Systems: Chronic Pain

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 is critical in evaluation of their pet's pain and in and pain relief.** However, owners generally have difficulty recognizing pain itself but can recognize the *impact* of pain, or the 'pain affect' on their pets. Thus, quality of life (QOL) scales are much more effective for pain identification by the owner. If the owner is unsure if a certain behavior might be pain related, they should be encouraged to take videos of their pet doing that behavior and have them send or bring the video to the clinic. Videos can be very helpful. Once the pet is at the hospital, the veterinarian can use the information from the video and can utilize specific pain exams (eg, joint palpation) to identify the presence of pain.

In addition to behavior, mobility should be included in the pain assessment. Specific questions (eg, does your cat still jump up to its favorite spot?; does your dog walk beside or ahead of you or does it lag behind? Is this normal for the dog?) should be included in chronic pain scales/questionnaires.

A validated chronic pain scales for cats, along with information for both veterinary professionals and owners is the Feline Musculoskeletal Pain Index (FMPI) at http://painfreecats.org/about-us/

The Client Specific Outcomes Measure (CSOM) is used for both dogs and cats and has become tool used not only by veterinary professionals and owners but also accepted by the US Food & Drug Administration (FDA), along with other regulating agencies, to determine efficacy of chronic pain drugs (example, frunevetmab, etc). https://pubmed.ncbi.nlm.nih.gov/17552444/

For diagnostics, very thorough videos demonstrating a complete cat diagnostic OA exam with joint palpation can be found at: https://www.zoetisus.com/conditions/petcare/oa-pain/feline-oa-pain#feline-exam-videos

The website https://www.galliprantvet.com/us/en/coast-tools outlines the COAST osteoarthritis scoring system for dogs with information for both owners and veterinarians and http://www.newmetrica.com/vetmetrica-hrql/.

Both Canine Arthritis Resources and Education (CARE) https://canineарthritis.org/ and Canine Arthritis Management https://canineарthritis.co.uk/ have information for veterinary professionals but also a very strong focus on client education.

In addition, quality of life (QOL) scales are not specific for pain but pain is one of the many causes of decreased QOL that owners should be aware of. These scales are often quite easy for owners to use and can

identify un- or under-treated pain and the resulting negative impact on the pet. Numerous QOL scales are available. Two open-access and easy to use examples are:

1) H5M2 scale https://www.tuftsyourdog.com/dogtrainingandbehavior/quality-of-life-hhhhhmm-scale/ The 5 H's are Hurt, Hunger, Hydration, Hygiene, and Happiness and the 2 M's are Mobility and More Good Days than Bad. The criteria are scored 0 to 10, with lower scores indicating a bigger impact on QOL; and

2) the Lap of Love scale which is similar and a bit streamlined https://www.lapoflove.com/how-will-i-know-it-is-time/lap-of-love-quality-of-life-scale.pdf

Future Technology

Wearable monitors, like accelerometers, could potentially be the most efficient way to monitor the patient's pain status. Some wearables may be simple, like many activity monitors or 'accelerometers'. However, even activity monitors need to be validated for dogs and cats and must be able to identify movement quality rather than simply quantity (eg, a painful patient that is restless and can't find a comfortable way to sleep will show high activity – but it is not 'normal' activity). Specific identifiers for cats will be needed since cats tend to move as much vertically as horizontally. Research in this technology is ongoing at Aniv8 (https://aniv8.com/ [US only for now]) A new monitor that uses biosignals to identify pain is PainTrace® at: https://biotraceit.com/paintrace-vet/ [US only for now]. When used for pain identification/assessment, this technology has far-reaching potential including not only diagnosing acute and chronic pain in patients but also tracking efficacy of analgesic therapy, assessing owner compliance in analgesic administration, promoting animal welfare and enhancing pain/analgesia research.

SUMMARY

Animals DO feel pain but are very adept at hiding pain so we must learn to look for pain. Physiologic, physical and behavioral signs of pain can be used to identify patients that need analgesic therapy. If unsure whether or not the animal is in pain, 'ask' the animal pharmacologically if it is in pain and monitor the patient's response to treatment. Future pain assessment tools are in development.

Lulich J.P.

DVM, PhD, DACVIM

TRIGGERS MARKERS AND TREATMENT OF ACUTE KIDNEY INJURY

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The kidneys are at high risk for ischemic and nephrotoxic injury because they receive a high proportion of cardiac output (20%), have a high metabolic (energy) demand, and potentially concentrate toxins in renal tubules. AKI is dynamic necessitating frequent monitoring, adjustments in fluid therapy high index of suspicion, Early identification allows removal and earlier repair processes to occur. Can occur on top of CKD.

Definitions:

Acute Kidney Injury is a rapid and abrupt decline in kidney function. Because creatinine is an insensitive marker of glomerular filtration rate at low levels of dysfunction, significant damage to the kidney and its function can occur with creatinine remaining in the normal range. If AKI remains unrecognized, kidney damage ultimately leads to acute kidney failure and its consequences, including death.

Acute Kidney Failure is the rapid accumulation of uremic toxins (e.g. azotemia) and dysregulation of fluid (e.g. inappropriately low urine specific gravity), electrolyte and acid base balance due to a recent hemodynamic, filtration, tubulointerstitial, or outflow injury to the kidneys. AKF and AKI can be used interchangeably.

Phases of AKI

Phase	Characteristics	Clinical Significance
Initiation	The inciting cause damages the kidney.	Clinical signs rarely evident Decreased renal function commonly overlooked Early intervention prevents damage
Extension	Continued damage even though the initial cause may be gone. Kidney function further deteriorates. Structural changes develop.	Intervention is losing its opportunity to reverse the outcome.
Maintenance	Established and measurable decreased kidney function. A critical amount of damage has occurred. Some may not be reversible. Lasts 1 to 3 weeks.	Typical time when most cases are diagnosed. Urine output may increase initially but commonly decreases necessitating strict fluid monitoring and reduction to prevent over-hydration.
Recovery	Make last weeks to months.	Initially heralded by an increase in urine volume necessitating

	Not all will recovery with a good quality of kidney function	careful fluid monitoring to prevent dehydration. CKD is a common consequence.

MECHANISMS OF RENAL DAMAGE

Several mechanisms can result in acute kidney damage. Of these ischemia and nephrotoxin exposure appear to be the most common. The kidneys are susceptible to ischemia and toxins because of their unique anatomic and physiologic features. The large renal blood flow (approximately 20% of the cardiac output) results in increased delivery of blood-borne toxins. The renal cortex is especially susceptible to toxin exposure because it receives 90% of the renal blood flow and contains the large endothelial surface area of the glomerular capillaries. In the process of reabsorbing water and electrolytes from glomerular filtrate, tubular epithelial cells may also be exposed to increasingly high concentrations of toxins. Likewise, toxins that are either secreted or reabsorbed by the kidney may accumulate in high concentrations within tubular epithelial cells. Finally, the kidneys also play a role in the biotransformation of many drugs and toxins. Biotransformation usually results in the formation of metabolites that are less toxic than the parent compound; however, in some cases metabolites (i.e. ethylene glycol) are more toxic.

Iatrogenic disease to the kidneys may also occur with unexpected trauma and infection. Knowing how to biopsy the kidney is just as important as knowing when biopsy is indicated. Unwarranted renal trauma can also occur with surgery to remove clinically insignificant nephroliths and ureteroliths. Iatrogenic urinary tract infections are often associated with use of urinary catheters (table 2).

Lastly, unwarranted kidney injury can result from unrecognized reversible kidney injury or inappropriate therapy for kidney disease. For example, failing to recognize ureteral obstruction until the development of hydronephrosis may result in a shorter lifespan.

Primary acute kidney failure may result from many causes most commonly results from ischemic and/or toxic renal insults. The term acute tubular necrosis (ATN) is used to describe the syndrome in which abrupt and sustained reductions in GFR result from ischemic or nephrotoxic injury. Reduced GFR is thought to result from a combination of vascular (renal vasoconstriction and reduced glomerular ultrafiltration coefficient) and tubular (renal tubular obstruction and back-leak of glomerular filtrate) effects, and cannot sometimes be immediately reversed by eliminating the initiating cause (e.g., renal ischemia due to hypovolemia). Post renal causes of acute kidney failure include urinary obstruction and rents in the urinary tract. It is essential that reversible causes of kidney failure be recognized and treated as early as possible.

Preventing Acute Uremia

The most effective method of preventing acute uremia is to recognize who is at risk and how to prevent it (table 1). Ignoring diagnostic tests or early treatment of common causes of acute kidney disease may result in irreversible kidney failure and possibly death.

Table 1. Potentially Reversible Causes of Acute Azotemia

Prerenal	Dehydration
	Hypoalbuminemia
	Hypoadrenocorticism
	Cardiac Failure

Renal	Ischemia: Prolonged hypovolemia, Nonsteroidal anti-inflammatory drugs, Thromboembolism
	Toxins: Aminoglycosides, Amphotericin B, Ethylene Glycol, Heavy metals, lily (cats), grapes and raisins (dog), radiocontrast agents, hypercalcemia, D3 rodenticides, superphosphate fertilizers, Ethylene glycol, pesticides, herbicides, solvents
	Infectious Agents: Bacterial Pyelonephritis, Leptospirosis, Borreliosis, Fungal pyelonephritis
	Endogenous metabolites: Hemoglobin, myoglobin
	Miscellaneous: Snake venom, shock,
	Glomerulonephropathy
Postrenal	Urinary obstruction
	Urinary tract Rupture

Treating Acute Kidney Disease

Treatment goals include limiting further renal damage and enhancing cellular recovery, improving renal oxygen delivery, and maintaining urine output. This includes maintaining acid-base abnormalities to improve survival.

General Measures

1. Identify and correct prerenal and postrenal causes.
2. Stop nephrotoxic drugs
3. Strictly monitor intake/output and daily weight.
4. Optimize cardiac output to maintain renal perfusion.
5. Optimize nutrition and treat any infections.
6. Indications for renal replacement therapy (RRT): volume overload, severe or progressive hyperkalemia, or severe metabolic acidosis refractory to medical management; advanced uremic complications (pericarditis, encephalopathy, bleeding diathesis); pulmonary edema

Fluid Therapy: The most effective therapy (besides avoidance and removal of nephrotoxins) is accurate management of fluid balance. This involves careful assessment of hydration, appropriate selection of fluids, frequent reassessment and fluid adjustments. Patients may be predisposed to dehydration during maintenance and recovery phases of acute kidney failure because involuntary urine losses are often great. In order to prevent dehydration, the volume of parenteral fluids administered and oral fluids consumed should equal the sum of: 1) urine volume, 2) contemporary fluid losses (e.g., fluid lost via vomiting, diarrhea), and 3) insensible fluid losses (20 to 25 ml/kg/day; fluids lot via respiratory, skin, and gastrointestinal tract). Because

estimation of contemporary and insensible fluid losses may be inaccurate, serial determinations of body weight are commonly used to guide fluid therapy.

Conversion of Oliguria to Nonoliguria: If oliguria persists despite correction of fluid deficits, therapy designed to increase urine volume is indicated because clinical management of nonoliguric patients is easier and their prognosis appears to be slightly better. Use of diuretics or vasodilators in nonoliguric patients is generally discouraged because they are rarely needed and therefore unnecessarily expose the patient to risk of fluid and electrolyte depletion, additional kidney injury, or adverse drug reactions.

A therapeutic trial with diuretics is indicated for most patients with oliguric acute kidney injury. Furosemide and mannitol are the diuretics most commonly used. Patients that fail to respond to one of these diuretics may respond to the other or a combination of both. Alternatively, diuretics may be used in combination with vasodilators such as dopamine.

Furosemide has been the most commonly used diuretic in canine and feline patients with oliguric kidney failure because it is relatively safe, readily available, and familiar to most veterinarians. Initially, it should be administered intravenously at a dose of 2-mg/kg body weight. If no substantial diuresis develops within one hour after administration, the dose may be doubled (4 mg/kg). If this dose also fails to induce diuresis, the dose may be further increased to 6-mg/kg body weight. If diuresis still does not ensue with very large doses of furosemide, an alternative diuretic (e.g., mannitol), or the combination of furosemide and dopamine may be considered.

If furosemide successfully induces diuresis, it may be repeated at 8 hour intervals as needed to sustain diuresis and promote potassium excretion. However, the need for continued furosemide therapy must be considered in light of its potential adverse effects. It has been suggested that furosemide should not be used in patients with suspected gentamicin-induced acute kidney failure because it may promote aminoglycoside nephrotoxicity.

Mannitol has at least three theoretical advantages over furosemide: 1) it may enhance kidney function by minimizing renal tubular cell swelling via its osmotic properties, 2) mannitol exerts its diuretic effects along the entire nephron and therefore may directly affect the proximal tubule, and 3) mannitol may expand the extracellular fluid volume. The major disadvantage of mannitol is the potential for vascular overload if oliguria persists. Therefore, mannitol should be avoided in over hydrated oliguric patients. Mannitol (20 or 25% solution) is administered intravenously over 5 to 10 minutes at a dose of 0.25 to 0.5 g/kg body weight. If substantial diuresis ensues, administration of mannitol can be repeated every 4 to 6 hours, or administered as a maintenance infusion (8 to 10% solution) during the initial 12 to 24 hours of treatment.

Limiting Uremic Signs: Clinical manifestations of uremia are ameliorated by a combination of dietary protein restriction and pharmacological control of uremic gastritis and vomiting. Adult dogs should receive approximately 8 to 12 percent of their calories as protein. Adult cats have a higher daily protein requirement than dogs, and therefore should receive approximately 20 percent of their diet calories as protein. Protein restriction minimizes production of nitrogenous waste products that may be responsible for many clinical signs of uremia. In addition, protein restriction may have a protective effect against additional ischemic or nephrotoxic kidney injury.

Ameliorating Uremic GI Signs
Antiemetics

a. Maropitant citrate *(Cerenia*® 1mg/kg SC q24hr) Selective serotonin antagonists (5-HT3) *(Anzemet – dolasetron;*
b. *Zofran – ondansetron; 0.1-0.2mg/kg q 8hr)*
c. Proton Pump Inhibitors (pantoprazole 1 mg/kg IV q24hr) or H2 Blockers are generally out of favor because they are not effective or because GI ulceration is low?

d. Sucralfate
e. Uremic stomatitis: 0.1-0.2% chlorhexidine solutions/gels q 6-12 h or a Sucralfate slurry

Use Antibiotics if When Infectious Diseases are Likely: Patients suspected of leptospirosis, Lyme's disease, and pyelonephritis should be treated immediately upon hospitalization. Waiting for confirmatory results while withholding correcting therapy may result is a less favorable outcome.

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What Every Clinician Needs to Know about Urolithiasis

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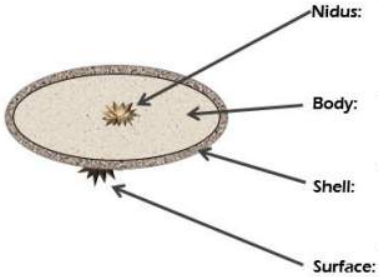
Uroliths (also known as calculi or stones) are solidified aggregates of mineral and non-mineral crystalloids that form in the urinary tract. The urinary tract is designed to eliminate wastes in a liquid form. Uroliths form when urine becomes oversaturated with crystallogenic precursors. Most uroliths are composed of biogenic minerals, but also form from drug metabolites, amino acids or over foreign substances such as suture material from a previous cystotomy.

What is the anatomy of a urolith?



	Description	Significance
Nidus:	Area of obvious initiation of urolith growth, which is not necessarily the geometric center of the sample.	In general, the mineral type(s) in the "nidus" layer should be the primary focus of preventative measures because the nidus is the area of urolith initiation. Preventing a nidus of foreign material such as suture, plant, etc. is also important to prevent urolith recurrence.
Body:	The major portion of the urolith.	The "body" layer comprises the largest bulk of the sample. If no nidus layer is listed (or the nidus is similar in composition to the body layer), this should be the focus of preventative measures.
Shell:	A complete outer concentric lamination of the urolith	Shell and/or surface layers represent the most recent activity in the urolith formation process. Often, shell and surface layers that are significantly different from the composition of the body layer reflect changes in diet, medication, or the patient's medical condition.
Surface:	An incomplete outer lamination of the urolith	See "Shell" significance above.

1. How to make the diagnosis

Medical imaging is required. Difficulty passing a urinary catheter and bladder palpation and not reliable, but done carefully is helpful. Two most common techniques is radiology and ultrasonography. These two procedures are not mutually exclusive – meaning both techniques may be necessary to make the diagnosis (e.g. non-radiopaque uroliths and uroliths in the urethra)

2. Predicting Urolith Composition

Knowledge of urolith composition is important because contemporary methods of detection, treatment, and prevention of uroliths and their underlying causes are based primarily on knowledge of urolith composition. This poses a problem when uroliths are not available for quantitative mineral analysis until they are removed. To overcome this problem we recommend predicting urolith composition on the basis of radiographic appearance, breed and gender of the patient, and evaluation of urinalysis and serum chemistry profile results. The Minnesota Urolith Center has developed an App to assist you. Go to your app store and select MN urolith for iphones and android devices. On the bottom activate CALCulate for predicting urolith composition based on breed, gender and age. Activate CALCuRad to input a picture of canine uroliths on

radiographs (if the CALCuRAD is not on the menu, force close (not remove the app) the app and then reopen it; it should be there now).

3. When To Dissolve Uroliths & When To Do A Cystotomy

These decisions are based on client preferences, stone type, and stone location. Because of the ease and success of struvite dissolution in the cat, struvite dissolution is the standard of care unless the stone is in the urethra or causing obstruction. Infection induced struvite uroliths in the dog requires more resources and time and is less effective (60%) but still has many advantages over surgical removal. Cystine, urate (due to genetic mutation) and xanthine (due to administration of xanthine dehydrogenase inhibitors) can also be dissolved medically (check out our recommendations at urolithcenter.org) and should be considered in all asymptomatic patients.

5. When To Perform Voiding Urohydropropulsion

This stone removal method is idea when the stones are small enough to easily pass through the urethra and the dog or cat is easy lifted in a vertical position (the spine is vertically positioned).

Performing Voiding Urohydropropulsion

1. Anesthetize the patient	They type of anesthesia selected may vary based on the likelihood of success and gender of the patient. Consider reversible short acting anesthetics (e.g. Propofol) for patients with very small uroliths that are easily removed. Patients likely to go to surgery/lithotripsy should be placed under inhalation anesthesia. Consider epidural anesthesia to facilitate relaxation of the urethra in male dogs.
2. Attach a 3-way stopcock to the end of the urinary catheter	The 3-way stopcock facilitates control of the volume of fluid entering the bladder and containment of fluid once the bladder is filled.
3. Fill the urinary bladder	Sterile physiologic solutions (LRS, normal saline) are injected through a transurethral catheter to distend the bladder. If fluid is expelled prematurely around the catheter prior to adequate bladder filling, the vulva and/or urethra can be gently occluded using your thumb and first finger. Placement of additional fluid may not be needed.
4. Position the patient such that the spine is approximately vertical	Repositioning the patient allows uroliths to accumulate at the neck of the bladder facilitating their expulsion. Anatomically, the urethra does not become vertical until the caudal spine is 20 to 25 degrees anterior of vertical, but this may not be clinically important.
5. Agitate the bladder (this is rarely needed)	Agitating the urinary bladder left and right is performed to dislodge uroliths loosely adhered to the bladder mucosa.

6. Express the urinary bladder	Apply steady digital pressure to the urinary bladder to induce micturition. Once voiding begins, the bladder is more vigorously compressed. Compress the urinary bladder dorsally and cranially (toward the back and head of the patient). Movement of the urinary bladder caudally toward the pelvic canal may cause the urethra to kink preventing maximal urethral dilation.
7. Repeat steps 2 through 6	The bladder is flushed repeatedly until no uroliths are expelled.
8. Medical Imaging	Radiography provides an appropriate method of assessing successful expulsion of uroliths. To enhance detection of remaining small uroliths consider a double-contrast cystography (only the lateral view is needed).

5. When to Culture the Urine

Diagnosing infection-induced struvite requires a urine culture. Although some prefer to culture the urinary bladder wall, this is not reliable and it is difficult to differentiate contamination from infection because bladder cultures are not quantitative.

6. When to Castrate the Dog

Cystine uroliths form because of inherited defects in renal tubular transporters of cystine. The transportation defect in dogs appears to be genetically heterogeneous (autosomal recessive SLC3A1, autosomal dominant-SLC3A1 & SLC7A9, and sex linked/androgen responsive). In many dog breeds the mutation has not yet been determined. Surgical or medical castration can resolve/cure cystinuria in the subset of male dogs with androgen dependent cystinuria. Androgen dependent testing is available in mastiffs, English bulldogs and French bulldogs, but is likely the cause in many other breeds. Castration also prevents the propagation of the genetic defect to progeny.

PUTTING THE BRAKES ON FELINE LOWER URINARY TRACT DISEASE

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"A well-defined problem is half solved." If we do not ask the right questions of our clients, perform physical examinations that are problem specific, select tests that are likely to reveal a cause, or treat without adequately making a diagnosis, we may remain trapped by our misconceptions and ineffective in our administration of care. The following will help you make smart and strategic decisions in the diagnosis and management of lower urinary tract disease.

Preventing Feline Idiopathic Cystitis

Idiopathic cystitis is characterized by lower urinary tract signs (pollakiuria, stranguria, periuria, and hematuria) that often resolve spontaneously within 4 to 7 days with or without treatment, and are likely to recur. Although our understanding of the pathogenesis of idiopathic cystitis has improved, the underlying cause remains unknown. A diagnosis of FIC can only be made once other common causes for dysuria (stones, behavioral urination, infection, cancer) has been eliminated. Goals for managing cats with idiopathic cystitis are to decrease the severity of clinical signs and to increase the interval between episodes of lower urinary tract signs. This can be facilitated by educating owners about known factors involved in the pathogenesis and outcomes of idiopathic cystitis, and implementing therapies to mitigate them.

Therapeutic Target	Therapy
Acute Pain (85-90%)	Buprenorphine: 0.02-0.03mg/kg SL q8-12h) Gabapentin 5-10mg/kg q12h
Recurrent Episodes of dysuria-up to 65%/1-2yr (Kruger 2003)	Therapeutic foods (c/d mulitcare®) reduced recurrent episodes of FIC by **89%** compared to a typical grocery store food (Kruger 2015) Environmental Enrichment and Stress Reduction reduced recurrent episodes of FIC by **72%**, but since this study had no control (comparison group), we cannot determine how this compares with a placebo. (Buffington 2006). Canned therapeutic food reduced recurrent episodes of FIC by **28%** compared to dry therapeutic food (Markwell 1989)
Life threatening Urethral Obstruction-up to 73% (Defauw 2011)	Similar to above for recurrent episodes of dysuria. Potential urethral obstruction is an indication to prescribe foods that minimize struvite crystals which is a common component of urethral plugs.
Chronic Pain (10-15%)	Gabapentin 5-10mg/kg q12h

Dissolve Feline Struvite Uroliths: Take The Challenge:

Should surgeon-minded veterinarians attempt medical dissolution when stones are rapidly dissolvable? Stone analysis at the Minnesota Urolith Center indicates that this is not happening. In 2018, 49% of the 17,294 feline submissions were struvite. In a clinical trial of 32 cats without urinary obstruction, complete dissolution of urocystoliths was achieved in 27± 2.6 (mean±SD) ; range = 7 to 52 days with a therapeutic dry food providing maintenance nutrition requirements (Prescription Diet c/d Multicare Feline Bladder Health) with no adverse effects (e.g. no urethral obstruction, food aversion) and at a fraction of the cost of surgical cystotomy. Here is the challenge: the next cat with bladder stones consistent with a composition of struvite (moderately radio dense), start therapeutic dissolution therapy (c/d multicare or s/d food). Repeat the lateral radiograph in 14 to 21 days. If the stone is smaller or dissolved continue the therapy. The cat and owner will thank you (in 2018 more than 8000 cats received unnecessary surgery). If the stone is unchanged, it is likely not struvite and requires removal (cystotomy, percutaneous cystolithotomy, laser lithotripsy) and submit for analysis.

Unobstructing the Feline Urethra

Urethral re-obstruction is the most common complication of unobstructing the feline urethra. Re-obstructions may result in euthanasia, increased expenses and further damage to the urinary tract. Minimizing re-obstruction starts with gentle, thoughtful care during the initial unobstruction. The tools to safely unobstruct the feline urethra and minimize reobstuction are provided.

Tool	Remarks	Preference
Sedation	Sedation should be considered for cats in pain. It facilitates physical examination, decompressive cystocentesis, IV catheter placement and reduce anxiety. Butorphanol (0.2 to 0.3 mg/kg IM) with Midazolam (0.2 mg/kg IM) is a suitable start. Not necessary in moribund cats.	Yes
Decompressive Cystocentesis	The benefits of cystocentesis can be lifesaving (correction of metabolic wastes including hyperkalemia and acidemia, reduced discomfort, decreased resistance to retrograde urethral flushing, and collection of a clean urine sample for analysis). Yet many practitioners avoid cystocentesis because of the fear of bladder rupture. Recent studies show that rupture is unlikely. 45 obstructed cats ultrasounded before and 15 min after cystocentesis found a scant amount of abdominal fluid in 15 cats before, and an additional 7 after cystocentesis; none had a ruptured bladder (Cooper 2013). In 47 obstructed cats radiographed after cystocentesis and catheterization, 57% had loss of peritoneal effusion but none had bladder rupture (Hall 2015). In a large study of 557 cats, 5 (1%) had a ruptured bladder but it was not stated if it happened spontaneously, following cystocentesis or following urethral catheterization (Hetrick 2013)	Yes
Pursue a Diagnosis Before Treatment	It is perplexing as to why so many cats with urethral obstruction are catheterized before an underling cause is pursued (Eisenberg 2013). Knowing the cause would 1. Confirm the diagnosis, 2. Determine the best strategy to stabilize cats (decompressive cystocentesis or urethral catheterization), 2. Determine when to unobstruct (before or at correction of the underlying cause), 3. Determine how to unobstruct (flush or force), 4. Select how long to leave the catheter in (1 day or longer), 5. Determine follow-up care (surgery or not).	Yes
Sufficient Anesthesia	Adequate anesthesia to unobstruct the urethra is crucial to avoid iatrogenic urethral trauma and urethral spasms. Many protocols are available (Ketamine (2 to 4 mg/kg IV, Diazepam (0.2 to 0.3 mg/kg) or midazolam (0.1 to 0.2 mg/kg) IV, and Acepromazine (0.05 mg/kg IV); inhalant anesthesia instead of IV). Use propofol (0.5 to 1 mg/kg IV) to top off regimens that are not blocking urethral contractions. Avoid protocols that potentially increase urethral tone (i.e. Dexmedetomidine, an α_2 agonist (Aro 2015)).	Yes, but avoid dexmedetomidine
Flush urethral and do not force catheters into the urethra	Passing catheters proximal to stones or through persistent intraluminal obstructions may damage the urethra. Clear the urethral lumen prior to passing a catheter into the urinary bladder.	Yes
Extend the distal urethra caudally while passing catheter	The feline urethra has a flexure which needs to be straightened to facilitate flushing and passage of urethral catheters. If not extended caudally, urethral flushing can be ineffective or catheters can be passed through the wall at the flexure.	Yes
Minimize time of indwelling catheters	For idiopathic obstruction and urethral plugs most catheters are only needed for 24 hours. However, catheters should be left in longer to clear azotemia, allow detrusor repair or to allow the underlying cause to resolve.	Yes
Intravenous fluid support	Intravenous fluid support is considered important to support cardiovascular function, assist renal clearance of excess wastes and electrolytes, and flush precipitates out of the urinary bladder. Balanced electrolyte fluids assist rapid return of acid-base abnormalities.	Yes

Therapeutic diets	Re-obstruction is a consideration for euthanasia, increased expenses and further damage to the urinary tract. Therapeutic diets are highly effective in preventing idiopathic cystitis, struvite urethral plugs, struvite uroliths, struvite crystalluria (Osborne 1991. Lulich 2013, Bell 2015, Kruger 2015).	Yes
Antispasmotics	There is little evidence to support a beneficial impact of urethral relaxants in the management of urethral obstruction. A double-blinded, placebo-controlled prospective study failed to demonstrate that prazosin (0.25mg/cat q 12 hr) made a difference in recurrence rate (Reineke 2017). It is important to know that this drug and others that decrease urethral spasms work on the proximal urethral which is not the site of disease. A better approach would be to gently unobstruct the urethra to minimize irritation. Drugs working on the distal urethral have not been evaluated; however in a study of 6 cats with obstruction, urethral pressures on average were not increased (Streater-Knowlen 1995).	No, unless catheterization induced trauma
Antibiotics	Studies indicate that at the time of urinary catheterization no first time obstructed cat was infected (Cooper 2013, Hugonnard 2013). However 13 to 33% develop infections following catheterization. These findings indicate that antibiotics should be withheld until urinary catheters are removed and the urine cultured. If empirical antibiotics are prescribed prior to culture results, they should be given short term since removal of the catheter is removing the underlying risk for infection.	No, or ultra-short term antibiotics following catheter removal.

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UTI from Simple Sporadic to Recurrent Infections

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A urinary tract infection (UTI) occurs when uropathogenic bacteria overcome host defenses and invade and persist (adhere and multiple) in any portion of the urinary tract that is normally sterile (i.e. mid to proximal urethra, urinary bladder, ureters, and kidneys) of uropathogenic bacteria.

Guiding Principles in the Diagnosis of UTI

1. Urine culture is the gold standard to diagnose a urinary tract infection.

   The identification of bacterial species, number of colony forming units per ml of urine and susceptibility is the most accurate an efficient way to diagnose a urinary tract infection.

2. Cystocentesis is the standard urine collection method to minimize contamination from extra-urinary sources. Ultrasound guided collection can help especially when the bladder is small or the patient is fat.

   When cystocentesis is less desirable (e.g. urinary cancer, thrombocytopenia), consider

   a. Clean midstream collection.
   b. Clean urethral catheterization in males

3. Not all positive urine cultures are urinary tract infections.

Typical scenarios for a positive urine culture

	Common Bacteria species	Number of species	Collection method	Urinalysis findings
<u>Subclinical Bacteriuria</u> Positive urine culture in the absence of clinical signs (i.e. clinical evidence of disease)	10^3 to $>10^5$ CFU/ml of urine Enterococcus and other common urinary bacteria	1	Cystocentesis Midstream Clean catheter in males	Unremarkable to inflammation and hematuria
<u>Established UTI</u> (Uropathogenic bacteria invade, persist and induce inflammation and damage)	$\geq 10^4$ CFU's of a common uropathogen (E.coli, Staph, Proteus, Klebsiella, Enterococcus, others)	1	Cystocentesis Midstream Clean catheter in males	Inflammation and hematuria

Emerging UTI (Uropathogenic bacteria invade)	≤10^4 CFU's of common uropathogens	1	Cystocentesis	No or minimal inflammation or hematuria
Contaminate (Bacteria introduced by improper sampling)	≤10^5 uncommon uropathogens, common skin flora	≥2	Catheterization in females, free catch, and owner caught samples	No or minimal inflammation

4. A true urinary tract infection is very likely if:

   a. High bacterial numbers (≥10^4 CFU's/ml of urine)

   b. Typical uropathogens (E.coli, Klebsiella, Enterococcus, Staphylococcus, Proteus)

   c. A single bacterial strain

   d. Clinical signs of disease (pollakiuria, urgency, renal pain)

   e. Pyuria (≥ 5-20 WBC/HPF = inflammation)

   f. Altered host defenses (e.g. immunosuppression, uroliths, cancer, anatomic defects, urine retention, and instrumentation)

   g. Identical bacterial strain on a previous culture (reproducible)

5. The urinalysis (bacteria on results) is neither a sensitive nor a specific method to diagnose bacterial urinary tract infection. Yet bacteriuria on the urinalysis is a common reason many veterinarians give antibiotics.

   The diagnosis of bacteriuria can be improved by

   a. Training laboratory personnel to differentiate bacteria from nonbacterial debris

   b. Gram stain urine sediment

   c. Wright stain urine sediment

   d. Automated bacterial recognition technology (?)

   e. If combined with inflammation (WBC's and RBC's)

   f. If combined with positive Point-of-Care testing (e.g. RapidBac™)

6. Urinalysis is not a good method of diagnosing UTI because

   a. Unidentified debris (especially cocci shaped debris) is misread as bacteria

   b. Cannot easily differentiate contamination from infection

   c. May not recognize emerging infections with low numbers of bacteria

   d. May not recognize bacteria in with low specific gravity (e.g. kidney failure)

   e. Cannot determine bacterial susceptibility to antibiotics

7. Types of urinary tract infections

Type		Definition	Clinical Significance
Sporadic (clinical)		≤2 infections per year Clinically healthy, except LUT signs No identifiable functional or anatomic abnormalities	Resolves with short duration of AB therapy Recurrence is unlikely Follow up cultures usually not recommended*. Healthy besides the infection
Recurrent Infection	Reinfection (different strain)	≥2 infections in 3 months or ≥ 3 infections per year with a different bacterial species	Antibiotics were effective Need to improve strategies to restore normal host defenses. Follow-up cultures needed
	Relapse (same strain)	≥2 infections in 3 months or ≥ 3 infections per year with the same bacterial species	Antibiotics were not effective Need to improve strategies to increase antibiotic effectiveness Follow-up cultures needed
Subclinical Bacteriuria		Culture positive No clinical signs	Treatment usually unnecessary and discouraged except in high risk situations

*The timing and decision to obtain follow-up cultures is determined by the response to antibiotic treatment and the clinical scenario (severe infections in debilitated patients are cultured earlier and more often).

Guiding Principles in the Treatment of UTI

1. The primary goal of therapy is a clinical cure (i.e. no clinical signs and no (or minimal) adverse effects of either administering or withholding therapy). You are balancing the need to give antibiotics with the risk of not giving antibiotics. A clinical cure does not always equal a microbiological cure. However, a microbiological cure (culture proven) is synonymous with a clinical cure (when the infection is the cause of clinical signs).

2. Antibacterials (antibiotics) are the foundation of therapy.

3. Types of Antibiotic Treatment

4. Adequate antibiotic concentration at site of infection is important to kill bacteria (eradicate infection)

5. Initial Antibiotic Strategy for sporadic infections or if location and underlying risk factors are unknown.

Give a high dose to ensure that the medicine reaches the site of infection

Give the shortest duration (3 to 5 days) to prevent resistence and because research indicates that it is just as effective as if given for a longer duraton

Give the antibitoic with the best in vitro susceptabilty

6. Antibiotic selection should consider *in vitro* effectiveness

Bacterial antibiotic susceptibility is highly predictive of antibiotic effectiveness. When selecting empirical antibiotics, use population statistics (antibiograms for your region).

7. Antibiotic selection should consider location of infection

When treating infections primarily in urine, water soluble antibiotics (penicillins, cephalosporins, nitrofurantoin) that reach high concentrations in urine are appropriate choices. Lipid soluble antibiotics that reach high concentrations in urine are also feasible.

When treating infections localized in tissue (kidney, prostate) consider lipid soluble antibiotics (trimethoprim-Sulfa, fluoroquinolones) with better tissue penetration or increasing the dose or dosing frequency (q 3 to 4x daily) of water-soluble antibiotics.

8. Antibiotic selection should consider virulence of organism

Some bacteria (e.g. Proteus, urease producing Staphylococcus, Corynebacterium urealyticum) are more destructive and typically require treatment with lipid soluble antibiotics with greater penetration, increased dose or dosing frequency of water-soluble antibiotics, or longer antibiotic duration to clear infections. In addition to intensifying antibiotic strategies, monitoring strategies (follow-up cultures) are also intensified to ensure AB success and recognize antibiotic resistance.

9. Antibiotic selection may incorporate the inhibitory quotient

The Cmax/MIC: In other words, the higher the Cmax is above the MIC the greater potential of killing both resident and more resistant mutants in the strain (concentration-dependent antibiotics (e.g. fluoroquinolones, aminoglycosides), and the longer that time-dependent antibiotics (cephalosporins, penicillins) are above the MIC.

10. Antibiotic duration should consider disease status

Antibiotics should be administered for the shortest duration necessary to clear the infection and the disease. Recently, there has been consensus to give antibiotics for 3 to 5 days regardless of the disease. This strategy is great for sporadic infections of the bladder or undetermined location and cause, because the strategy is designed to minimize develop of antibiotic

resistance and adverse effects. When other disease factors are known, they should be considered when determining antibiotic class, dose and duration to be successful.

Disease	Initial Antibiotic Duration
Sporadic bladder infections of undetermined cause	3 to 5 days
Kidney infections	1 to 2 weeks
Prostate infections	2 to 4 weeks?
Infection induced struvite stones	Until mostly dissolved (2 to 3 months?)

11. Infections are likely to recur (and maybe persist) if predisposing conditions cannot be identified and eliminated.

12. Effectiveness of antibiotic therapy for recurrent infections, in which underlying risk factors cannot be eliminated, is unpredictable.

    For best results:

    a. Select antibiotics based on culture and susceptibility results, and their ability to reach the site of infection at adequate concentrations (i.e. high concentrations in the urine, tissue, or both)

    b. Reculture often (e.g. a few days after starting antibiotics and 1-2 weeks after stopping antibiotics) to assess therapy and development of resistance.

    c. Reconsider novel strategies to identify and eliminate underlying risk factors (e.g. contrast imaging studies, neurologic exam, residual urine volume, CT scan, observe urine voiding, cystoscopy)

    e. Avoid antibiotic strategies that were ineffective previously; select a different strategy (different antibiotic class, higher dose or longer duration).

    f. Combine antibiotic strategies (e.g. short-term high dose antibiotics immediately followed with low-dose long-term nightly antibiotics)

    g. Reassess treatment goals when infection and its underlying risks are impossible to eliminate (e.g. prioritize patient comfort over microbial cure (e.g. intermittent intravesicular therapy for persistent infections in male dogs or dogs with permanent cystostomy tubes), or consider an antibiotic holiday).

13. Antibiotic Strategies

Drug Selection	**↑ Urine Concentration**	**↑ Tissue & Urine Concentration**	**Inhibitory Quotient**	**Avoid AB classes that didn't work previously**
	Penicillins Cephalosporins Nitrofurantoin	Quinolones Trimethoprim Sulfas Cefpodoxime	Cmax/MIC Peak/MIC AUC/MIC	To not make the same poor selection of therapy

Dose	**High**	**Medium**	**Low**
	ABs with a wide margin of safety	Abs with a narrow margin of safety	Nightly (prevention after bacterial eradication)

Duration	**Short**	**Medium**	**Long**	**Nightly**	**Intermittent**
	3-7 days	7-14 days	Until disease corrects	At bedtime	2days:q2wks

Route	**Oral**	**Intravenous**	**Intravesicular**
	Common	Uncommon	To eradicate or control clinical signs for persistent bladder infections

14. Urine culture strategies to monitor antibiotic effectiveness

The timing and decision to obtain follow-up cultures is determined by the response to antibiotic therapy and the clinical scenario (high risk infections in debilitated/high risk patients are cultured earlier and more often).

Clinical Scenario	**Timing of follow-up culture**
Sporadic cystitis	No follow up culture planned
Recurrence of Clinical Signs	At recurrence and before restarting AB's
Persistence of Clinical Signs	2 to 3 days after starting AB's
High risk disease (e.g. pyelonephritis, prostatitis, Corynebacterium)	3 to 5 days after starting AB's to ensure desired effectiveness
Dissolving infection-struvite	4 to 6 weeks into therapy
Monitoring low-dose nightly therapy	Every 1 to 2 months
Ensuring effective response to antibiotics (e.g. eradication after recurrent infections or dissolving struvite stones)	7 to 14 days after finishing antibiotic therapy

	Urine	Catheter	Bladder Wall	Uroliths
What	Cystocentesis (voided?) Pyelocentesis Catheter	Not recommended	With negative urine culture & persistent clinical signs	To differentiate infection from sterile struvite urolith

	Before Treatment or return of urinary signs	Early During Therapy (day 3)	Late during Therapy (3 -5 days before stopping)	Post Therapy (7-14 days post-therapy)	Intervals (q1-3 months)
When	Diagnostic, repeat with unclear results (most important culture)	Test of *in vivo antibiotic* effectiveness for high-risk infections (e.g. pyelonephritis)	Test of *in vivo* antibiotic effectiveness before stopping therapy	Dx Recurrence of infection	*In vivo* test for nightly AB therapy. Dx recurrence early to minimize consequences of late diagnosis (e.g. ineffective therapy).

Follow-up cultures after treating Sporadic infections are not preformed until urinary signs recur

1. International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. Vet Journal 2019;247:8-2

UNOBSTRUCTING THE FELINE URETHRA: The SAFE method

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Feline urethral obstruction is a common life-threatening emergency in cats. Aetiologies associated with this disease include urethroliths, urethral plugs, urethral strictures, blood clots and urethral neoplasia. However, in many cats a cause for urethral obstruction is not apparent which raises the concern that some cats may have a functional obstruction caused by urethral spasms or urethral swelling from edema and inflammation.

We use the following acronym, S.A.F.E. as a reminder of the important steps to safely unobstruct the urethra of male cats.

S=Stabilize First (table 1)

A= Accurate Diagnosis

F=Flush, don't force catheters through the urethra

E= Extend the urethral caudally when inserting catheters to flush the urethra

Stabilize First

Cats with urethral obstruction and bladder over-distension are often experiencing a high degree of pain and anxiety. To facilitate physical examination, radiography and safe bladder decompression; provide prudent amounts of analgesia (butorphenol 0.2 to 0.3 mg/kg and midazolam 0.2mg/kg IM or IV; for cats experiencing higher degrees of anxiety consider adding 2 to 5mg/kg of ketamine; some have advocated buprenorphine (5 to 20 µg/kg) but the onset of analgesia make take up to 20 minutes). Then, consider placing an IV access line, complete the physical exam, and perform abdominal radiography to verify bladder size and to determine the cause of urethral obstruction. In very sick cats, these steps can be combined with stabilization of the patient (table 1) which often includes decompressive cystocentesis. Once stabilized, patients can be more safely anesthetized (a variety of protocols are available; strive to avoid drugs that may increase urethral tone (e.g. dexmedetomidine) and consider drugs that can be rapidly administered in case additional anesthesia is needed (e.g. propofol). Consider regionally anesthetizing the urethral using an epidural technique of lidocaine. (1) Epidural anesthesia reduces the need for high levels of general anesthesia thereby reducing anesthetic-adverse events. (1)

Table 1. CORRECTING METABOLIC CONSEQUENCES OF URETHRAL OBSTRUCTION

Consequence	Indications to treat	Therapy
Hypothermia	Core temperature less than 99oF or cardiac decompensation	Heating pad Heat lamps Infuse only warm saline

Hypovolemia	Azotemia Cardiovascular collapse	Replace deficits in 2 to 12 hours with 0.9% saline. Consider an initial bolus of fluids to rapidly correct hypovolemia if needed (10 to 30 ml/kg). Although saline has been recommended because patients are often hyperkalemic, any balanced replacement electrolyte solution will help.
Azotemia	If serum creatinine is greater than 2 to 3mg/dl	Replace fluid deficits with balanced electrolyte solutions Decompressive cystocentesis to promote renal excretion
Acidemia	If blood pH <7.1-7.2	Administer 1/3 to ½ of the dose of NaHCO3 (0.3 x BW in kg x base deficit) administered over 15 min. Rapid or excessive administration of bicarbonate may exacerbate hypocalcemia.
Hyperkalemia	Weakness or shock due to cardiovascular depression	To promote intracellular translocation of potassium: Correct metabolic acidosis with sodium bicarbonate (mmol = 1/3(0.3 x BW in kg x base deficit) Administer 0.1 U/kg regular insulin IV with 1 gram of glucose per unit of insulin administered. To antagoize adverse cardiac effects: 50 to 100 mg/kg Calcium gluconate slow (2-5min) IV. Concomitant hypocalcemia and acidemia contribute to worsened heart function.
Hypocalcemia	Hypocalemic tetany or hyperkalemic cardiac decompensation	50 to 100mg/kg calcium gluconate slow (2 to 5 min) IV with cardiac monitoring

ACCURATE DIAGNOSIS

Knowing the cause of urethral obstruction is essential to develop a feasible therapeutic plan (tables 3 and 4) for alleviating obstruction and preventing recurrence. Therefore, survey radiography is an essential diagnostic step for all cats. Remember to include the entire urethra. Urethroscopy may provide a more accurate method to verify, localize and determine the cause of obstruction, but is technically difficult and cumbersome during an emergency.

Early diagnosis of the causes for urethral obstruction can improve client communication and refine therapeutic options. If urethroliths are detected, the client should be informed of the cat's need for a cystotomy once the cat has been stabilized and the urethra unblocked. Cystotomy adds substantially to the cost of care. Therefore, informing clients of the presence of uroliths prior to spending money to unblock the urethra is helpful to make appropriate care decisions. A diagnosis

of uroliths is also an indication that the one-time urethral unblocking method with outpatient care (Seitz et. al. 2018), and the unconventional unobstruction method of decompressive cystocentesis and pharmacological relaxation without urethral flushing, are inappropriate treatment options (Cooper et al.2010). Urethral plugs contain a variety of substances (e.g. protein, cells, and crystals) that become trapped in the matrix of the plug, but also provide information on disease processes contributing to plug formation. A diagnosis of a urethral plug can alert clinicians to collect a sample of the plug for microscopic and mineral analyses to assist formulation of therapy to minimize recurrence. In addition, cats with urethral plugs may benefit from gentle massage of the distal urethra to break up the plug and facilitate its antegrade expulsion without urethral flushing or catheterization. Urethral massage would not be expected to assist the expulsion of urethroliths.

FLUSH, DON'T FORCE

There are several techniques to un-obstruct the urethral lumen (tables 3 and 4). Selection of the procedure depends on the cause of the obstruction and the severity of life-threatening metabolic abnormalities. In some cases cost may also dictate the extent of diagnosis, treatment, and monitoring.

Use open-ended catheters to clear the urethra. I prefer the olive-tipped catheters. To prevent urethral trauma, do not force catheters through the urethral lumen. First, clear the lumen by using a catheter to flush sterile saline. Once cleared, a lubricated catheter of appropriate size should easily traverse the urethral lumen and enter the urinary bladder.

EXTEND THE URETHRA CAUDALLY

To prevent damage to the urethral, stretch the urethra caudally and dorsally before advancing catheters. Pulling the urethra caudally eliminates the flexure in the distal urethral that is easily ruptured during forceful catheterization.

General Recommendations

1. Insure that the patient is suitably prepared for anesthesia (e.g. normothermic, normotensive, normokalemic, and less azotemic, etc.)
2. Administer appropriate and sufficient anesthesia to abolish urethral pain to facilitate urethra manipulation
3. Make every effort to protect the patient from iatrogenic complications associated with urethral catheterization (infection, trauma).

Retrograde Flushing While Occluding the Distal Urethra (generally the most effective)

1. If the bladder distended even moderately, perform decompressive cystocentesis* using a 22gauge, 1.5 inch needle attached to an intravenous collection set, 3-way stop cock and syringe.

2. Select an olive-tip urethral catheter (or other suitable catheters). Assemble the urethral catheter, intravenous extension tubing, and small syringe (3 to 12ml) filled with normal saline. Evacuate air from lines by flushing saline through the assembled supplies.
3. Exteriorized penis caudally and dorsally (i.e., parallel with the spine).
4. Without using excessive force, slowly insert the tip of the urinary catheter into the urethra and advance the catheter to the site of obstruction.
5. With the catheter in place, occlude the urethra around the catheter shaft using your first finger and thumb. Placing a moistened gauze sponge or pad between the urethra and your fingers will minimize trauma to the surface of the urethra.
6. Stretch the urethra caudally and dorsally while an assistant depresses the plunger of the syringe to flush the urethra clear of its obstruction. By preventing reflux of solutions out of the external urethral orifice, this maneuver dilates the urethra and flushes the plug into the urinary bladder.
7. Once the urethral lumen is cleared, advance the catheter slowly toward the urinary bladder. Additional flushing may be needed to continue to clear the urethral. When the tip of the catheter reaches the urinary bladder, empty the bladder.

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CLINICAL DIAGNOSIS AND MANAGEMENT OF BLEEDING DISORDERS – PART I

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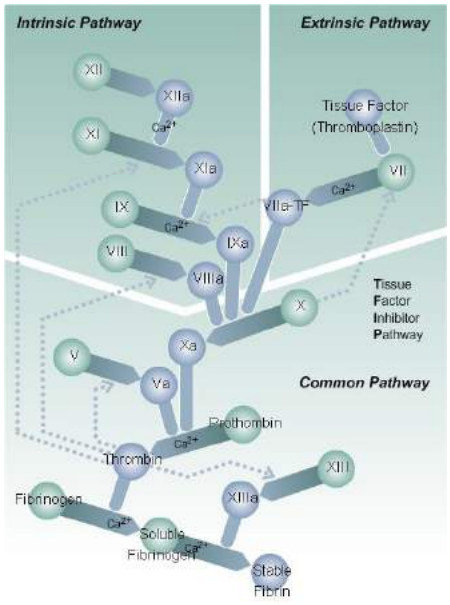
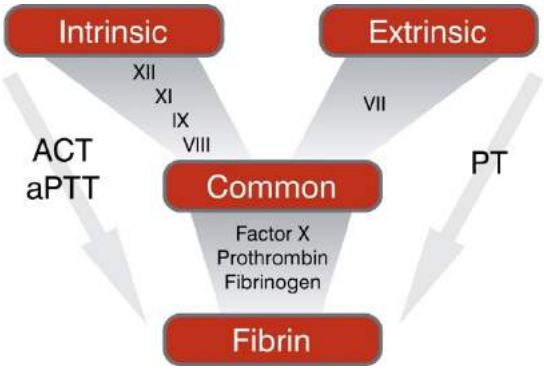
Bleeding disorders are a common presentation in dogs and less commonly in cats and may be inherited or acquired. Furthermore, thrombotic conditions are being increasingly recognized. These lectures will focus on the clinical diagnostic approach and management to a bleeding animal. There are several point-of-care and reference laboratory tests permitting the separation between primary and secondary hemostatic defects as well as a specific diagnosis even in clinical practice. Particularly challenging is the diagnosis of Disseminated Intravascular Coagulation (DIC), a syndrome observed with a variety of disorders and still not completely understood and not really treatable.

Bleeding diatheses are generally separated into primary and secondary hemostatic disorders and in some cases both systems are affected, such as in disseminated intravascular coagulation (DIC). Primary hemostatic disorders include not only the common thrombocytopenias but also thrombopathias, vasculopathies, and hereditary von Willebrand disease. Secondary hemostatic disorders include all coagulation factor deficiencies involved in fibrin formation and are strictly speaking the 'coagulopathies'. They may also be acquired often invoving several factors such as in liver disease and anticoagulant rodenticide poisoning or a specific coagulation factor deficiency may be inherited.

Platelet and vascular problems often present with surface hemorrhage such as petechiations and ecchymoses, while coagulopathies generally cause hematomas and cavity bleeds. Excessive hemorrhage at an injury or surgery site and bleeding from multiple places are suggestive of bleeding disorder, and there are a several breed predilections for specific hereditary defects.





Hemostatic tests are indicated whenever an animal is bleeding excessively or repeatedly, prior to surgery when an increased bleeding tendency is suspected in patient, to monitor therapeutic interventions, and for genetic screening in certain breeds or families with a known common bleeding disorder. Hemostatic abnormalities should be assessed prior to instituting therapy whenever possible or at least appropriate blood samples should be collected pretreatment as therapy will change test results. Excellent venipuncture with discarding of the first few drops of blood (to avoid platelet activation and tissue factor influence) and extended compression over jugular, saphenous or femoral vein is required to avoid iatrogenic bleeding.

The **cuticle bleeding time** is simple to perform in dogs and crudely assesses overall hemostasis, but is not standardized. A minimal database includes a **packed cell volume** and **total protein** evaluation, and **evaluation of a blood smear** can provide a **platelet estimate** and identify platelet size and clumping as well as schistocytes (as seen with DIC). A simple and inexpensive in clinic activating clotting time (ACT) test can assess all coagulation factors except Factor VII (hereditary deficiency in Beagles and other breeds). The results can also provide some measure of the extent of blood loss and the requirement for red blood cell, plasma or platelet transfusions.

Tools for Primary Hemostastic Defects

Platelet counts can be estimated by a microscopic examination of a blood smear or specifically counted by a hematology instrument. Since 8-15 platelets (1 platelet equals 20,000/µL) are normally found per high power oil emersion microscopic field, an absence to low number of platelets suggests a severe thrombocytopenia. Various modern impedance and laser hematology instruments have the ability to count platelets and measure their mean size including platelet size distribution and platelet crit; they may have been validated, but some have difficulties in differentiating large platelets from erythrocytes (particularly in cats). Furthermore, platelets can readily be activated which results in platelet aggregation, hence, platelet counts need to be confirmed by a careful review of a blood smear

including the feather edge for platelet clumps (preferably with fresh non-anticoagulated blood). Hemorrhage is generally not observed unless the platelet count is <40,000/µL (normal 150-500,000/µL) or there is also a coagulopathy like DIC present.

Thrombocytopenia, a common cause of surface hemorrhage in dogs, can result from impaired thrombopoiesis, increased platelet destruction and consumption, and sequestration of platelets (e.g. splenomegaly). Reduced platelet production may be isolated or associated with an overall decreased hematopoiesis due to many drug reactions (estrogens, chemotherapeutics, azathioprine), infections (Ehrlichia, Babesia and many others), and myelophthisis (leukemia, myeloma, myelofibrosis), but remains often idiopathic (immune-mediated?). Accelerated platelet destruction is commonly associated with immune-mediated thrombocytopenia (IMT, including idiopathic thrombocytopenia purpura [ITP]), but enhanced platelet consumption may also be observed with neoplasia, vasculitis, and disseminated intravascular coagulation (DIC). IMT can be divided into primary, also known as idiopathic thrombocytopenia purpura (ITP), and secondary forms triggered by infections (Ehrlichia, Rickettsia, and Babesia, Anaplasma spp., vaccines), drugs, and cancer). Anticoagulant rodenticide poisoning can also be associated with mild to moderate thrombocytopenia. However, acute and chronic blood loss is not resulting in any major consumptive thrombocytopenia unless there are concomitantly a vasculopathy and/or DIC present. Thrombocytopenia occurs rarely in cats and is generally associated with drug exposure (e.g. griseofulvin, methimazole), viral infections, or malignant diseases.

A diagnosis of thrombocytopenia is made by a platelet estimate on a blood smear or complete blood cell count, but any thrombocytopenia must be verified by a review of a blood smear. Spurious thrombocytopenia may due to instrument limitations; e.g. megaplatelets in Cavalier King Charles and few other breeds, and platelet aggregates with many illnesses and collection techniques; also Greyhounds have generally a mild thrombocytopenia. Classic signs of thrombocytopenia include petechiation, ecchymosis, epistaxis, and gastrointestinal blood loss. The most severe thrombocytopenias are seen with IMT/ITP, but often cause only mild hemorrhage. Following a careful history, a search for an underlying cause is warranted to identify an infection (blood smear, serology, PCR) or cancer (also involving lymphnodes and spleen). Bone marrow examination is safe, but may rarely reveal a specific cause on initial presentation.

A diagnosis of ITP is mostly based upon excluding other causes of thrombocytopenia, but platelet-associated antibodies can also be determined to support an immune mechanism for thrombocytopenia. Detection of platelet-associated antibodies further supports an immune-mediated thrombocytopenia, but this test is rarely available. Serum titer, antigen, and PCR tests for tick-born (e.g. ehrlichiosis, babesiosis, leishmaniasis) and other infectious diseases are indicated in certain countries or areas. The presence of schistocytes and thrombocytopenia suggests DIC, where intravascular fibrin strands fragment erythrocytes. Because von Willebrand disease is such a common mild primary hemostatic defect in dogs, plasma vWF measurements by ELISA through a commercial laboratory are indicated. For breeding purposes, DNA testing is also available for some canine breeds involving specific mutations/variants.

Finally, in light of normal platelet count and plasma vWF values, a prolonged buccal mucosal bleeding time (BMBT) indicates a thrombopathia. Disposable devices are available that facilitate making 1-2 standard 1 mm deep mucosal incisions. The platelet function analyzer (PFA100) is an

expensive in-clinic tool to functionally assess platelet dysfunction, VWF deficiency, and other primary hemostatic defects. Electron microscopic and platelet aggregation and nucleotide studies allow further characterization of platelet dysfunctions in specialized laboratories. For a couple of hereditary thrombopathias even a DNA test is now available such as for Glanzmann thrombasthenia in Great Pyrenees and Otterhound, and thrombopathia in the Spitz, Basset, Landseer and Swiss Mountain dog, and macrothrombocytopenia in Cavalier King Charles and others.

Coagulation Tests – Secondary Hemostasis

Whereas the whole blood clotting time test is insensitive and mostly inaccurate, there are several standardized coagulation screening tests that are useful to define coagulopathies even in clinical practice. Nearly all coagulation tests assess the function of certain parts of the coagulation system in fresh whole blood or fresh (or frozen) plasma to generate fibrin in a fibrometer devise. Recalcified citrated plasma is used and many tests are comparing a patient sample directly with a simultaneously obtained control or pooled plasma sample (plasma from 10 animals). Generally coagulation times, which is measuring the time to clotting (fibrin formation), are much shorter in small animals than in humans. Thus, every coagulation test needs to be run on an instrument for animals and validated for the animal species.

The intrinsic and common pathways are assessed by either the activated coagulation time (ACT) or activated partial thromboplastin time (aPTT or PTT). Factor XII of the intrinsic cascade is activated by diatomaceous earth (celite) in the ACT test and by kaolin or other contact phase substrates in the aPTT test. The extrinsic and common pathways can be assessed by the prothrombin time (PT) test. In these assays different tissue factors (thromboplastins) are activating factor VII, which in turn will lead to fibrin formation.

Hemostatic screening tests and simplified groups of bleeding disorders

	Platelets	BMBT	PTT	PT	TT
Thrombocytopenia	**D**	**I**	**N**	**N**	**N**
Thrombocytopathia & vWD	**N**	**I**	**N**	**N**	**N**
Intrinsic coagulopathy	**N**	**N**	**I**	**N**	**N**
Extrinsic coagulopathy (FVII)	**N**	**N**	**N**	**I**	**N**

Combined coagulopathies (DIC, liver, rodenticide)	**D**	**I/N**	**I/N**	**I/N**	**I/N**

N = normal; I = increased (prolonged) time; D = decreased

Until this century, the ACT tube test was the only point-of-care test available for clinical practice, whereas PTT and PT tests were performed in commercial laboratories. There are now several point-of-care coagulation instruments (e.g. IDEXX Coag DX and the Abaxis VetScan VSpro) introduced that are capable of determining without delay on small amounts (50 µL) of fresh citrated whole blood the aPTT and PT, thereby making separation of citrated plasma and shipment of frozen plasma to the reference laboratory for initial coagulation screening unnecessary. In practice, a reasonable and simple approach for a bleeding animal to be screened for a coagulopathy would be to measure the ACT or PTT first as either of those test detects all coagulopathies (except for hereditary factor VII deficiency in Beagles and a few other breeds), but the aPTT is more standardized and the ACT can only be run on fresh non-anticoagulated whole blood. If the aPTT (or ACT) is prolonged, a PT test would be indicated to differentiate between an intrinsic and common pathway defect or a combined coagulopathy involving several coagulation factors.

Although hereditary coagulopathies can be suspected based upon the pattern of coagulation test abnormalities, specific factor analyses are needed to confirm a precise diagnosis. A young male animal who is bleeding and has a mildly prolonged aPTT but normal PT likely has hemophilia A or B (factor VIII or IX deficiency), an X-chromosomal recessive disorder. However, factor XI deficiency is associated with the same test abnormalities and is inherited by an autosomal recessive trait (e.g. Kerry blue terriers and Maine Coon cats). For several hereditary coagulopathies, DNA tests are already available (http://research.vet.upenn.edu/penngen), while for others the specific plasma factor deficiency can be determined through special laboratories (e.g. the Comparative Hemostasis Laboratory at Cornell University). Finally, factor XII deficiency, particularly common in domestic shorthair cats, and prekallikrein deficiency cause marked aPTT prolongations but are not associated with any excessive bleeding tendency.

Animals poisoned with anticoagulant rodenticides that are bleeding or are at risk for bleeding will have severe prolongations in all of the above coagulation tests, but would have a normal thrombin time (TT). The thrombin time is independent of vitamin K-dependent coagulation factors and is a functional assay for fibrinogen to form fibrin. The protein induced by vitamin K antagonism or absence (PIVKA) test is a modified PT test and not diagnostic for rodenticide poisoning, but a toxicological investigation (product identification, blood toxicology analysis) may confirm the specific rodenticide poison and allow for more precise treatment. Moderate thrombocytopenia may also be associated with rodenticide poisoning. Liver diseases may result in varied coagulopathies due to impaired coagulation factor synthesis and vitamin K malabsorption.

Similarly, disseminated intravascular coagulopathies due to many different disorders are associated with variably prolonged (and rarely shortened) coagulation times. More helpful to the diagnosis of DIC are the recognition of schistocytes, thrombocytopenia, low fibrinogen and antithrombin III levels, and increased D-dimers and fibrin split (degradation) products. Finally, thromboelastography (TEG or ROTEM) techniques can be used in the emergency room, intensive care units, and referral centers to assess overall hemostasis and particularly thrombotic or fibrinolytic tendencies in fresh citrated whole blood.

CLINICAL DIAGNOSIS AND MANAGEMENT OF BLEEDING DISORDERS – PART II

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Bleeding disorders are a common presentation in dogs and less commonly in cats and may be inherited or acquired. There are several point-of-care and reference laboratory tests permitting the separation between primary and secondary hemostatic defects as well as a specific diagnosis even in clinical practice. Depending on the specific diagnosis of the bleeding disorders, severity of the bleeding and anemia, different therapeutic options are available. Local hemostasis, special drug therapies, and transfusion support may be considered. Many can be handled in clinical practice while others may have to be sent to a referral center to receive intensive therapy.

In any clinical setting, hemorrhage is a very common clinical problem in dogs and less so in cats. Depending on the (internal or external) site, acuteness, and degree of bleeding, dogs may have overt signs of hemorrhage, show specific organ failure (e.g. thoracic hemorrhage, hemoabdomen), and/or signs related to the systemic effects of hypovolemia, anemia and/or hypoproteinemia. Differentiating between normal and abnormal hemostasis by clinical and laboratory assessment is crucial; animals with a bleeding tendency often exhibit recurrent and/or multiple sites of hemorrhage. Similarly, differentiating between primary (thrombocytopenia, -pathias, von Willebrand's disease, and vasculopathies) and secondary (hereditary and acquired coagulopathies) hemostatic defects is important to choose the correct therapy. It should be noted that many tests can be used in an emergency setting and may also be applied to monitor the response to treatment and course of the underlying disease.

Therapeutic considerations for the bleeding patient

- Resuscitate and emergency care – do not more harm
- Local hemostasis to prevent further blood loss
- Transfusion with packed Red Blood Cells (pRBCs) in case of severe anemia and tissue hypoxia.
- Specific blood component therapy, like fresh plasma, to correct hemostatic deficiencies
- Specific drug therapy where available
- Withdrawal of any offending agents and/or treat underlying disease
- Supportive agents such Yunnan Baiyao (Yunnan Paiyao), aminocaproic acid, desmopressin

The general principles of resuscitation and emergency care apply to animals with hemorrhage such as restoring hydration, opening airway, offer oxygenation, and adjusting body temperature. For rehydration, crystalloid fluids are typically used as colloids have anticoagulant effects and may worsen the bleeding. In case of dangerously low oncotic pressures, fresh frozen plasma (FFP) may be used. With peracute blood loss, PCV changes are not observed for hours until fluid shifts occur or after the animal is rehydrated with intravenous fluid administration. Dogs with acute hemorrhagic

gastroenteritis may lose more fluid than RBCs and become hemo-concentrated until they are rehydrated. Thereafter, they are anemic and often severely hypoproteinemic.

While ligatures, hemostats, and compression can locally stop visual bleeding from trauma or surgery, surgical intervention should be only cautiously considered in order to not cause more harm to the patient. Thus, adequate hemostatic function should be first assured or restored with appropriate blood products or medical treatment, whenever possible. There are also a variety of commercially available local hemostatic agents that might be applied at a wound, such gelatin, thrombin, bone wax, and fibrin glue. Yunnan Baiyao (Yunnan Paiyao – supposedly hemostatic) and epsilon aminocaproic acid (antifbrinolytic) have been used in clinical practice to improve hemostasis and impair fibrinolysis.

Animals with massive blood loss may benefit from pRBCs or whole blood transfusions. Ideally, dogs are initially DEA 1 typed to provide type specific blood products and possibly crossmatched, if they had received blood previously (>4 days). There is no specific PCV at which to transfuse, but rather the overall clinical assessment of tissue oxygenation is determining the transfusion trigger in each patient. The simple formula of **volume to transfuse = desired PCV rise x kg Body Weight x 2** is adequate to estimate the target PCV in dogs. In case the expected PCV rise is not achieved, continued blood loss, fluid shifts, and an acute hemolytic crisis may account for the deficit. Animals with chronic blood loss generally have well adapted to their low hematocrits and may cope well with a PCV as low as 10%. Their heart, however, functions at maximal capacity (large cardiac output) to compensate for the anemia. These animals are generally not dehydrated and additional fluids may result in severe volume overload and cardiac decompensation. Thus, the fluid and blood volume as well as rate of administrations should be appropriately chosen, and the dog's cardiovascular system should be carefully monitored. Interestingly, it has been shown that a rise in PCV will also ameliorate bleeding, likely due to the fact that RBCs are a major part of any clot.

In case of thrombocytopenia, platelet products are rarely used for a variety of reasons. Platelet concentrates and platelet-rich plasma (unchilled, <8 hours gently agitated) need to be freshly prepared and are rarely available. Frozen as well as lyophilized platelets were offered in some countries, but their efficacy has been questioned. While the normal survival of platelets is 7-10 days in circulation, typically transfused platelets are short-lived, particularly in dogs with immune-mediated thrombocytopenia. Large quantities of platelet transfusions are needed to make a difference in the platelet count (platelet count rise ~ 20,000/10 mL blood/kg body weight) and allo-sensitization may occur after repeat transfusions. Nevertheless, platelet concentrates or platelet-rich plasma are used to stop life-threatening bleeding due to severe thrombocytopenia. And in case there is a combined hemostatic deficiency and anemia, fresh whole blood that has not been chilled could be given (chilling platelets inactivates platelets). Platelet support may also be needed in dogs with hereditary thrombopathias, such as Glanzmann thrombasthenia, P2Y12 deficiency, and acquired thrombopathias (e.g. drug induced).

There are a variety of specific treatments for thrombocytopenia but there is no clinically available/affordable drug stimulating platelet production. As many thrombocytopenias are caused by infections, dogs need to be serologically and by Real-Time PCR examined for infections. And accordingly they are potentially presumptively treated, for instance with doxycycline until the specific microorganism is found and a specific treatment can be instituted. It should be noted that Babesia is more frequently associated with thrombocytopenia than hemolytic anemia. And indeed, there are many emerging infectious agents to consider, and double infections can cause more serious signs.

With respect to immunosuppression, glucocorticosteroids remain the best option despite their negative side effects. Aside initial dexamethasone and prednisolone/prednisone thereafter at their respective immunosuppressive doses (dexamethasone is 6-8 times more potent than prednisone), a high dose dexamethasone pulse regiment could be tried for four days, but likely has considerable

side-effects. On the other hand, vincristine is a useful additional agent. It is inexpensive, safe, and rapidly effective by massively increasing the platelet count within days. It is a tubulin inhibitor permitting more rapid release of platelets from marrow and inhibiting macrophage activity particularly in spleen and without bone marrow suppression. The main concern is perivascular necrosis which can be readily avoided, if a catheter is placed and flushing is used. A single strictly intravenous injection is usually sufficient but could be repeated after one week. Other alternatives are limited except for human intravenous immunoglobulin which seems to work similarly well as vincristine but is extremely expensive and not approved for dogs. Additional medications may include melatonin and thrombopoietic agents, but there is no data. Platelet transfusions raise the platelet count less than in other diseases likely due to the rapid antibody-coating of platelets and their removal, but may still ameliorate serious bleeding. Splenectomy may be a last resort and histopathology may offer also another mean of diagnosing an underlying cause.

Dogs which can be seriously bleeding due to von Willebrand disease are best treated with cryoprecipitate at 2-5 ml/kg every 6-8 hours until hemorrhage is controlled. In milder cases or to prevent hemorrhage during minor surgery in dogs with von Willebrand disease, desmopressin (DDAVP) at a dose of 1 µg/kg subcutaneously once (or repeated once on the second day) has been shown to shorten the buccal mucosal bleeding time and hemorrhage despite only marginally changing the plasma von Willebrand factor concentration.

While for any coagulopathy fresh or fresh frozen plasma could be administered (10 mL/kg or to effect) for some coagulopathies other therapeutic options should be considered. Coagulopathies due to rodenticide poisoning and several hereditary coagulation factor deficiencies (like Factor VII, IX, and XI deficiency) can be treated with cryo-poor plasma, while Hemophilia A (FVIII) and fibrinogen deficiency require cryoprecipitate. Depending on the cause of vitamin K deficiency higher or lower doses of vitamin K are administered (1-5 mg/kg twice daily). Vitamin K1 rather than K3 should be used. Oral absorption is very fast and effective and subcutaneous or intravenous injections may be considered, if nothing per os can be administered or gastrointestinal absorption is impaired (cholestasis, inflammatory bowel disease, antibiotics). Porcine and human coagulation factors have been experimentally studied in bleeding dogs and have also been used anecdotally in clinics. Human recombinant FVIIa may be used if FFP is not available in some coagulopathies although its efficacy and safety have not been extensively studied in dogs. Finally, the hemophilic dog has served as an excellent large animal model to develop and assess the efficacy and safety of hemophilia A and B and these studies have led to successful treatments in human hemophiliacs. It is foreseeable that gene therapy could be applied to the canine patients beyond experimental studies.

The management of DIC remains unrewarding unless the trigger can be removed or the underlying disease can be controlled. Rehydration is of utmost importance to assure adequate blood flow and tissue oxygenation. The use of unfractionated or Low Molecular Heparin or aspirin continue to be highly controversial. There are no controlled studies showing clinical efficacy of these agents in DIC. Similarly, the use of fresh frozen plasma or other plasma products in an attempt to replenish antithrombin III and consumed clotting factors is controversial and unless the animal exhibits overt signs of hemorrhage may be contraindicated.

In conclusion, simple and inexpensive in-practice tests are available to diagnose and differentiate hemostatic disorders. Platelets, vWF, coagulation factors as well as the vascular tissue you may be affected. While transfusions to correct anemia as well as provide the missing platelets and coagulation factors, there are also various drug therapies which may control bleeding.

CANINE TRANSFUSION THERAPY

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Veterinary clinicians and clinical pathologists play a key role in providing safe and effective transfusion therapy. Blood typing is clinically important to ensure blood compatibility and therefore is recommended for any dog in need of a transfusion or considered to become a blood donor. Moreover, previously transfused dogs also should be crossmatched. Unless blood typing is performed regularly in practice, blood may be sent to a clinical pathology laboratory for typing.

Selecting heathy blood donors and screening them against infectious and other diseases is critical for the safety of donor and the blood to be transfused. Blood collection and processing into blood components requires skills and training. There is no specific transfusion trigger and ideally only those components missing are transfused to support the patient. All blood components should be administered via filter and at a calculated volume and certain rate.

Canine Blood Types

Blood types are genetic markers on erythrocyte surfaces that are antigenic and species specific. A set of blood types of two or more alleles makes up a blood group system. Dogs have likely more than a dozen blood group systems mostly known as dog erythrocyte antigens (*DEA*). However, there is *no DEA 2* blood group and some may be rather labeled high frequency or common red blood cell (RBC) antigens (e.g. *DEA 4*) and some have not yet received an international *DEA* designation (e.g. *Dal* and *Kai 1 & 2*). Canine erythrocytes are either positive or negative for a blood type (e.g., *DEA 1+* or *DEA 1-*), and these blood types are codominantly inherited. Recent studies with a monoclonal antibody showed that the *DEA 1* blood group is a continuum from *DEA 1-* to weakly to strongly *DEA 1+*. The biochemical structure of the DEA 1 remains still unknown. Recent surveys revealed that most dogs are *Dal+* but the *Dal-* type is not restricted to Dalmatians but is also seen in Doberman Pinschers, Corso, Lhasa Apsos, and Shih Tzus. In related studies in dogs two new blood types, *Kai 1* & *Kai 2*. Most dogs were *Kai 1+* and only few dogs were Kai 2+ or Kai 1-/Kai 2-.

The clinically most important canine blood type is *DEA 1*, which elicits a strong alloantibody response after sensitization of a *DEA 1-* dog by a transfusion and thus can be responsible for a hemolytic transfusion reaction in a *DEA 1-* dog previously transfused with *DEA 1+* blood. Furthermore, transfusion reactions against other blood types or common antigens have rarely been reported. They include reactions against the *DEA 4, Dal, Kai 1* and other common RBC antigens; other clinically important blood types may be found in the future. Only limited surveys on the frequency of these blood types have been reported, which suggest possible geographic and breed-associated differences.

Clinically the most antigenic blood type in dogs is the DEA 1. Transfusion of *DEA 1+* RBCs to a *DEA 1-* dog invariably elicits a strong alloantibody response. Following a first transfusion, anti-

DEA 1 antibodies develop after more than 4 days and may cause a delayed transfusion reaction (rarely clinically documented). However, a previously sensitized *DEA 1*- dog can develop an acute hemolytic reaction after a second transfusion with *DEA 1*+ blood. Transfusion reactions also may occur after a sensitized dog receives blood that is mismatched for a RBC antigen other than DEA 1 (e.g. *DEA 4* and *Dal*). However, in most cases the incompatible blood type has not been determined. Because administration of a small (<1 ml) amount of incompatible blood can result in life-threatening reactions, the practice of giving small "test volumes" of donor blood to assess blood-type compatibilities is not recommended. In contrast, pregnancy does not cause sensitization in dogs, because of a complete placenta, and does not induce alloantibody production; thus dogs with prior pregnancies can be used safely as blood donors.

Canine Blood-Typing Procedures

Because of the strong antigenicity of *DEA 1*, typing of donors for *DEA 1* is recommended and *DEA 1*- patients should only receive *DEA 1*- blood. Whenever possible, the recipient also should be typed to allow the use of *DEA 1*+ blood for *DEA 1*+ recipients. Canine blood typing tests are generally based on serologic identification by agglutination reactions in tube or on a card but chromatographic strip and gel column methods are also offered. A blood typing card kit has been available as a simple in-practice kit to classify dogs as *DEA 1*- or *DEA 1*+ (DMS laboratories). DMS also offers *DEA 4 & 5* card kits as well as *Dal* typing. Simple immunochromatographic and gel minitube kits became available in the mid-2000s from Alvedia. In addition cartridge based tests are available from Abaxis/Zoetis. Kai 1 & 2 can be typed by a kit from KABB in South Korea.

Caution should be exercised whenever the patient's blood is autoagglutinating or has a low hematocrit (<10%). If autoagglutination is not too severe, it does not appear to affect the Alvedia strip technique because only free RBCs are moving up the strip. Prior to typing, clinicians and technicians should check for autoagglutination of blood with buffer/saline in a tube or on a slide. Autoagglutinating blood may be first washed three times with ample physiological saline to overcome the apparent autoagglutination similar to what is done for the Coombs' and crossmatch testing. However, if autoagglutination after three washes persists at more than 1+, it is considered to reflect true autoagglutination, which may preclude typing (as well as Coombs' testing and crossmatching), because it always looks like DEA 1+ blood. In such circumstances, DEA 1- blood should be used, until the patient does not agglutinate anymore and can be retyped. Finally, recently transfused dogs may display a mixed field reaction, with only the transfused or recipient cells agglutinating if they were DEA 1 mismatched.

Blood Crossmatching Test

Whereas blood typing tests reveal the blood group antigens on the red blood cell surface, blood crossmatching tests assess the serologic compatibility or incompatibility between donor and recipient. Thus, the crossmatch test checks for the presence or absence of naturally occurring and induced alloantibodies in serum (or plasma) without determining the blood type and thereby does not replace blood typing. These alloantibodies may be hemagglutinins and/or hemolysins and can be directed against known blood groups or other RBC surface antigens. Many laboratories commonly use a standardized tube or microtiter plate crossmatching procedure, but the interpretation of the

agglutination reaction is highly variable. The crossmatching test requires some technical expertise, may be accomplished through a veterinary laboratory along with blood typing, and is done with washed EDTA-anticoagulated blood from recipient and potential donor(s). The laboratory and in clinic gel column and strip kits were found to be simple, sensitive, and standardized methods to crossmatch dogs and cats.

The major crossmatch tests search for alloantibodies in the recipient's plasma against donor cells, whereas the minor crossmatch test looks for alloantibodies in the donor's plasma against the recipient's RBCs. Generally fresh EDTA-anticoagulated blood or tube segments from stored collection bags are used for this purpose in dogs. The presence of autoagglutination or severe hemolysis may preclude the crossmatch testing. A major crossmatch incompatibility is of greatest importance, because it predicts that the transfused donor cells will be attacked by the patient's plasma, thereby causing a potentially life-threatening acute hemolytic transfusion reaction. Because fatal reactions may occur with less than 1 ml of incompatible blood, compatibility testing by administering a small amount of blood is not appropriate. A minor crossmatch incompatibility should not occur in dogs if canine donors have not been transfused previously and is also of lesser concern because donor's plasma volume is small, particularly with packed red cell products, which is diluted markedly in the patient. Do not use previously transfused dogs as donors.

The initial blood crossmatch between two dogs that have never before received a transfusion should be compatible, because dogs do not have naturally occurring alloantibodies. Therefore, a crossmatch may be omitted before the first transfusion in clinical practice for dogs. Previously transfused dogs should always be crossmatched, even when receiving again blood from the same donor. The time span between the initial transfusion and incompatibility reactions may be as short as 4 days and the induced alloantibody can last for many months to years (i.e., years after the last transfusion alloantibodies may be present). The practice of transfusing patients with the least compatible unit does not have any scientific basis. Nevertheless, some minor agglutination results in crossmatching a patient may be unrelated to alloantibodies and unspecific (e.g., patient's RBC damage by uremia and other illnesses, donor cells after extended storage of unit in the refrigerator).

Although transfusion of blood and its components is usually a safe and temporarily effective form of therapy, there is always a risk for potential hazards as it is a biological product and not a drug. Adverse reactions usually occur during or shortly after the transfusion and can be due to any component of whole blood. Most transfusion reactions can be avoided by carefully selecting only healthy donors; using appropriate collection, storage, and administration techniques; performing blood typing and crossmatching; and administering only the needed blood components.

Transfusion Reactions

While transfusion of blood and its components is usually a safe and temporarily effective form of therapy, there is always a risk for potential hazards. Adverse reactions usually occur during or shortly after the transfusion and can be due to any component of whole blood. Most transfusion reactions can be avoided by carefully selecting only healthy donors, using appropriate collection, storage, and administration techniques, performing blood typing and crossmatching, and administering only needed blood components. The most common clinical sign of transfusion reaction

is fever, followed by vomiting, urticaria, and hemolysis. Hemolytic transfusion reactions can be fatal and are, therefore, most important, while fever and vomiting are usually self-limiting. Adverse effects of transfusions can be divided into non-immunologic (pyrogen-mediated fever, transmission of infectious agents, vomiting, mechanical hemolysis, congestive heart failure, hypothermia, citrate toxicity, pulmonary complications) and immunologic reactions (acute and delayed hemolytic transfusion reactions, urticaria to anaphylaxis, acute respiratory distress, graft versus host disease). Note that some clinical signs may be caused by both mechanisms. Despite the variety of blood types and the limited degree of compatibility testing in clinical practice, hemolytic transfusion reactions are rarely reported.

Blood Donors and Sources

Many larger veterinary hospitals have permanent canine and/or feline blood donors to cover their transfusion requirements or in special cases fresh whole blood or platelet-rich plasma (concentrate) is needed. Several larger voluntary blood donor programs have emerged with client or staff owned dogs. More than a dozen commercial canine blood banks have been established in the United States and deliver overnight blood products.

Autologous (self) transfusion refers to the donation of blood by a patient four weeks to a few days prior to surgery when major surgical blood loss is anticipated. Blood can also be collected immediately prior to surgery. The patient will be hemodiluted with crystalloid and colloid solution and receives the blood when excessive bleeding occurs or after surgery. Autotransfusion is another autologous transfusion technique in which freshly shed blood salvaged intra-operatively or following trauma can be reinfused after careful filtering. Because it should only be done with fresh (intraoperative) bleeding and is technically difficult, it is rarely performed.

Blood donors should be young adult, lean, and good tempered animals, and weigh at least 23 kg for dogs (to donate 450 ml; smaller dogs may donate proportionally less); have no history of prior transfusion; have been regularly vaccinated (but not within a month of last vaccine), and are healthy as determined by history, physical examination, and laboratory tests (complete blood cell count, chemistry screen, and fecal parasite examination every 6-12 months) as well as free of infectious diseases (testing in dogs depends on geographic area but may include regular microfilaria, Brucella, Hemomycoplasma, Babesia, Ehrlichia, Anaplasma, Borrelia, Leishmania). Donors should receive a well-balanced, high performance diet, and may be supplemented twice weekly with ferrous sulfate (Feosal, 10 mg/kg), if bled frequently (no more than every 6-8 weeks). Packed cell volume (PCV) or hemoglobin (Hb) should be >40% and >13 g/dl, respectively, in canine donors.

Blood Collection and Component Preparation

Canine donors are generally not sedated. After clipping and surgical scrub, blood is collected aseptically by gravity or blood bank vacuum pump from the jugular vein over 5-10 minute period. Blood bank plastic bags containing citrate-phosphate-dextrose-adenine (CPD-A1) with or without satellite bags for blood component separation are optimal. These commercial blood bags represent

a closed collection system in which the blood does not come into contact with the environment at any time during collection or separation into blood components, thereby minimizing the risk of bacterial contamination and allowing storage of the blood products. The maximal blood volume to be donated is 20 ml blood/kg or one regular blood bag unit of 450 ± 45 ml per ≥ 25 kg dog. There are also 250 and 150 ml bags available.

Blood components are prepared from a single donation of blood by centrifugation generally within 8 hours from collection; thereby, fresh whole blood can be separated into packed red blood cells, platelet-rich plasma or concentrate, fresh frozen plasma, cryoprecipitate and cryo-poor plasma. Fluctuations in storage temperature alter the length of storage; thus, temperature needs to be monitored and the refrigerator/freezer are not too frequently opened. Partially used or opened blood bags should be used within 24 hours because of the risk of contamination.

Administration of Blood Products

For routine transfusion in the treatment of anemia, it is not necessary to warm blood after removal from the refrigerator. A temperature-controlled waterbath (37°C) is ideal to warm frozen blood products. A warm water bowl in which the water is periodically changed may be used to warm blood products. Care should be taken to maintain a aseptic conditions and to not overheat the blood products; thus, do not use microwave.

Blood bags are connected to blood infusion sets that have an in-line microfilter. A long (85 cm) blood infusion set with a dripping chamber and a short infusion set for small dogs to connect with syringes are available. Use a latex-free infusion sets for platelet administration to avoid aggregation. Microfilter with 170 µm pores are commonly used to remove clots and larger red blood cell and platelet aggregates. Finer filters with 40 µm pores will remove most platelets and microaggregates and clog after <100 ml. Leukocyte reduction filters (expensive) may be used to decrease febrile adverse reactions to WBC components prior to storage.

Blood components are best administered intravenously with an indwelling catheter (16-22 gauge depending on size of the animal). An intramedullary (or intraosseous) infusion at the trochanteric fossa (or other sites) may be used when no venous access can be obtained while the intraperitoneal administration is not recommended. Avoid concurrent administration of drugs or fluids other than physiologic saline through the same catheter in order to prevent lysis of erythrocytes and blood coagulation.

The rate of transfusion depends on the hydration status, degree of anemia, and general health condition of an animal. Initial rate is slow, starting with 1-3 ml over the first 5 minutes to observe for any transfusion reactions, even with blood typed and/or crossmatched transfusions. In animals with cardiac failure, do not exceed 4 ml/kg/hour. Transfusion of a single bag should be completed within 4 hours to prevent functional loss and bacterial growth. Volume of blood component to be administered depends on the type of deficiency and size of the animal. In anemia: Volume (ml) of whole blood = 2 x PCV rise desired (%) x body weight (kg) or in other words, administration of 2 ml

whole blood/kg body weight raises the PCV by 1%. If packed red blood cells are used without prior resuspension in a red blood cell preservative, closer to half the volume is administered, since packed red blood cells have a PCV of 70-80%. In the absence of bleeding and hemolysis, at least 80% of transfused erythrocytes survive 24 hours (required blood bank standard) and transfused erythrocytes may be thereafter expected to have a normal life-span (~110 days in dogs). Response to transfusion is carefully monitored by obtaining PCV/Total Protein readings prior to, immediately, 2, 4, 6 and 24 hours post-transfusion, and observing the clinical parameters of a patient.

In thrombocytopenia or thrombopathia, platelet transfusions are only used with life-threatening bleeding. One unit of Platelet Concentrate, Platelet Rich Plasma or Fresh Whole Blood will increase the platelet count by ~10,000/µL in a recipient weighing 25 kg. Platelet counts are monitored prior, 1 hour and 24 hours after the platelet transfusion. Even if the platelet count does not increase as expected the platelets may have sealed the injury site and stopped the bleeding.

In coagulopathies and von Willebrand's disease, Fresh Frozen Plasma at 6-10 ml/kg is an initial dose to stop bleeding or avoid excessive bleeding during surgery. In some cases, larger volumes may be needed to control bleeding. Depending on the coagulopathy (and haf-life of coagulation factor), repeated administration of FFP may be required every 6-24 hours. Thus because of the short half-life of factor VII and VIII and von Willebrand factor, deficient animals need to be treated twice to four times daily. Other coagulopathies may be treated daily. Cryoprecipitate at a dose of 1 Cryoprecipitate unit/10 kg or 2-4 ml/kg body weight twice daily is ideal to treat hemophilia A as well as von Willebrand's disease. Plasma support should be provided for an additional 1-3 days after the bleeding has been controlled to allow for wound healing and prevent rebleeding. In addition to transfusions, specific drug therapies for bleeding patients are covered in sessions on bleeding.

In conclusion, after a specific diagnosis of the anemia and bleeding, has been made, diseased animals may be blood typed for *DEA 1* (and crossmatched if previously transfused) to assure blood compatibility and avoid sensitization. Appropriately collected blood from healthy screened donors may be transfused as whole blood or one of its components. During transfusions patients need to be carefully monitored for transfusion reactions as well as efficacy like increase in hematocrit or ceasing the bleeding. Many patients may only be saved by transfusions and if not available in a clinical practice a referral to a clinic with transfusion support is recommended.

CLINICAL APPROACH TO THE DIAGNOSIS OF ANEMIA

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Anemia is an extremely common clinical sign and laboratory test abnormality in dogs and cats which is associated with many different diseases. Specific clinical signs of anemia include pallor, hemorrhage, and icterus. Unspecific signs are lethargy and exercise intolerance. Despite severe anemia many animals may only show mild clinical signs particularly when the anemia is chronic. In order to recognize the type, degree, and erythroid regeneration of the anemia in animals, it is important to appropriately appreciate the hematological peculiarities of dogs and cats. When compared to dogs, the normal packed cell volume in cats is lower (Dogs PCV 35-56%; 0.35-0.56/L vs Cats PCV 30-48%; 0.30-0.48/L), feline red blood cells (RBCs) are considerably smaller (Dogs MCV 62-76 fL vs Cats 38-50 fL), central RBC pallor is small in cats (therefore one cannot see spherocytes in cats), bone marrow iron stores are visually lacking in cats , and there are mostly mild regenerative marrow responses observed with any anemia in cats.

Polychromasia on a regular blood smear and reticulocytosis based upon a special vital stain are the best parameters to assess erythroid regenerative bone marrow response with an absolute reticulocyte count (normally <60,000/µl). All types of anemia start off as non-regenerative for the first two days but then regeneration is developing in hemolytic and blood loss anemias. Note nucleated RBCs may be proportionally increased with reticulocytes or may independently be elevated due to bone marrow endothelial damage, as for instance in lead poisoning, sepsis, and myelodysplasia. The evaluation of PCV, total protein, and blood smear are most valuable. However, a complete blood count (CBC) and other specific tests are desirable to better classify the anemia, reach a precise diagnosis, and to monitor the response to therapy. It should be noted that a microscopic blood smear which may detect RBC abnormalities and inclusions, is not a regular part of a CBC. Veterinary clinicians and technicians benefit from reviewing a blood smear from an anemic animal.

A CBC with reticulocyte count of modern laser/flow hematology analyzers is ideal to best assess hematological disorders, but expensive for clinical practice. Thus, either a smaller impedance hematology analyzer or referral of sample to a reference laboratory may be achievable in any clinic. Moreover, other tests are likely needed to reach a precise diagnosis. These may include serum chemistry screen, urinalysis, bone marrow and other hematopoietic tissue cytology or biopsy, hemostatic tests, iron parameters, infectious disease screen by serology and PCR tests, toxicological analyses, direct Coombs' test, genetic/DNA tests, imaging, and blood typing and crossmatching. Some of these tools will be exemplified in this or other lectures at this congress.

Blood loss anemias are common in dogs but far less frequently seen in cats. They happen with endo-/ectoparasites, trauma/surgery, and cancer. Moreover, chronic external blood loss can result in iron deficiency particularly in the very young animals due to the small iron stores. Iron deficiency is characterized by microcytosis and hypochromasia (and frequently

thrombocytosis). Skin, gastrointestinal, and other tumors may also cause external blood loss and iron deficiency anemia. In contrast, acute blood loss anemias are generally regenerative after 3-4 days and remain regenerative even when iron is lost. While in the above cases hemorrhage is caused by vascular injury, there are also a variety of bleeding disorders to consider. Hemostatic disorders may be acquired but there are also many hereditary bleeding disorders.

Thrombocytopenia is rare in cats but common in dogs and may be immune-mediated or caused by infections and cancer. Accurate platelet counts can be difficult to obtain, particularly in cats and with impedance analyzers due to the large size platelets and tendency to aggregate in cats. Thus, any platelet count needs to be confirmed with an estimate from a microscopic blood smear examination (20,000 platelets/µL equals 1 platelet seen on a high power microscopic field). Platelet counts are normally a little higher in cats than in dogs (normal 150,000-500,000/µL) with bleeding typically only occurring when the platelet count is less than 40,000/µL. **Thrombopathia** – impaired platelet function – may be triggered by aspirin or similar drugs, renal failure, and/or rarely be inherited.

Coagulopathies can be readily screened for by prothrombin time (PT) and partial thromboplastin time (PTT) or activated coagulation time (ACT). Anticoagulant rodenticide poisoning, heparin exposure, and hepatic disorders are common and important coagulopathies. There are also several hereditary coagulopathies, such as X-chromosomal hemophilia A and B as well as Factor VII and XI deficiency. Noteworthy, Factor XII deficiency, seen commonly in cats, does not cause a bleeding tendency. Generally, the prothrombin and partial thromboplastin times provide sufficient information to differentiate the coagulopathies, although specific factor analyses may be needed. Thromboelastography is more suited for thrombotic and fibrinolytic tendencies.

Hemolytic anemias are regenerative and associated with hyperbilirubinemia -uria. There may also be evidence of intravascular hemolysis, but hemolyzed plasma/serum may be artifactual (poor handling, heat exposure, and long storage of blood samples). There are many causes of hemolytic anemias and not just infections and immune-mediated diseases:

• Infections (e.g. Babesia, hemoplasma)

• Immune (primary (auto- and allo-immune) and secondary (drugs, infections, cancers)

• Toxic (e.g drugs, onions)

• Metabolic (e.g hypophosphatemia)

• Hereditary (e.g. pyruvate kinase and phosphofructokinase deficiency)

Immune-mediated hemolytic anemias (IMHA) are common in dogs but rare in cats. Autoagglutination (which is persistent after 3 x washing with saline), marked spherocytosis (can only be noted in dogs), and/or species-specific Coombs' tests are the best diagnostics to document an immune destruction of erythrocytes. IMHA can be primary (auto-immune) or secondary associated with infections, cancer, and drugs. Blood type incompatibilities can result in hemolysis in dogs after being sensitized by a prior transfusion. In contrast, an A-B mismatch in cats can cause an acute

hemolytic transfusion reaction at first transfusion as well as hemolysis of newborn (neonatal isoerythrolysis during first few days) at first breeding. Transfusing canine blood to cats (xenotransfusion) causes always severe hemolytic transfusion reactions and is therefore not recommended.

There are several important **differential diagnoses for hemolytic anemias** and thus specific treatment options depend on the cause of hemolysis. Various triggers such as drugs and chemicals may be identified and can be rapidly removed. However, other diagnoses may require tests at reference laboratories, such as for serology and real-time PCR for infectious diseases and genetic tests for hereditary erythrocyte defects. It is, therefore, not unusual to start with a combination of prednisolone and doxycycline as initial treatment of hemolytic anemias to cover the bases until test results are back and specific and proper therapy can be instituted. For hereditary hemolytic anemias, it is most important to avoid harmful treatments and offer a safe environment. Thereby, some anemic animals with hereditary erythrocyte defects may live for many years with good quality of life.

Lastly, **non-regenerative anemias** due to decreased erythro- or overall hematopoiesis can be associated with a variety of disorders. Indeed, mild non-regenerative normochromic-normocytic anemia is commonly seen with many organ diseases and is mostly well tolerated. However, many middle-aged to older cats (less commonly dogs) with chronic renal failure develop a moderate to severe anemia. The main cause is a lack of renal production of erythroproietin, but uremic toxins affecting RBC stability and impairing erythropoiesis as well as blood loss from gastrointestinal ulcers also play a role. Transfusion and/or human recombinant erythropoietin (darbepoetin) may reverse the anemia and associated clinical signs but not the renal failure. However, repeat transfusions are generally needed and animals may become refractory to transfusions, as they develop alloantibodies against the transfused RBCs. Moreover, companion animals can develop antibodies against the recombinant human erythropoietin, which leads to a severe and hardly reversible pure red cell aplasia. While dogs and cats are rarely truly deficient, iron, folate, and cobalamin may be replenished as needed. Finally, mild non-regenerative anemia is commonly observed with anemia of inflammation with organ diseases, a variety of infections and cancers.

PECULIARITIES OF FELINE ANEMIAS

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Anemia is an extremely common clinical problem in cats and is associated with many different conditions. It is well recognized that various infections can cause hemolytic anemias in cats. And while primary (auto-) immune-mediated hemolytic anemias (IMHA) are uncommon in cats, there are other hemolytic anemias including chemically induced Heinz body and methemoglobinemias and hereditary erythrocyte defects, such as PK deficiency, increased osmotic fragility, and porphyria. Bleeding disorders are far less common in cats than dogs, but there are a few unique considerations such as coagulopathies associated with hepatic disorders. And of course non-regenerative anemias caused by renal and bone marrow issues are of major consideration in cats. This session will review the approach to anemic cats illustrated by case examples.

Anemia

Despite severe anemia many cats may only show mild clinical signs particularly when chronic. In order to recognize the type, degree, and regeneration of the anemia in cats, it is imperative to appropriately appreciate the hematological peculiarities of cats. When compared to dogs, the normal hematocrit or packed cell volume in cats is lower (Hct/PCV 30-48%; 0.30-0.48/L), feline red blood cells (RBCs) are considerably smaller (MCV 38-50 fL), central RBC pallor is small (therefore one cannot see spherocytes in cats), bone marrow iron stores are visually lacking, and there are mostly mild regenerative marrow responses observed with any anemia in cats.

Erythroid regeneration: There are aggregate reticulocytes by vital stain which are also reflected as polychromasia on a regularly stained blood smear. They are short-lived in circulation (one day as in dogs). However, cats also have punctate reticulocytes (<10 punctates), which may linger around in circulation for a couple of weeks. The best parameter to assess a regenerative bone marrow response is the absolute reticulocyte count (normally <60,000/µL), which refers to the presence of aggregate reticulocytes and is equal to the degree of polychromasia. Note nucleated RBCs may be proportionally increased with reticulocytes or may occur independently due to bone marrow endothelial damage as for instance with lead poisoning, sepsis, and myelodysplasia. While the evaluation of PCV/Hct, total protein, and blood smear are most valuable, a complete blood count (CBC) and specific tests are generally desired to classify the anemia, reach a specific diagnosis and to monitor the response to therapy.

A CBC with reticulocyte count by a modern hematology analyzers is ideal to best assess hematological disorders, but other tests are likely needed. These may for instance include serum chemistry screen, urinalysis, bone marrow and other hematopoietic tissue cytology or biopsy, hemostatic tests, iron parameters, infectious disease screen by serology and PCR, toxicological analysis, direct Coombs' test, and genetic/DNA tests as well as imaging.

Non-regenerative Anemias

Non-regenerative anemias due to decreased erythro- or overall hematopoiesis can be associated with a variety of disorders. It should be noted every anemia starts of as non-regenerative normocytic normochromic for the first couple of days. Indeed, mild non-regenerative normochromic-normocytic anemia is commonly seen with many organ diseases and is mostly well tolerated.

Many middle-aged to older cats develop chronic renal failure with a moderate to severe anemia. The main cause is a lack of renal production of erythropoietin, but uremic toxins affecting RBC stability and erythropoiesis as well as blood loss from ulcers may also play a role. Transfusion can alleviate the anemia and associated clinical signs. Moreover, human recombinant erythropoietin (darbepoetin) can reverse the anemia but cats may develop antibodies against the recombinant human erythropoietin, which leads to a severe and hardly reversible pure red cell aplasia. Iron supplementation and control of hypertension may be needed. It should be noted the renal failure will neither be helped by transfusion nor erythropoietin.

FeLV infections may end in a pure red cell aplasia or myelodysplasia to aplasia (and far less commonly leukemia), while FIV exhibits less effects on the bone marrow. Cancer associated anemias may have many causes, but may result in aplastic or myelophistic bone marrows. Finally, mild non-regenerative anemia is commonly observed with anemia of inflammation with organ diseases and a variety of infections and cancers.

Blood Loss Anemias and Bleeding Disorders

In contrast to dogs, blood loss anemias are less commonly observed in cats, albeit they happen with ectoparasites, trauma, and surgery. In fact, many cats drop their PCV during and shortly after surgery which may in part be due to blood loss, but also unexplained erythrocytic lysis and sequestration. Moreover, external blood loss can rapidly result in iron deficiency particularly in kittens (even with repeat phlebotomies for diagnostic purposes), due to their small iron stores. However, the classic microcytosis and hypochromasia seen in dogs with iron deficiency may be very difficult to appreciate in cats. The most common reason for blood loss is flea infestation, while maggots, ticks, and hookworms are less likely leading to major external blood loss. Skin and other tumors may also cause local bleeding. Separate lectures cover extensively the diagnostic approach and management of bleeding disorders.

Thrombocytopenia is rare in cats but may be induced by drugs (methimazol) and rarely infection (except for a new agent in Japan) and cancer. Also immune-mediated thrombocytopenia seems to occur rarely. Accurate platelet counts can be difficult to obtain and particularly with impedance analyzers due to the cats' large size platelets (compared to small erythrocytes) and tendency of platelets to aggregate. Thrombopathia refers to impaired platelet function and may be

triggered by aspirin or similar drugs (cats appear particularly sensitive to platelet injury but less likely to aspirin or steroidal ulceration). Hereditary thrombopathias and von Willebrand disease are extremely rarely seen in cats.

Coagulopathies due to hepatic failure are much more common and severe in cats than dogs. In contrast anticoagulant rodenticides are rarely ingested by cats and thus this toxicity is rarely seen in cats. Furthermore, there are several hereditary coagulopathies such as hemophilia A and B in domestic and purebred cats as well as Factor XI deficiency in Maine Coon cats and a vitamin K-dependent coagulopathy in Devon Rex and Sphinx cats. Interestingly, domestic and exotic shorthair cats often have a coagulation factor XII deficiency; while this causes a markedly prolonged partial thromboplastin time, this is clinically not associated with a bleeding tendency. Generally, the prothrombin and partial thromboplastin times provide sufficient information to differentiate the coagulopathies, although specific factor analyses may be needed.

Hemolytic Anemias

Hemolytic anemias in cats are often hard to recognize as the degree of bone marrow regeneration and the evidence of hyperbilirubinuria and hyperbilirubinemia are often mild (any bilirubinuria is important in a cat). In fact, icterus in cats is much more likely due to hepatic failure than hemolysis, and intravascular hemolysis is only seen with acute toxicities. While the normal feline spleen is very small, it can get fairly enlarged in some cases of hemolytic anemia.

A variety of **viral, bacterial, and parasitic infections** can induce hemolytic anemias. The most common cause are hemomycoplasma infections, but also other bacteria and hemoparasites such as Cytauxzoons and Babesia may have to be considered. Likewise FeLV and FIP may be associated with hemolysis and indeed coinfections may result in more severe hemolysis and illness. Thus, careful screening by cytological examination of blood smear, serology, and PCR and other antigen tests is generally recommended. Until a definitive diagnosis is made, cats may be treated with doxycycline but marbofloxacin should not be used unless there is a definite diagnosis of persistent hemoplasma infection after a full course of doxycycline. And of course, these antibiotics will not be effective against hemoparasites. Because these infectious diseases are typically covered from clinical signs to therapy in many other lectures, they will be only mentioned here.

There is a syndrome of **increased erythrocytic osmotic fragility** seen in Abyssinian, Somali and other non-pedigreed and purebred cats with massive splenomegaly, hyperproteinemia and lymphocytosis. Osmotic fragility testing is only offered by a few laboratories, mostly because it is a time consuming test. However, checking the degree of lysis after a few hour storage of EDTA blood may indicate increased erythroid fragility. Erythrocytic **pyruvate kinase (PK) deficiency** is a common hereditary disease causing intermittent hemolytic anemia in Abyssinian, Somali, and other purebred and even non-pedigreed cats. Interestingly, all PK-deficient cats have the same PK gene mutation identified by us >20 years ago and a simple DNA test has been available to detect homozygous affected and asymptomatic heterozygous carriers. There is also **porphyria**, a heme synthesis defect, which causes hemolysis but most remarkably erythrodontia with dark and fluorescing teeth in cats. Urinary metabolic or mutation-specific DNA testing permits a definitive diagnosis. Porphyria may be

dominantly or less commonly recessively inherited, and cats may live for years with this condition requiring no specific treatment.

Table – Feline Hemolytic Anemias

- **Infections**
  - Mycoplasma hemofelis, (also hemominutum, turicensis)
  - Cytauxzoon felis and others
  - Feline Leukemia Virus infection
  - Feline Infectious Peritonitis
  - Bacterial infections including abscesses

- **Immune**
  - Alloimmune – neonatal isoerythrolysis and acute transfusion reactions
  - Autoimmune or primary hemolytic anemia (rare compared to dogs)
  - Secondary (drugs [methimazol], infection, cancer)

- **Toxic**
  - Drugs - acetaminophen, lidocaine spray, Propofol, etc.
  - Onions and garlic

- **Metabolic**
  - Hypophosphatemia

- **Hereditary**
  - Pyruvate kinase deficiency
  - Increased osmotic fragility
  - Porphyria (Siamese and DSH cats)

In contrast to dogs, **primary (auto-) immune-mediated hemolytic anemia** seems to occur rarely in cats, but may be seen with other triggers, such as infections, drugs (methimazol), and cancer (lymphoma) as secondary IMHA. Their species-specific direct antiglobuilin (Coombs') test is positive. In addition, some show autoagglutination that may break up when adding saline and most after 3x washing with physiological saline when caused by unspecific *in vitro* agglutination, such as possibly induced by EDTA-anticoagulant and exposure to cold. More important than primary IMHA is *anti-A* alloantibody associated hemolysis. Neonatal type *A* and *AB* kittens nursing from a type *B* queens will frequently develop acute hemolysis of the newborn, also known as **neonatal isoerythrolysis** during the first hours to three days of life. Classic signs are acute death, massive pigmenturia due to hemoglobinuria, and occasionally they may develop icterus and a tail tip necrosis and survive. Similarly important are *A-B* mismatched **acute hemolytic transfusion reactions**. They can happen at the first transfusion due to preformed *anti-A* alloantibodies and rarely others like *Mik* or after sensitizing by prior transfusion but not pregnancy. Thus, *AB* typing (and crossmatching of a previously transfused cat) is critical prior to breeding and transfusing cats. Transfusing canine blood to cats (i.e. xenotransfusion) causes always severe acute hemolytic reactions with RBCs only surviving <4 days and is, therefore, not recommended.

Toxic hemolysis – Feline erythrocytes are very sensitive to oxidative damage as their and the overall metabolism is limited. For conjugation they do not have a glucuronidation and quickly deplete their sulfation process. Moreover, the feline hemoglobin has multiple sulfa groups which can become targets to oxidative damage. Thus, toxic effects may cause intra- and extravascular hemolysis. Classic features may be **Heinz body** and methemoglobinemia. Heinz bodies refer to precipitated hemoglobin which may attach to membranes. Eccentrocytes indicate more massive oxidation where parts of erythrocytes lack any hemoglobin. Heinz bodies are seen as refractile bodies on regularly stained blood smears, but are best identified with a vital stain like new methylene blue – there are large and small Heinz bodies which need to be differentiated from Howell Jolly bodies and other inclusions. Heinz bodies may be seen along with methemoglobinemia.

Methemoglobin which indicates oxidation of heme iron from Fe^{2+} to Fe^{3+} cannot carry oxygen. While normal venous blood turns bright red when exposed to air (e.g. on filter paper), blood containing methemoglobin remains dark brownish. And of course there are in-clinic and laboratory instruments which can measure methemoglobin concentration. A prime example the accidental or inappropriate administration of paracetamol but even large quantities of onions may elicit oxidative damage to erythrocytes and other tissues. Acetylcysteine and methylene blue (quick and highly effective but has a narrow therapeutic index) are excellent antidotes.

In conclusion, variety of peculiarities to the anemias are seen in cats. Specific diagnostics as well as treatments are available to manage these anemic cats and their many illnesses effectively.

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FELINE TRANSFUSION THERAPY

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Transfusion support is critical for the feline patient, most commonly to correct anemia and less often bleeding. Nevertheless, blood transfusions are overall still less frequently administered to cats than dogs for a variety of reasons. Recently, guidelines on feline blood transfusions as well as original studies on topics related to transfusion, donor selection, and blood type compatibilities relevant to clinical feline practice have been published. In this session, the peculiarities of feline blood types, blood collection and processing, and blood transfusion and transfusion reactions will be presented and illustrated with practical case examples. Neonatal isoerythrolysis and xenotransfusions will also be covered.

Compared to dogs, cats can tolerate anemia better and bleed less frequently except for those cases with feline hepatopathies and trauma. Recruiting healthy donors is more difficult (occult heart disease, viral infections), blood collection requires sedation and special small bag collection systems, and component therapy is less commonly practiced in clinics. There is no specific trigger PCV, but rather the overall clinical picture with a PCV of <20% is used. Cats have important naturally occurring alloantibodies and may experience life-threatening complications with a first transfusion. Beside acute hemolytic transfusion reactions, the anemic cat is also more sensitive to volume overload and can experience other transfusion reactions. Excellent transfusion practice with quality control and monitoring of transfused feline patients is critical to provide effective and safe transfusion support.

Blood Typing

The major feline blood group system is known as the feline *AB* or by some *ABC* blood group system – to not confuse with the human *AB* system and in recognition of the unique *AB (C)* type. The *ABC* blood group system contains 3 alleles: type *A*, type *B*, and the rare type *AB* (or also known as *C* type). Type *A* is dominant over *B*. Thus, cats with type *A* blood have the genotype *A/A* or *A/b* (also rarely A/a^c), and only homozygous *b/b* cats express the type *B* antigen on their erythrocytes. In the rare *AB (C)* cat, a third allele (a^c) recessive to the *A* allele and/or codominant to *b* allele leads to the expression of both *A* and *B* substances. Noteworthy, *AB (C)* cats are not produced by mating of a type *A* to a type *B* cat, unless the *A* cat carries the rare a^c allele. Cats with type *AB (C)* blood have been seen in many breeds, but particularly in Ragdolls, and also domestic shorthair cats in some geographic regions like Israel.

Most domestic shorthair cats have type *A* blood, but the proportion of type *B* cats can be substantial in certain geographical areas. The frequency of *A* and *B* blood types varies greatly between different breeds, but likely not much geographically in purebred cats (depends on catteries). Kitten losses due to *A-B* incompatibility and changes in breeding practices influence the frequency of *A*, *B* and even *AB (C)* in various breeds. Most blood donors have type *A* blood, but some places also

keep cats with the rare type *B* and type *AB* as donors. All blood donors must be *AB (C)* typed or, if not available or previously transfused, crossmatched to patient in order to assure blood compatibility even for a first transfusion. Naturally-occurring alloantibodies have been well-documented in type *B* and to much lesser extend type *A* cats and absolutely require that blood typing (or if not available crossmatching) be performed prior to both blood transfusion and breeding to assure appropriate blood compatibility.

In contrast to dogs, cats can have naturally-occurring alloantibodies. All type *B* cats as of 3 months of age have very strong naturally-occurring *anti-A* alloantibodies, which can be detected by hemolysis and hemagglutination assays. Kittens receive alloantibodies only through the colostrum from type *B* queens, and all type *B* kittens develop high alloantibody titers (>1:32 to 1:2048) after a few weeks of age. These alloantibodies are strong hemolysins and hemagglutinins, and are of the IgM and, to a lesser extent, IgG classes. They are responsible for serious acute hemolytic transfusion reactions and neonatal isoerythrolysis (hemolysis of the newborn) in type *A* or *AB (C)* kittens born to type *B* queens. Type *A* cats have no or only weak *anti-B* alloantibodies; their alloantibody titer is usually very low (1:2 to 1:32). Nevertheless, they can also cause hemolytic transfusion reactions, but have not been associated with neonatal isoerythrolysis. Type *AB (C)* cats have no alloantibodies. Furthermore, additional blood group systems have been identified, such as the common *Mik* red blood cell antigen in domestic shorthair cats. *Mik-* cats may also produce naturally occurring *anti-Mik* alloantibodies.

Examples of blood type A and B frequency in cats in certain countries and breeds*

		Percentage (%)			Percentage (%)	
DSH cats		**Type A**	**Type B**	**Purebred cats**	**Type A**	**Type B**
USA	Northeast	99.7	0.3	Abyssinian	84	16
	North Central	99.6	0.4	Am. shorthair	100	0
	Southeast	98.5	1.5	Birman	82	18
	Southwest	97.5	2.5	British shorthair	64	36
	West Coast	95.3	4.7	Burmese	100	0
Argentina		97.0	3.0	Cornish rex	67	33
Australia		73.7	26.3	Devon rex	59	41
India (Bombay)		88.0	12.0	Exotic shorthair	73	27
Europe	(examples)			Himalayan	94	76
	Austria	97	3	Japanese Bobtail	84	16
	England	97	3	Maine Coon	97	3
	Finland	100	0	Norwegian Forest	93	7
	France	85	14	Oriental shorthair	100	0

Germany	94	6	Persian	86	14
Hungary	100	0	Scottish Fold	81	19
Italy	89	11	Siamese	100	0
Netherlands	96	4	Somali	82	18
Scotland	97	3	Sphinx	83	17
Switzerland	100	0	Tonkinese	100	0
Turkey	75	25	Turkish Angora/Van	50	50

*Ignoring the rare *AB (C)* cats in several breeds(particularly Ragdolls) with type *B* cats

Blood typing relies on identification of surface antigens on erythrocytic membranes, leading to agglutination and hence can distinguish *A, B* or *AB (C)* phenotypes. Several different reagents may be used but monoclonal antibodies against the type *A* and and mostly the lectin *Triticum vulgaris* against the type *B* antigen are currently used in typing kits versus sera in the past.

A genetic test had also been offered for identification of the *b* allele, but it was inaccurate. More recent research shows a more complex pattern and requires a unique panel of several genetic markers (patented by Laboklin but also offered by other laboratories) which is allowing precise identification of type *A, B,* and *AB (C)* phenotypes in most purebred cats. Genotyping is very important to domestic cat breeders to use informed breeding strategies in order to avoid certain blood type pairings – like a type *B* queen to type *A* or *AB* (C) tom – and thereby preventing neonatal isoerythrolysis (NI).

Noteworthy, due to the presence of naturally-occurring alloantibodies, there are no feline universal donor cats. All donors and patients need to be typed, even if it is “only” a domestic shorthair cat and a first transfusion. Simple *AB (C)* blood typing cards, chromatographic strip cartridges and (mini-) gel tube kits (Alvedia DME and DMS Laboratories) are available for in clinical practice use, besides yet a less well established cartridge method (Zoetis/Abaxis or QuickVet) which require an instrument for typing. Larger veterinary diagnostic laboratories frequently use the same in-clinic kits. Removal of plasma and washing with saline may overcome autoagglutination which could interfere with interpretation. Also with severely anemic samples some plasma may need to be removed to have enough erythrocytes to show agglutination or binding. Careful adherence to the typing instructions and some practice are needed to assure accurate results and interpretation.

Blood Crossmatching Tests

In contrast to dogs where a first transfusion without typing and crossmatching is generally compatible (still can sensitize a dog), blood incompatibilities have been related to the *AB* blood group system even at a first transfusion and may also be related to other blood types (like *Mik*) following blood transfusions. They have been recognized through crossmatching or, unfortunately, as a result

of observing acute hemolytic transfusion reactions. Standard laboratory tube, immunochromatographic and gel column crossmatching techniques have been fairly well established, and in-clinic (minitube) gel tube (Alvedia and DMS) kits are now available. Screening feline blood donors and patients for the presence of naturally occurring (*ABC*, *Mik* potentially other blood group systems) or transfusion-induced alloantibodies proves necessary in clinical practice. The presence of severe and persistent autoagglutination or severe *in vitro* lysis may preclude crossmatch testing or interpretation of results. Hence, samples should be examined for autoagglutination or lysis before performing typing and crossmatching.

The major crossmatch tests for alloantibodies in the recipient's plasma against donor cells, whereas the minor crossmatch test looks for alloantibodies in the donor's plasma against the recipient's RBCs. Mixing a drop of donor/recipient blood with recipient/donor plasma will detect *A-B* incompatibilities (except type *B* kittens after maternal *anti-A* antibodies have waned produced naturally occurring alloantibodies only within weeks and surely by 3 month of age), if typing is not available. Again, proper techniques for crossmatching and experience are required. A-B mismatches are generally readily recognized, but detection of other less severe incompatibilities may be harder to note. A major crossmatch incompatibility is of greatest importance, because it predicts that the transfused donor cells will be attacked by the patient's alloantibodies in the large volume of patient plasma, thereby causing a potentially life-threatening acute hemolytic transfusion reaction. As fatal reactions may occur with as little as 2 ml of incompatible blood, compatibility testing by administering a small amount of blood is not appropriate. The major and minor crossmatch can show incompatibilities prior to any transfusion due to the presence of naturally occurring alloantibodies in type *B* cats, not only for the *A-B* mismatch, but also incompatibility with the *Mik* and possibly other blood group systems once a cat was sensitized.

Because type *AB (C)* cats are very rare encountered (except Ragdolls and some geographic regions), *AB (C)* donors are very rarely available. However, these cats have been safely transfused with type *A* (but never type *B*) blood. However, as type *A* cats may have weak *anti-B* antibodies, a major and minor crossmatch is recommended.

Previously transfused cats should always be crossmatched, even when receiving *A-B* matched blood and potentially receiving blood from the same donor as they can still develop alloantibodies against unknown types. Similar to humans, dogs and other species, cats likely have many blood group systems. The time span between the initial transfusion and development of induced alloantibodies causing incompatibility reactions may be as short as 4 days but lasts for many years (i.e., years after the last transfusion alloantibodies may be present). Obviously, a blood donor should never have received a blood transfusion to avoid any donor sensitization against other blood groups.

Xenotransfusion

Xenotransfusion refers to interspecies transfusion, and ancient to most recent studies showed they are always incompatible. Therefore, they are never performed in humans and are therefore not

recommended in any species. Nevertheless, occasionally anemic cats are given canine blood, either because apparently no feline blood is available or the feline blood is incompatible (*A-B*, *Mik* and other mismatches). There are no studies documenting the benefits of xenotransfusion versus supportive care and recruitment of a compatible donor or referral to a clinic for *A-B* matched compatible transfusion support. Acute hemolytic transfusion reactions have rarely been reported in cats similar to *A-B* mismatched transfusion reactions. Clinicians only rarely carefully monitor feline patients receiving a (xeno-) transfusions and do not like to report on iatrogenic complications or blame the patient illness for the loss. Extensive studies have shown that both canine and feline blood contain naturally-occurring alloantibodies against the other species. Thus, crossmatch studies between dogs and cats are always incompatible. Xenotransfusions are always incompatible and documented to be very short-lived (<4 days) in cats as seen with *A-B* mismatches. Even large/wild felids thought to potentially offer larger volumes of blood have alloantibodies against domestic cats and other felid species. They appear to have an *AB (C)* blood group system. Even severely anemic cats (hematocrit of <10%) can do well, if they are hydrated and may be safely referred to another clinic where they have stored feline blood or donors as well as typing and crossmatching available. Products similar to Oxyglobin, a highly purified bovine hemoglobin solution, should be again shortly available as it has been in the past FDA approved for dogs and found to be extremely helpful when feline compatible blood was not available.

Feline Blood Donors

There are few but an increasing number of commercial blood banks worldwide that offer feline blood products by pick-up or overnight service. Some are affiliated with veterinary teaching hospitals and larger clinics. Also many hospitals have a small in-house colony and/or involve the staff's or client's healthy cats to donate based upon the human blood banking practice (pets help pets). In some countries animal blood banks are not permitted or highly restricted to only specific target donations. While not as tightly regulated as in human blood banking, any animal blood bank will require governmental and animal welfare approvals and informed consent for client-owned animals. Healthy, young adult (1-6 years), good tempered cats of at least 4 kg (and lean body condition) can be recruited. Due to the high risk of infectious diseases, indoor cats free of fleas and intestinal parasites and regularly screened for any infectious diseases are preferably selected. A freely roaming cat in a veterinary hospital would not be a good donor candidate, because of the potential of having acquired some infections from patients at the clinic.

Blood donors should be regularly examined and also for potential occult diseases. Donations from cats with occult cardiomyopathy, common in certain feline breeds, should be avoided, because the stress with collection and associated fluid shifts may cause overt disease and death. Like for dogs, blood donors must have no prior history of prior transfusion, have been regularly vaccinated, and are healthy as determined by history, physical examination, and laboratory tests (preferably complete blood cell count, chemistry screen, and fecal parasite examination prior to every donation or every 6-12 months). Feline donors also must be free of ecto- and endoparasites and other infections. Guidelines for infectious disease screening have been published. However, testing depends on the specific geographic area and emerging diseases, but may include regular FeLV, FIV, FIP, Hemomycoplasma, Anaplasma, Bartonnella, and Cytauzoon testing. Donors should receive a well-balanced, high performance diet, and may be supplemented twice weekly with ferrous sulfate

(Feosal, 10 mg/kg), if bled several times a year. Packed cell volume (PCV) or hemoglobin (Hb) should be >35% and >12 g/dl in cats and these parameters should be carefully monitored over time. Blood donations should not make any donor cat anemic.

Blood Collection

Guidelines on blood collections have recently been published. Cats are regularly sedated by intravenous injection in order to reduce the stress and improve handling and collection of blood over several minutes. Several sedation protocols using multiple drugs have been proposed. Some sedatives, such as acepromazine, interfere with platelet function and induce hypotension, and, hence, they should be avoided.

Blood is collected aseptically by gravity or potentially assisted by a gentle blood bank vacuum pump from the jugular vein over 5 to 10 minute period. Large plastic syringe containing 1 ml CPD-A or 3.8% citrate per 9 ml blood and connected to a 19 gauge butterfly needle is commonly used for cats. This represents an open blood collection system in which connections allow exposure of blood to the environment. Because of the potential risk for bacterial contamination, blood collected via an open system should not be stored for more than two days. Because of the small blood volume (6-8 ml/kg bodyweight), the maximal blood volume to be donated is 50 ml blood (one typical feline unit) per ≥ 5 kg cat or maximally 10-12 ml/kg body weight.

Some clinics have developed their own closed blood collection system and recently commercial small volume closed systems that permit component preparation into packed red blood cells and fresh frozen plasma as well as storage (<21-28 days and 1 year, respectively) have been introduced. Blood components are prepared from a single blood donation by simple centrifugational separation generally within 4 hours from collection.

Blood Administration

Guidelines on blood administration to cats have recently been published. The regular principles used in transfusing dogs are applied to cats. No food and drugs are given during the transfusion. Bblood is administered through blood filter via a separate line without any drugs or other fluids. Because of the small volumes of feline units, shorter infusion tubing with a small filter are used instead of the large infusion sets. Infusion pumps may not be approved for blood, are associated with very long infusion sets, and may damage blood cells, and are thus not generally recommended. Infusions may be given via syringe pump, instead of drip which can be very slow. In that case transferring the blood into the 60 ml syringe may be preceded by filtering the blood at time of transfer.

Transfusion reactions

Despite assuring blood compatibility particular attention is given to the first few milliliters of blood infused when first reactions can be observed. Monitoring is done frequently early on (every 15 min) including attitude, temperature, pulse, and respiration, and then as needed PCV, plasma hemoglobin, urine dipstick, like in dogs. Templates for monitoring transfusions are available.

Febrile transfusion reactions may be frequently seen but are fortunately often mild and self-limiting. Hyperthermia may be caused by hemolytic transfusion reactions but also allergic reactions to plasma and white blood cells. Febrile reactions may be also associated with other allergic reactions like urticaria and very rarely anaphylaxis. Acute hemolytic transfusion reactions are most feared and may be related to blood type incompatibilities (see above), but may also be caused physical hemolysis of a unit during collection, storage, and administration. Other transfusion reactions may also occur: Nausea and vomiting may be observed but may be triggered by simultaneous feeding or drug interactions. Thus, during a transfusion, no food (water can be offered) and no drugs, unless absolutely essential, should be given. Hypocalcemia due to the citrate anticoagulant used is not expected, unless massive transfusions are administered and/or the animal has hepatic failure and is unable to metabolize citrate. And of course transmission of infectious diseases from donor, such as hemomycoplasma infections, or sepsis due to a bacterially contaminated unit may occur but can be mostly avoided by screening and appropriate blood banking techniques.

In conclusion, while there are a few intricacies to cats such as small size, unique blood group systems, viral infections), adapting protocols from human and canine transfusion medicine allow for safe and effective support to critically ill, anemic and/or bleeding cats.

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Interpretación clínica de las alteraciones ácido-base

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Puntos claves de la presentación:

La regulación del **equilibrio ácido-base** y sus alteraciones más frecuentes son un tema difícil de entender y, debido a esto, muchas veces los clínicos abandonan su estudio. Intentaremos hacer entender las bases del equilibrio ácido-base haciendo hincapié en los términos de conocimiento imprescindible y el abordaje clínico de las alteraciones simples.

El equilibrio ácido-base es el balance del **ion hidrógeno (H^+)**. Su regulación es similar a la de los otros iones del organismo. Hay que recordar que el control preciso de las concentraciones de iones de hidrógeno necesita de la intervención de buffer (amortiguadores o tampones) ácido-base en los riñones, en la sangre, en las células y en los pulmones.

Un ion de hidrógeno es un protón liberado a partir del átomo de hidrógeno. Los iones o moléculas que contienen átomos de hidrógeno y que pueden liberar iones en una solución reciben el nombre de **ácidos (HCl^-, H_2CO_3, ...).** Un ácido fuerte es que se disocia rápidamente y libera grandes cantidades de H^+ a la solución. Una **base** es un ion o una molécula que puede aceptar iones de hidrógeno **(HCO_3^-, HPO_4^-, ...)**. Las proteínas funcionan como una base. Una base fuerte reacciona de forma rápida y fuerte con el H^+ y por tanto lo elimina de la solución.

El metabolismo normal del organismo produce una cantidad de ácidos diarios, 20000 mmol de ácidos volátiles (ácido carbónico) procedente del CO_2 que son eliminados por los pulmones y 80 mmol de ácidos fijos o no volátiles que son eliminados por los riñones. **La concentración final de H^+= [H^+] =40 nmol/L (35-45)** ha de ser muy estable y su mantenimiento es fundamental para el funcionamiento normal del organismo. Debido a que esta concentración es un número muy bajo, aparece una escala relacionada con el pH. **El pH es el logaritmo negativo de la concentración del ion hidrogeno.** Hay que recordar que, al ser una escala logarítmica, pequeños cambios el pH implican grandes cambios en la concentración de ion de hidrógeno y, que al ser un logaritmo negativo, los aumentos de [H^+] implicarán un descenso del pH y viceversa.

[H^+] = 40 +/- 5 nmol/L → pH = 7.4 +/- 0.04

Por tanto, acidemia y alcalemia son aumentos o disminuciones de la [H^+] y que los valoramos por el pH sanguíneo.

Para mantener este equilibrio básico de la [H^+] hay una serie de mecanismos fisiológicos. Estos mecanismos se pueden dividir según el tiempo en que tardan en actuar y la duración de su acción. Los podemos dividir en tres grupos principales:

A) Actúan en pocos segundos, pero su duración es corta. Son los buffer intracelulares o extracelulares. Entre otros: **H_2CO_3, Na HCO_3, Na_2HPO_4, Na H_2PO_4, hemoglobina y proteínas (albúmina).**
B) Actúa en minutos. Su rendimiento no siempre es suficiente para mantener el equilibrio. **Control respiratorio del CO_2**
C) Se inician a las 12 horas y tiene su máxima expresión a los 2-3 días. Es duradera y muy efectiva. **Regulación renal de H^+, bicarbonato y electrolitos.**

Para mantener el equilibrio se han producir cambios en los buffer, pulmón y riñones según la fórmula básica del equilibrio ácido-base:

$$[H^+] = 24 \times CO_2/HCO_3^-$$

Componente respiratorio: pCO_2 = 40 +/- 4 mmHg

Retención del **CO_2** implica elevación de la **$[H^+]$** y por tanto disminución del **pH**

Eliminación del **CO_2** implica disminución de la **$[H^+]$** y por tanto incremento del **pH**

Existen alteraciones del componente respiratorio cuando se manifiestan disfunciones en los pulmones, el diafragma, los músculos respiratorios, la pleura o el control a nivel del SNC. Una alteración en el pCO2 indica una alteración respiratoria pero no una patología.

Componente metabólico o no respiratorio: $[HCO_3^-]$ = 24 +/- 4 mEq/L

La eliminación o retención de los ácidos no volátiles o fijos (H_3PO_4, H_2SO_4, NH_4^+) en los riñones controla el exceso o falta de H^+. El riñón también controla los niveles de HCO_3^- mediante la eliminación de Na^+ o K^+, cambiándolo por Cl^- o con la producción de H_2SO_4. Una alteración en el HCO_3^- indica una alteración metabólica pero no una patología.

La acidosis y la alcalosis son procesos (respiratorios o metabólicos) que cambian la producción, eliminación o retención de los ácidos y las bases pero que no siempre van relacionados con un pH anormal. **Las alteraciones simples son la acidosis metabólica, la alcalosis metabólica, la acidosis y la alcalosis respiratorias.** Estos procesos pueden ocurrir simultáneamente, como mecanismo de compensación o porque es un proceso mixto (complejos). Es muy importante recordar que la compensación de la alteración no siempre es sinónima de corrección de la alteración. La compensación mejora el pH, pero no siempre lo devuelve a un pH normal.

Acidosis metabólica: **HCO_3^-** bajo con **CO_2** normal (no compensado) o bajo (compensado)

Alcalosis metabólica: **HCO_3^-** alto con **CO_2** normal (no compensado) o alto (compensado)

Acidosis respiratoria: **CO_2** alto con **HCO_3^-** normal (no compensado) o alto (compensado)

Alcalosis respiratoria: **CO_2** bajo con **HCO_3^-** normal (no compensado) o bajo (compensado)

El pH puede ser normal si no hay alteración ácido-base, por que hay una respuesta buena a la compensación (raro) o porque hay una alteración mixta o compleja. La eficacia en la respuesta de regulación es diferente entre hombres y animales. En perros la respuesta es más eficaz en la acidosis respiratoria crónica, menos eficaz en la acidosis metabólica e igual en las demás. En los perros la respuesta frente a la alcalosis respiratoria es un 60% más eficaz que frente a la acidosis respiratoria.

Anión gap

El organismo es eléctricamente neutro, por tanto, ha de existir el mismo número de cationes y de aniones. Como existen unos aniones (Cl^- y HCO_3^-) y unos cationes (Na^+ y K^+) en mayor cantidad y más fáciles de cuantificar, el resto de los aniones (UA) y cationes (UC) no cuantificables necesarios para llegar a la neutralidad reciben el nombre de **anión gap**.

$$\mathbf{UA - UC = 12 = (Na^+ + K^+) - (Cl^- + HCO_3^-)}$$

Pueden existir alteraciones metabólicas con o sin alteración del anión gap. El anión gap varía si hay cambios de los iones no cuantificables o de los cuantificables que no han sido corregidos por cambios en los iones de signo opuesto.

Iones fuertes

Son los iones que están totalmente disociados. Sus alteraciones pueden producir cambios en el equilibrio ácido-base.

Aniones: **Na^+, K^+, Ca^{2+}** y **Mg^{2+}**

Cationes: **Cl^-, SO_4^{2-}, proteínas** y **ácidos orgánicos no cuantificables (láctico, cetoácidos)**

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Enfermedades trasmitidas por artrópodos en gatos

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Puntos claves de la presentación:

- En general, a diferencia de cuando tenemos un perro en la consulta, a los veterinarios nos cuesta incluir a las patógenos transmitidos por vectores artrópodos cuando visitamos a un gato.

- Nuca nos olvidamos de la PIF, de la leucemia felina o de la inmunodeficiencia felina, pero, ¿y la bartonelosis, la leishmaniosis, la hepatozoonosis, la hemoplasmosis, la filariosis, la ehrlichiosis, la babesiosis, la rickettsiosis, …?

- Hay múltiples publicaciones que refieren grados variables de prevalencia de todos estos patógenos en gatos en España, pero todos coinciden en que ¡todas estas enfermedades existen en gatos en nuestro país!

- Por ejemplo, se considera que la prevalencia de infección por Leishmania en gatos es aproximadamente la mitad de la descrita en perros en la misma zona.

- Hay múltiples lesiones, signos clínicos, alteraciones de laboratorio o lesiones asociadas a estas enfermedades transmitidas por artrópodos en los gatos, pero la fiebre, anemia, uveítis, tos, disnea o proteinuria son de los más frecuentes.

- Cuando tengamos alteraciones clínicas, que si fuese un perro, no harían pensar o incluir estas enfermedades en el diagnóstico diferencial, hemos de hacer lo mismo si es un gato.

- Por tanto el enfoque clínico en gatos para el diagnóstico de estas enfermedades se basa en tres etapas: 1) sospechar o pensar en esto patógenos; 2) excluir las otras patologías más frecuentes que pueden dar las mismas alteraciones clínicas; y 3) realizar pruebas de diagnóstico para confirmar la infección.

- En general, a diferencia de los perros, en los gatos la serología no es la prueba diagnóstica más útil para confirmar la presencia de estos patógenos, siendo la observación directa del agente infeccioso con microscopio en las lesiones o la detección de su ADN mediante la PCR, las pruebas más útiles.

- El agente de hemoplasmosis más frecuente en nuestro país es Candidatus Mycoplasma haemominutum y su infección puede ser asintomática, por lo que su detección en sangre debe ser interpretada con prudencia en un caso con signos clínicos.

- Las infecciones por Ehrlichia y Anaplasma spp. deben incluirse en el listado de diagnósticos diferenciales en gatos con fiebre, anorexia y letargia que viven en zonas endémicas.

- Aunque las infecciones por Rickettsia spp. en gatos se han asociado con fiebre y otros signos clínicos, su importancia clínica aún plantea muchos interrogantes.

- La bartonelosis en gatos puede cursar con endocarditis, miocarditis, fiebre, linfadenopatía, osteomielitis y uveítis, siendo frecuente la detección de hiperglobulinemia en la

analítica sanguínea. La existencia de altas tasas de seropositividad en la población general hace necesario el empleo de otras técnicas como cultivo o PCR para no sobrediagnosticar la enfermedad.

- Aunque en Estados Unidos la cytauxzoonosis felina es una enfermedad grave, en nuestro entorno puede cursar con un amplio abanico de signos, incluyendo infecciones leves.

- Hepatozoon spp. puede infectar a gatos europeos, asociándose en algunos estudios con fiebre y anemia y sin que se conozca detalladamente el tratamiento de elección en la especie felina.

- Los gatos con leishmaniosis suelen presentar signos cutáneos, si bien también se describen signos viscerales muy variados. El tratamiento con alopurinol a largo plazo suele ser clínicamente eficaz, si bien la curación parasitológica es infrecuente. Los antimoniales también pueden emplearse de manera eficaz en gatos con leishmaniosis.

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Enfoque clínico de la fiebre de origen desconocido en gatos

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Puntos claves de la presentación:

- La fiebre o sus consecuencias, como apatía o menos apetito, son signos clínicos frecuentes en los gatos. Sin embargo, debido a lo inespecíficos que son, frecuentemente los veterinarios abusamos del concepto: “fiebre de origen desconocido (FOD)”.
- FOD significa una fiebre que no resuelve espontáneamente, que no responde a antibióticos y que permanece como idiopática a pesar de la realización de un mínimo de pruebas diagnósticas.
- Actualmente se ha adoptado esta definición de medicina humana para la FOD: “Gato con una temperatura >39,2ºC durante, a) al menos 3 semanas sin una causa aparente después de al menos tres visitas; o b) tres días de hospitalización sin un diagnóstico a pesar de la valoración de la historia clínica, el examen físico y un mínimo de pruebas diagnósticas (hemograma, bioquímica sérica y urianálisis).”
- Cuando tenemos gatos con una temperatura rectal >39,2°C existen dos posibilidades: hipertermia o fiebre.
- La hipertermia está causada por un incremento de la actividad muscular, por un aumento de la temperatura ambiental, por estrés o por una mayor tasa de actividad metabólica como por ejemplo el hipertiroidismo.
- En cambio cuando hay fiebre, hay una alteración en la termorregulación en el hipotálamo debido a la acción de los pirógenos que finaliza con un aumento de la temperatura corporal.
- Los pirógenos más frecuentes son la interleuquina-1 y el factor de necrosis de los tumores producidos por los leucocitos, principalmente macrófagos y neutrófilos.
- La información publicada sobre FOD en gatos es muy limitada, de hecho no hay estudios retrospectivos, a pesar de la larga lista de diagnósticos diferenciales posibles frente a un gato con fiebre.
- Sabemos que la causa más frecuente de FOD en gatos es una infección (bacterias, virus, hongos y parásitos), seguido de algunas neoplasias (linfoma) o inflamaciones graves (lesiones traumáticas extensas, pancreatitis), y siendo muy poco descrita asociada a enfermedades inmunomediadas (anemia o trombocitopenia).
- También se han descrito cambios en la termorregulación asociados a lesiones intra-craneanas, incluida el traumatismo, y al uso de algunos fármacos (tetraciclinas, sulfamidas, penicilinas o levamisol).
- A pesar de todo esto, entre un 10% y un 15% de los gatos con FOD permanecen sin diagnóstico a pesar de la realización de una extensa batería de pruebas diagnósticas.
- Los virus son una de las causas infecciosas más frecuentes de FOD en gatos, especialmente la PIF y los virus de las vías respiratorias altas.
- Los virus de la leucemia y la inmunodeficiencia felinas se han de valorar en cada gato con fiebre, sin embargo, los resultados se han de interpretar correctamente porque no siempre son la causa de la fiebre en ese momento.
- No debemos olvidar que algunos gatos pueden tener fiebre asociada a una bacteriemia por *Salmonella* o *Campylobacter* sin presentar diarrea, especialmente si hay gran cantidad de neutrófilos en la citología rectal.
- Finalmente, hay numerosos patógenos transmitidos por diferentes artrópodos (pulgas, garrapatas, mosquitos, flebotomos) que causan FOD en gatos que hay que considera e incluir en el diagnóstico diferencial.
- El enfoque clínico de la FOD se debe personalizar a cada gato en base a la historia clínica, tipo de vida, zona geográfica, examen físico y el resultado de un mínimo de pruebas diagnósticas.

- Es fundamental una buena comunicación con los propietarios para obtener el máximo de información, pero también para que entiendan que obtener un diagnóstico definitivo en una FOD implica normalmente un alto coste de tiempo y dinero.
- Si está con algún tipo de fármaco y es posible, lo ideal sería suspenderlos al menos durante 48-72 horas, y si la fiebre continua pasada ese tiempo se puede excluir que sea como consecuencia de una reacción medicamentosa.
- La historia y fechas de vacunación del gato deben evaluarse adecuadamente ya que en gatos, al igual que en perros, esta descrita la presencia de fiebre asociada a las vacunas.
- Saber el tipo de vida (*indoor/outdoor*), los viajes realizados, si usan antiparasitarios internos y externos, el tipo de alimentación (comercial, casera, cruda, etc.) o la preferencia de presas (insectos, roedores, pájaros, caracoles, etc.) que tiene el gato, es muy importante para aclarar nuestro diagnóstico diferencial y decidir que pruebas diagnósticas pueden ser más interesantes.
- Basado en la historia clínica anterior y si después de la exploración física no se localiza la causa de la FOD, por ejemplo un absceso, se recomienda realizar siempre un hemograma, una analítica sanguínea completa, un urianálisis con UPC +/-cultivo de orina, citología rectal y serologías de VLFe/VIF.
- No se recomienda el uso de antibióticos empíricos sin haber realizado al menos las pruebas diagnósticas anteriores.
- El protocolo de trabajo para intentar el diagnóstico de una FOD se basa en tres fases.
- Fase1. Todo lo que hemos hablado anteriormente más considerar si es necesario realizar radiografías torácicas y abdominales. Al final de esta fase se podría plantear el uso empírico de antibiótico si se sospecha de alguna infección que pudiera responder a éste, por ejemplo la doxiciclina.
- Fase 2. Repetir o realizar ahora algunas de las pruebas diagnósticas de la Fase 1. Realizar ecografía abdominal +/- ecocardiografía si hay soplo cardíaco. Realizar citologías/biopsias de cualquier masa, nódulos linfáticos, médula ósea (si hay alteraciones en el hemograma) o fluido en cavidades. Realizar artrocentesis, cultivos de sangre y de heces, serología o PCR de enfermedades infecciosas, y radiografías de huesos y articulaciones.
- Fase 3. Repetir o realizar ahora algunas de las pruebas diagnósticas de la Fase 1 o 2. Realizar ecocardiografía aunque no haya soplo, realizar broncoscopia y/o lavado broncoalveolar, citologías de líquido cefalorraquídeo y de médula ósea (aunque no haya alteraciones en el hemograma). Valorar la posibilidad de un TAC o RM de cuerpo completo o de una toracoscopia/laparoscopia/laparotomía.
- Si no hay diagnóstico al final de la Fase 3, se podría valorar el probar con tratamientos empíricos (antibióticos, prednisolona, etc.)
- Si hay un diagnóstico definitivo, el tratamiento ha de ser específico para esa enfermedad.
- Los tratamientos empíricos con antibióticos se deben basar en el tipo de tejido u órgano afectado, o en el tipo de agente infeccioso del que se sospecha.
- El tratamiento empírico con prednisolona ha de ser considerado en gatos con FOD cuando las pruebas diagnósticas no ofrecen luz, o no se han podido realizar, y no ha respondido a antibióticos.
- Los antipiréticos generalmente no se recomiendan porque la mayoría son AINE, que en gatos enfermos pueden ser contraproducentes si hay deshidratación o anorexia, y porque la fiebre puede tener un acción beneficiosa ya que reduce la acción de algunos patógenos y mejora la eficacia de algunos antibióticos.

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Manejo clínico de las hepatopatías en gatos y perros

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Puntos claves de la presentación:

- Las principales funciones del hígado son el metabolismo de carbohidratos, proteínas y grasas, la desintoxicación, la secreción y el almacenamiento. Por lo tanto, mantener un hígado saludable es un factor crucial para la salud general y el bienestar de vida de los animales.
- Es un órgano vital y complejo del cuerpo, se vuelve susceptible a muchos efectos adversos, incluidos medicamentos, productos químicos, agentes infecciosos o enfermedades autoinmunes.
- La enfermedad hepática incluye hepatitis, colangitis, necrosis, derivación porto sistémica, neoplasia, y fibrosis o cirrosis.
- La enfermedad hepática puede presentarse con una variedad de condiciones clínicas, desde gravemente enfermo hasta sin signos clínicos.
- Los signos clínicos son generalmente inespecíficos y pueden ser depresión, pérdida de peso, ictericia, signos gastrointestinales, urinarios y/o neurológicos
- Se diagnostica mediante el uso de la historia clínica y el examen físico, las pruebas de función hepática y las técnicas de diagnóstico por la imagen.
- Sin embargo, para la identificación de hepatopatías específicas, diagnóstico definitivo de enfermedad hepática, se requiere el examen histopatológico para establecer el tratamiento recomendado.
- El hígado de perros y gatos puede verse afectado por una gran variedad de agentes infecciosos como virus, bacterias, parásitos, hongos y protozoos.
- Cuando se excede la capacidad de almacenamiento hepático del cobre, se produce una inflamación parenquimatosa seguida de muerte celular con liberación de cobre al plasma que causa hemólisis. Además, el cobre libre es tóxico y tiene el potencial de crear especies reactivas de oxígeno que causan hepatitis crónica y cirrosis.
- El hígado es el órgano principal del metabolismo de los medicamentos y, por lo tanto, es un lugar común para las reacciones adversas a los medicamentos.
- La hepatitis reactiva es un trastorno inflamatorio del hígado inducido por un proceso extra-hepático.
- La diabetes mellitus, el hiperadrenocorticismo y el hipertiroidismo pueden causar deterioro de la función hepática debido a sus efectos sobre el órgano.
- La derivación portosistémica es una malformación congénita de la vascularización del hígado tanto en perros como en gatos.
- La lipidosis hepática felina es la acumulación de grasa en las células del hígado, a medida que la grasa se moviliza de las reservas corporales como fuente de energía.
- La colangitis es la inflamación del sistema biliar y es el trastorno hepático primario más frecuente en gatos, aunque también se puede dar en perros. Las dos formas principales de colangitis en gatos son neutrofílica y la linfocítica.
- La fosfatasa alcalina es principalmente un indicador de enfermedad hepática colestásica, pero también aumenta con la destrucción ósea grave y debido a la inducción de los esteroides.
- La alanina aminotransferasa es una enzima específica del hígado que se encuentra en el citoplasma de las células hepáticas. Se encuentra casi exclusivamente dentro de los hepatocitos, por lo que el aumento de la ALT sérica indica una lesión hepatocelular importante en perros y gatos.
- Los aumentos de GGT se observan con mayor frecuencia en perros y gatos con enfermedad hepática colestásica.
- Las pruebas de función hepática ayudan a determinar la salud del hígado midiendo los niveles de albúmina, bilirrubina, ácidos biliares, urea, colesterol, glucosa o pruebas de coagulación.
- La radiografía y la ecografía abdominal son las modalidades de diagnóstico por la imagen utilizadas con más frecuencia para la evaluación del sistema hepatobiliar en perros y gatos, pero ahora se utilizan con más frecuencia otras técnicas de imagen como es la tomografía computarizada.

- La ecografía abdominal se considera el procedimiento de diagnóstico por imágenes más práctico para detectar una enfermedad hepatobiliar, aunque no es muy específica o sensible para todas las hepatopatías.
- La biopsia hepática y la histología es el examen final en el árbol diagnóstico y proporciona un diagnóstico definitivo, pronóstico de las lesiones y selección del tratamiento más adecuado.
- Los medicamentos antiinflamatorios como la prednisona o la prednisolona, algunos diuréticos como la espironolactona, los antihipertensivos como amlodipino o telmisartan, las dietas de prescripción bajas en proteínas, la fluidoterapia, los antibióticos o los llamados heaptoprotectores como antioxidantes o SAMe, se utilizan para el tratamiento de las enfermedades hepáticas.
- Algunos tratamientos quirúrgicos como la colecistectomía, extirpación quirúrgica de la vesícula biliar, también se utilizan para el tratamiento de cálculos biliares y de otras afecciones de la vesícula biliar.

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Uso de los inmunosupresores en enfermedades infecciosas de perros y gatos

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Puntos claves de la presentación:

- Las enfermedades inmunomediadas más frecuentes son hipersensibilidad, autoinmunidad, inmunodeficiencia y neoplasias del sistema inmunitario.
- Todas se producen por una alteración en el equilibrio normal del sistema inmunitario.
- Las enfermedades inmunomediadas tienen un impacto muy grande en medicina humana, aunque parecen menos frecuentes en perros, y muy poco documentadas en gatos. Sin embargo hay un porcentaje de nuestros pacientes que presentan este tipo de enfermedades.
- Todas estas enfermedades inmunomediadas son multifactoriales siendo la genética, la desregulación de la respuesta inmunitaria y los factores ambientales los factores desencadenantes más importantes.
- Dentro de los factores ambientales, los agentes infecciosos son uno de los más importantes en perros y gatos, especialmente los patógenos transmitidos por artrópodos.
- Es difícil encontrar siempre una correlación entre enfermedad inmunomediada y patógeno porque no existe una prueba perfecta para el diagnóstico de la enfermedades infecciosas transmitidas por artrópodos. La combinación de la historia clínica, el examen físico, las pruebas de laboratorio y la respuesta al tratamiento, son necesarias para la confirmación o no del diagnóstico.
- Las enfermedades inmunomediadas producidas por patógenos, algunas veces persisten una vez el agente infeccioso se ha eliminado, y esto es muy importante para decidir el tratamiento y dar un pronóstico en cada caso.
- Debido a que el diagnóstico de las enfermedades vectoriales es complejo, tal vez muchas de las enfermedades inmunomediadas tienen a un patógeno como factor activador.
- Sin embargo, no ha sido posible confirmar que todos estos patógenos produzcan enfermedades inmunomediadas, ya que algunas de las pruebas de confirmación, como la prueba de Coombs, pueden dar falsos positivos secundarios a las reacciones inflamatorias intensas y graves asociadas a estos patógenos.
- Hay diversos mecanismos, algunos demostrados en estudios experimentales, mediante los cuales estos patógenos pueden activar una enfermedad inmunomediada.
- Permitir un *bypass* a la estimulación normal de los linfocitos B, la presencia de los súper-antígenos o la capacidad de mimetizar moléculas activadoras, son algunos de los mecanismos más frecuentes asociados a patógenos transmitidos por artrópodos para activar/desarrollar una enfermedad inmunomediada.
- Se piensa que la interacción inicial de sustancias del artrópodo con el sistema inmunitario del perro o gato, ya modula la respuesta inmunitaria de cara a que posteriormente se pueda desarrollar enfermedad inmunomediada asociada al patógeno transmitido.
- Tanto los mecanismos como los signos clínicos de las enfermedades inmunomediadas secundarias a este tipo de patógenos son aún más complicados o graves cuando en un mismo animal hay coinfecciones.
- En las fases iniciales de la dirofilariosis felina se pueden confundir los signos clínicos con una enfermedad inmunomediada como la bronquitis alérgica, cuando en realidad es una enfermedad respiratoria asociada a la respuesta inmunomediada frente a los adultos inmaduros que llegan a los vasos pulmonares. En cambio, una vez la infección pulmonar se ha establecido, las dirofilarias son capaces de crear una inmunosupresión que permite al gato tolerar este patógeno, prácticamente asintomático.
- En la dirofilariosis también hay una respuesta especifica inmunomediada con producción de IgG frente a una proteína de superficie de la *Wolbachia* que contribuye a las lesiones pulmonares y renales; por tanto el tratamiento de esta bacteria en fases iniciales de enfermedad puede ayudar en la mejoría clínica más rápida y en la reducción de la microfilaremia.

- La anemia hemolítica es el signo clínico más grave asociado a babesiosis. Posiblemente la enfermedad inmunomediada secundaria a la presencia de la *Babesia* es el mecanismo principal, ya que la gravedad de la anemia no va asociada a la cantidad de patógenos presentes.
- El hecho que perros infectados con *Babesia gibsoni* son positivos a la prueba de Coombs por anticuerpos que se fijan a componentes de la membrana del glóbulo rojo y no de la *Babesia*, confirma la anterior idea.
- La anemia hemolítica asociada a la hemoplasmosis en gatos parece más asociada a una enfermedad no autoinmune, ya que una adecuada respuesta inmunitaria frente al patógeno produce una destrucción de los glóbulos rojos porque los hemoplasmas están pegados a ellos. Sin embargo, hay evidencias que demuestran que en algunos gatos con hemoplasmosis se encuentran auto-anticuerpos de la membrana de los glóbulos rojos parecido a lo que pasa en *Babesia*.
- La gravedad del cuadro clínico secundario a *Hepatozoon canis* va asociado al número de parásitos presentes, y esto, al grado de inmunosupresión que tenga el perro, normalmente asociado a la presencia de otras co-infecciones.
- La gran variedad de signos clínicos asociados a *Leishmania* es debida a la interacción entre el parásito y el sistema inmunitario del perro. Por ejemplo, la excesiva producción de anticuerpos desarrolla lesiones en los tejidos iguales que las asociadas a la hipersensibilidad tipo II y tipo III presentes en muchas enfermedades autoinmunes.
- Diversos mecanismos inmunomediados parecen estar relacionados con la ehrlichiosis y la anaplasmosis, ya que la gravedad de los signos clínicos no va siempre asociada a la cantidad de patógeno presente en el perro, y es frecuente la positividad a las pruebas de Coombs y ANA. Sin embargo, si todos estos auto-anticuerpos son verdaderos o no, no ha sido totalmente demostrado.
- El primer y mejor tratamiento de las enfermedades inmunomediadas asociadas a patógenos trasportados por artrópodos es la eliminación del agente infeccioso lo más rápidamente posible .
- Desde un punto de vista clínico, tenemos que plantearnos en cada caso si es necesario un tratamiento específico para la enfermedad inmunomediada o no. Algunas veces será necesario utilizar, junto al tratamiento frente al patógeno, el uso de inmunosupresores, mientras que en otros casos sólo será necesario un tratamiento sintomático antiinflamatorio o con otros fármacos.
- En los casos que hay trombocitopenia grave o anemia hemolítica con la presencia o sospecha de un patógeno transmitido por artrópodos, la recomendación es iniciar tratamiento con prednisona o prednisolona al menos a 1 mg/kg/12h. Pero en la mayoría de casos la respuesta clínica es rápida y se puede reducir el tratamiento en pocos días o semanas.
- En la mayoría de casos en los que hay glomerulonefritis, poliartritis o uveítis, la recomendación a día de hoy, es de añadir tratamiento con prednisona o prednisolona a una dosis antiinflamatoria, mientras se trata el patógeno que ha causado la lesión.
- En situaciones de vasculitis, sobretodo cuando se mantienen una vez tratado el patógeno, el tratamiento recomendado no incluye los corticoesteroides, y se recomienda el uso de doxiciclina (si no se ha usado para el tratamiento del patógeno) más pentoxifilina durante meses.
- El pronóstico de las enfermedades inmunomediadas asociadas a patógenos transmitidos por artrópodos es bueno en la mayoría de los casos y el uso de inmunosupresores se limita a las primeras semanas. Sin embargo hay algunas situaciones clínicas que muchas veces no responden y tienen un pronóstico reservado o grave, como por ejemplo en la uveítis exudativa o nodular asociada a la leishmaniosis.

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Manejo clínico de la leptospirosis canina

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Puntos claves de la presentación:

- La leptospirosis es una enfermedad reemergente zoonosis bacteriana que presentan una distribución mundial, a excepción de las áreas polares.
- Está causada por espiroquetas del género *Leptospira* spp. que son móviles y con un extremo en forma de gancho característico.
- En la naturaleza se han descrito especies saprófitas (aquellas que no infectan a animales) y patógenas.
- La clasificación taxonómica es compleja y, muchas veces confusa. La más utilizada es la clasificación serológica y actualmente se han identificado 9 especies patógenas que afectan a seres humanos, animales salvajes y domésticos, con un total de 150 especies.
- Dentro de estas nueve especies, hallamos mas de 250 serovares y aquellos que tienen relación antigénica se agrupan en serogrupos. Los diferentes serovares están adaptados a los animales que actuarán de reservorio por lo que la identificación de los serovares es de gran importancia desde un punto de vista epidemiológico.
- Sobre el ciclo epidemiológico, las leptospiras las podemos encontrar en el ambiente en suelos húmedos y aguas superficiales, pudiendo permanecer durante meses en el ambiente.
- La infección del huésped accidental se puede dar tanto por contacto directo, a través de las mucosas o heridas cutáneas, con orina de animales infectados o contacto indirecto a través de las superficies contaminadas que puede desarrollar la enfermedad dependiendo del serovar causante e inmunidad del hospedador.
- Algunos perros mostrarán signos clínicos leves mientras que otros desarrollaran un cuadro clínico grave o incluso, pueden llegar a morir debido a la enfermedad. Una vez han entrado en el organismo se diseminan vía hematógena por el organismo causando una fase febril, con bacteriemia que puede durar varios días.
- Cuando el número de leptospiras llega en cantidad suficiente a los tejidos, aparecen los signos clínicos que pueden ser: **lesión renal aguda**, donde presentan poliuria, polidipsia, deshidratación, vómitos, diarrea, anorexia, apatía y/o dolor abdominal. Se ha descrito también anuria/oliguria; **lesión hepática,** con signos clínicos inespecíficos (PU/PD, diarrea, anorexia, apatía) y como signos clínicos más característico, ictericia; **tendencia hemorrágica**, donde observamos hematemesis, hematoquecia, hemoptisis, melena, epistaxis y petequias. El mecanismo por el que se observa esta presentación tanto en perros como en humanos no se ha determinado completamente, aunque la presencia de fallo hepático, coagulación intravascular diseminada o daño directo de las espiroquetas sobre la vasculatura podrían ser el origen; s**índrome de hemorragia pulmonar**, donde observamos taquipnea y disnea aguda, se ha descrito principalmente en perros de Europa y en humanos parece tener un componente inmunomediado y está asociado con alta mortalidad.
- Estos cambios han hecho que en los últimos años el veterinario clínico no sólo deba incluir a *Leptospira* en el diagnóstico diferencial de los perros con azotemia o ictericia, sino que además debe sospechar de leptospirosis ante un gran número de otros signos clínicos, por ejemplo: poliuria- polidipsia, fiebre recurrente, petequias, hemoptisis, ojo rojo, ceguera, abortos, disnea, tos, cojeras, vómitos, diarrea, apatía, anorexia, dolor abdominal, proteinuria o trombocitopenia.
- Por tanto, para el veterinario clínico no es fácil realizar un diagnóstico definitivo, porque se ha de sospechar de leptospirosis en muchos casos que hasta ahora no se incluían en el diagnóstico diferencial.
- MAT es el método más utilizado porque la visualización directa o el cultivo de *Leptospira* tienen una sensibilidad muy baja. Sin embargo, la serología detecta la respuesta inmunológica del perro frente a *Leptospira*, lo que significa que puede ser que el contacto fuese previo a la presencia de los signos clínicos que presenta el perro actualmente o que en otros casos estos anticuerpos fuesen debidos a la vacunación previa.

- Las técnicas moleculares como la PCR pueden ser útiles en algunos casos porque permite la detección de las leptospiras en sangre u orina especialmente durante esos primeros 15-21 días donde la sensibilidad de la serología es baja porque puede que aún no se haya producido una seroconversión.
- Si entendemos que la vacunación produce anticuerpos que detectamos en la serología, que los niveles de anticuerpos no son 100% específicos de cada serovar y que la PCR detecta *Leptospira* pero no indica qué serovar es, nos daremos cuenta de que en estos momentos el diagnóstico clínico de la leptospirosis canina es difícil y es el fruto del análisis conjunto de los signos clínicos presentes, de los resultados de estas pruebas diagnósticas y de la exclusión de otras enfermedades.
- Hoy en día está ampliamente demostrado que la eficacia del tratamiento en conseguir una desaparición total de los signos clínicos y de las leptospiras se reduce a medida que se retrasa el inicio de este.
- Las recomendaciones actuales sobre la leptospirosis canina, el tratamiento considerado de primera elección es la doxiciclina a la dosis de 5 mg/kg cada 12 horas durante, al menos, 15 días. Algunos autores recomiendan tratamientos mas largos, de hasta 4-6 semanas de duración, para estar seguros de la eliminación de la leptospiras del parénquima, especialmente renal.
- Si por algún motivo no se puede utilizar la doxiciclina, el segundo tratamiento de elección es la ampicilina intravenosa a la dosis de 20 mg/kg cada 6-8 horas. Esta dosis se debe reducir si existe azotemia y, posteriormente, debido a que la ampicilina es menos eficaz frente a *Leptospira* y que no se recomienda su uso vía oral, siempre se debe iniciar un tratamiento de al menos 15 días con doxiciclina una vez que ya se pueda utilizar y el diagnóstico de leptospirosis se haya confirmado.
- El control de la leptospirosis es importante, no sólo para la salud de nuestras mascotas, sino desde una perspectiva de salud pública.
- Las vacunas actuales parece que ofrecen una buena eficacia preventiva frente a los serovares que llevan en su composición. Sin embargo, el conocimiento actual de la presencia de estos nuevos serovares en los perros y la descripción de casos de leptospirosis en perros vacunados correctamente con los serovares *Icterohaemorrhagiae* y *Canicola*, nos debe hacer reflexionar sobre la potencial utilidad de introducir nuevos serovares en el plan de vacunación de la leptospirosis canina.
- Parece claro que la vacunación anual con varios serovares de los perros con alto riesgo de desarrollar leptospirosis estaría recomendada para limitar las posibilidades de padecer esta enfermedad.

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Examen Neurologico y neurolocalizacion

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Objetivos de la presentación

1) Listar las partes del examen neurológico
2) Listar los segmentos neurológicos principales
3) Conocer las señales de lesiones en cada parte del sistema nervioso
4) Hacer una diagnosis neuroanatomica (neurolocalizacion)
5) Poder hacer listas de diagnosticos diferenciales basado en la neurolocalizacion

Puntos Principales

El examen neurológico existe para ayudarnos a localizar la lesión en el sistema neurológico. Hay seis componentes del examen neurológico.

1) Mentacion
2) Paso y postura
3) Nervios craneales
4) Propriocepcion
5) Reflejos segmentales
6) Rango de movimiento y palpación

Mentacion

Un animal debe tener mentacion normal, que también se describe como alerto y apropriado. Obtundacion quiere decir que el animal tiene la mentacion reducida, pero todavía responde de una manera normal, aunque de una manera disminuida. Un animal puede estar obnubilado por razones neurológicas o sistémicas. Estupor, la próxima clasificación, se define como un animal que no responde a estimulos normales, pero si responde a estimulos nocivos. Un animal comatoso esta vivo, pero no responde a nungun estimulo, ni nocivos.

Paso y postura

Cuando se evalua el paso, buscamos ataxia y paresia y es muy importante distinguir paresia de cojera. Hay tres tipos de ataxia: vestibular, cerebeloso y proprioceptivo. La ataxia vestibular se describe como un marinero borracho – camina sin coordinación y con inclinación a un lado u otro. Este casi siempre se ve con otras senas como la cabeza ladeada o nistagmo. La característica mas grande de ataxia cerebelosa es la hipermetría – estos animales exhiben movimientos exagerados, a veces tremores de intento y pueden perder la respuesta de amenaza pero no son ciegos. Ataxia proprioceptiva se ve con lesiones de la medula espinal, y de vez en cuando, con lesiones en el tronco encefálico caudal (bajo en nucleo de VIII). Ataxia proprioceptiva tiene hipometria, y casi siempre, paresia.

Es importante describir la postura de la cabeza y el cuerpo. Aquí es donde describimos la cabeza canteada o mantenida baja, si están recostados, si tienen un vaivén del tronco o si temblores. Kyphosis, torticollis, lordosis and scoliosis. Decerebrate, decerebellate, schiff-sherrington.

Nervios craneales

I: Olfativo. No se examina.
II: Optico. Se prueba con una gestura amenazante, con un laberinto, y con el reflejo pupilar a la luz.
III: Oculomotor. Responsable para la inervación de la pupila (parte parasimpático) y de los musculos extraoculares.
IV: Trochlear. Inerva el musculo oblicuo dorsal.
V: Trigeminal. Es el nervio responsable por sensación de la cara y cabeza. Tiene función motor (V3) a los musculos masticatorios.
V1: Oftalmico. Sensación a la cornea y el tabique nasal.
V2: Maxilar. Sensacion a la cara.
V3: Mandibular. Motor a los musculos masticatorios (maseter, temporalis, pterigoides) y sensación a parte de la lengua.
VI: Abductor. Inerva el musculo recto lateral y el bulbo retractor del ojo.
VII: Facial. En nervio responsable por la inervación de los musculos de expresión facial.
VIII: Vestibulococlear. Nervio con dos partes, coclear responsable por la audición, y vestibular, responsable para el balance y la orientación de la cabeza y el cuerpo en relación a la fuerza de gravedad.
IX: Glosofaringeo. Lleva sensación de la lengua caudal, el membrano tympano y la faringe, también sabor de la lengua caudal, información del seno y cuerpo carotideo. Inerva la glandula parótida.
X: Vago. Lleva control parasimpático al corazón, los pulmones y el sistema digestivo. Inerva la faringe.
XI: Accesorio. Inerva los musculos trapecio y esternocleidomastoideo.
XII: Hipogloso. Inerva la mayoría de los musculos de la lengua.

Propriocepcion

Propriocepcion es el saber donde esta el cuerpo sin verlo. Esto es una función sensorial, y ascendente, muy importante. Hay varias maneras de evaluar proprioception. Propriocepcion consciente se evalua con la colocación de un pie al revez – si el animal lo corrige, esta normal. Si no lo corrige o lo hace muy lentamente, es anormal.

Tambien uno puede hacer que salten en un pie de una manera lateral: se levanta una pierna y se empuja al lado. El animal debe iniciar un salto en cuanto que el cuerpo pasa el limite vertical. Se puede hacer un movimiento de caretilla que evalua función proprioceoptiva y motora.

El impulso postural extensor evalua las vías motoras vestibuloespinales. Esto se hace con animales pequenos que uno puede levantar. Se levanta el animal (aguantándolo en las axilas) de una manera vertical; en animal debe levantar las piernas. Al bajar el animal hacia el piso, debe extender las piernas buscando el piso. Al tocarlo, toma un par de pasos hacia atrás para poner el cuerpo en una orientación apropiada.

Reflejos segmentales

Los reflejos segmentales que se pueden evaluar con confianza en las extremidades en el perro solamente son la retracción y la patelar.

El reflejo perineal se evalua al levantar la cola y ligeramente se estimula la piel lateral al ano. Un reflejo normal incluye contracción de la cola y el ano.

El reflejo normal de paniculus se puede provocar al limite mas caudal aproximadamente al nivel de las alas del ilion. El musculo del tronco cutáneo es inervado por el nervio toracio lateral, que sale de la medula espinal al nivel de T1-T3. Los nervios espinales segmentales traen la sensación a la medula, y la señal sube hasta T1-T3 donde sale el nervio motor.

Rango de movimiento y palpación

La mayoría de información de rango de movimiento se puede acumular observando como se mueve el animal. Si mantienen la cabeza baja y no doblan el cuello, ya se sabe que tienen dolor cervical. Un animal debe poder doblar el cuello tanto que pueden tocarse el tronco con la nariz, pero esto a lo mejor no es posible en un buldog!

Neurolocalizacion

El sistema nervioso se puede dividir en trozos pada poder localizar una lesión. La primera división es entre el cerebro, la medula espinal y la unidad motora. Aquí siguen las divisiones principales que se usan para hacer una neurolocalizacion y las señales clínicas que se ven con disfunción en ese lugar.

Cerebro

Cerebro anterior: convulsiones, ceguera (CN II), dar vueltas, compulsión, cambio de personalidad (demencia, agresión/agradable), defectos proprioceptivos. No se debe ver ataxia de ninguna forma, ni paresia.

Cerebelo: ataxia cerebelar (hipermetría), postura de hancho, temblores de intentcion, perdida del reflejo de amenaza (pero son visual), inclinación de la cabeza, nistagmo. No se debe ver paresia con una lesión puramente en el cerebelo ni se debe ver defectos proprioceptivos.

Tronco encefálico: defectos en los nervios craneales (III-XII), paresia, ataxia (puede ser vestibular si afecta esos nucleos, o prioprioceptiva si es caudal al nucleo de CN VIII), defectos proprioceptivos, y una disminución mental (defecto del sistema de activación reticular). Porque los nucleos de CN VIII son tan grandes (hay 4 en cada lado!), les recomiendo evaluar el sistema vestibular en varias maneras.

Medula espinal

C1-C5: ataxia proprioceptiva y paresia que afecta las cuatro patas. Los reflejos segmentales deben ser intactos a hiperactivos.

C6-T2: ataxia proprioceptiva y paresia que afecta las cuatro patas. Los reflejos segmentales deben ser intactos a disminuidos.

T3-L3: Las piernas torácicas son normales, pero las piernas pélvicas ensenan ataxia proprioceptiva, paresia, y deben tener reflejos segmentales intactos a hiperactivos.

L4-S3: Las piernas torácicas son normales, pero las piernas pélvicas ensenan ataxia proprioceptiva, paresia, y deben tener reflejos segmentales intactos a disminuidos.

Aquí también se pueden ver defectos en la función perineal, la función de la cola, la vejiga y el esfínter anal.

Unidad motora: Nunca se debe ver ataxia con lesiones en la unidad motora.

Raiz nerviosa: se ve paresia y defecto o ausencia en los reflejos segmentales. Aquí se tiene que considerar que las raíces motora y sensorial son separadas.

Nervio periférico: se ve paresia y defecto o ausencia en los reflejos segmentales.

Union neuromuscular: se puede ver intolerancia al ejercicio, paresia, y el paso se pone muy rigido.

Musculo: condiciones musculares en general causan paresia y un paso rigido, pero los reflejos segmentales se mantienen.

No se nos debe olvidar que también existe la posibilidad de una lesión **multifocal**. Esto puede llegar a ser porque hay una condición que esta causando problemas en mas de un lugar a la vez. Tambien se ve cuando hay dos problemas simultaneo, pero no relacionados.

Manejo farmacéutico de convulsiones

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Resumen

Ataques epilépticos son un problema común en medicina veterinaria. Hay varias manifestaciones de ataques epilepticos, pero las manifestaciones no indican nada hacia la causa. Filiacion, base de datos minima y lo que encuentren en el examen neurológico, muchas veces seguido por tomografía o resonancia magnética, son las cosas mas útiles para descubrir la causa de ataques epilépticos. En general, todos ataques epilépticos se tratan la misma manera, pero el tipo y tiempo de tratameinto debe variar dependiendo de la causa. Existen varias medicinas anticonvulsivas por escoger. Uno tiene que medir los efectos buenos y malos en cada caso.

Objetivos

1) Familiarizarse con las clasificaciones de los ataques epilépticos

2) Familiarizarse con las causas comunes basado el Filiacion

3) Revisar caracteristicas de los anticonvulsantes comunes

Convulsiones se clasifican como generalizada, parcial, compleja parcial o psicomotor. Una convulsion generalizada, previamente dicho “grand mal,” da señales bilaterales y refleja que los dos hemisferios cerebrales están involucrados. Una convulsion parcial refleja que la actividad eléctrica inapropiada es restringida a un hemisferio cerebral; por eso, solamente una parte del cuerpo es afectado. Una convulsion compleja parcial, también dicho convulsion límbico o psicomotor, manifesta con cambios mentales y algún tipo de accion repetitiva (manifestación motor) como chasquido de labios. Estas convulsiones casi siempre tienen una componente emocional significante, una falta de consciencia normal (no necesariamente inconsciente), y pueden manifestar como agresión, miedo, vocalización or corridas histéricas.

La gran mayoría de convulsiones ocurren una a la vez, como eventos solitarios y discretos. Convulsiones repetidas agudas (acute repetitive convulsiones, ARS), también dicho racimos, es definido como 2 o mas convulsiones dentro de 5-24 horas distinto al patrón normal del paciente. Status epilepticus (SE) es definido como convulsiones continuas por un minimo de 5 minutos.

Al momento, la terminología para los desordenes convulsivos esta cambiando. Epilepsia quiere decir que hay convulsiones recurrentes debido a una causa intracraneal. Lo que se ha previamente conocido como epilepsia idiopática en la medicina veterinaria ahora se dice

epilepsia genética o primaria donde se sabe o es muy sospechado que hay un defecto genético. Epilepsia estructural abarca epilepsia sintomática, que son convulsiones que resultan debido a cosas como tumores, malformaciones, trauma o meningitis. Epilepsia incognita, también dicho criptogenica o epilepsia probable sintomatica, se usa para casos donde no se encuentra una lesión obvia, pero algo untrastructural o sutil es sospechado. Convulsiones reactivas, causadas por un desorden extracraneal como hipoglucemia, trastornos de electrolitos o toxicidades, no son considerados una epilepsia porque la causa se encuentra afuera del cerebro.

Los gatos son distintos. Epilepsia primaria o genética probablemente infrecuente en el gato. Pero, muchos gatos con ataques epilépticos tienen un examen neurológico normal y toso los analsis (incluyendo RM) normales. La terminología preferida para esos casos es unknown epilepsia. Gatos que tienen ataques epilépticos con un examen neurológico normal por mas de dos anos pero nunca se han hecho análisis avanzados son considerados tener epilepsia presuntiva desconocida.

Como doctores, no hemos visto la mayoría de nuestros pacientes epilépticos tener un ataque. Hacemos la diagnosis de un ataque epiléptico basado en la historia que nos da la familia. Por esta razón, es critico hacer preguntas apropiadas para confirmar que el episodio en realidad es un ataque epiléptico y no otra cosa. Si quedamos con dudas basado en la historia que nos han dado, hoy en día, yo le pido a la gente que saquen un video con el teléfono. Esto me ha hecho la vida mas fácil.

Una buena historia y un examen general son muy importante, rápidamente seguidos con un examen neurológico. Aunque tratamos todo ataque epiléptico igual, es muy importante conocer la causa para saber como dirigir tratamiento y poder dar una prognosis apropiada.

La primera pregunta que uno se tiene que hacer es si la causa es extra-craneal o intracraneal. Aquí es donde el examen general y análisis de sangre ayudan muchísimo. Un hemograma completo, perfil quimico serico y analisis de orina puede revelar varias anormalidades. Evaluacion de la presión de sangre, nivel de tiroide en los gatos, radiografia del torax también ayudan mucho. Animales con causas extracraneales no necesariamente requieren tratamiento para los ataques epilépticos contalde que el problema principal se este corrigiendo. Causas extracraneales incluyen hipoglucemia, hipocalcemia, and hepatopatías, incluyendo portosystemic shunts. Causas comunes intracraneales de convulsiones incluyen procesos idiopáticos, condiciones inflamatorias, varias neoplasias y malformaciones. Causas menos comunes incluyen infecciones, eventos vasculares, y errores innatos del metabolismo.

Animales con epilepsia primaria o genetica, por definición, van a tener un examen neurológico normal entre ataques. Si el examen neurológico es anormal, es 16.5x veces mas grande el chance que haya una causa estructural causando los ataques epilépticos! Es muy importante acordarse de que aunque un animal tenga un examen neurológico normal NO quiere decir que tiene un cerebro normal! Una lesion en un área silente del cerebro puede causar ataques epilépticos, pero no otra anormalidad que se vea clínicamente. Aproximadamente 80% de perros que empiezan a tener ataques epilépticos a mas de 7 anos tienen una causa estructural; el 20% que queda tiene epilepsia

desconocida o criptogenica (empiezan a tener convulsiones a mayor edad pero tienen el cerebro estructuralmente normal).

Los gatos, como siempre, son diferentes. En los gatos domesticos, epilepsia sintomática es lo mas común, componiendo 40-50% de casos de convulsiones. Epilepsia presumida ser idiopatica y convulsiones reactivas son igual como causas segundas y terceras, entre 25-50% cada uno. Sincope cardiaco es la causa cuarta de "convulsiones," pero estos en realidad so gatos con arritmias severas, como bloqueo del AV de tercio grado o "sick sinus syndrome." En gatos, convulsiones focales y generalizados aparecen con frecuencia igual. Una convulsion generalizada en un gato es muy parecido a un perro; se va ver ptialismo, movimientos tonicos-clonicos, micción, defecación, pero los gatos pueden vocalizar durante la convulsion. Los gatos también pueden tener ataques epilépticos generalizados con el minimo de actividad motor; puede haber espasmos pequenos de parte de la cara y ptialismo, pero la clave in estos casos es que los gatos casi siempre la temperatura elevada. Epilepsia de causa desconocida en gatos tiene la supervivencia mas alta que en perros con aproximadamente 45% que obtienen remisión. En breve, vemos gatos que tienen algo parecido a la epilepsia general en perros, pero los gatos parecen ser mucho mas fácil manejarlos.

La lista de diagnosticos diferenciales por convulsiones de causas intracraneales va variar basado en la filiación, pero la lista siguiente sirve de guía:

<1 ano: Metabolico (hypoglycemia), Congenital (hidrocefalia), Infeccioso
1-5 anos: Genetico/Idiopatico, Inflamatorio, Neoplasico
>6 anos: Neoplasico, Inflamatorio, Criptogenico
Geriatrico: Neoplasico, Vascular, Criptogenico

La raza del animal también se debe considerar cuando pensando en la causa de ataques epilépticos. Un perro joven de raza grande (Labrador, pastor alemán) probablemente tiene epilepsia genetica mientras que un perro joven o adulto terrero o raza de jugete probablemente tiene meningitis o encefalitis inflamatorio. En un perro adulto braquicefalo con una historia nueva de convulsiones, uno se debe de preocupar por neoplasia encefálica primaria, un tumor glial en particular. En contraste, el perro mayor de raza dolicocéfalo tiene mas alto riesgo de meningioma.

Terapias medicas

Los objetivos principales de terapia medica son reducir la frecuencia y la severidad de las convulsiones. Remision completo es muy infrecuente en los perros. Un ataque epiléptico solo, en general, no es muy peligroso, pero convulsiones agrupadas y status epilepticus si son situaciones emergentes. Actividad epiléptica prologada puede acabar en danos a las neuronas, hipertermia, coagulación intravascular diseminada y muerte. Vigilancia no es recomendado en un animal con convulsiones a no ser que las convulsiones son individuos y lejos cronológicamente.

En la situación emergente, una benzodiazepina inyectable como diazepam o midazolam es ideal. Una inyección de 0.5mg/kg IV debe parar una convulsion activa. Si acceso a la vena no es disponible, 1-2mg/kg de diazepam se puede dar por recto or nasal para parar la convulsion. Diazepam solo ejerce efectos anticonvulsivos for aproximadamente 15 minutos – suficiente tiempo para obtener resultados preliminares y una historia medica. Bolos de diazepam se pueden repetir, pero si hace falta mas de dos o tres veces, una medicina anticonvulsiva de mas largo plazo se debe considerar. Diazepam no es una buena opción en el perro o el gato. Los perro desarrollan tolerancia a diazepam oral tan temprano como a los 5 dias, y entonces ya no tiene efecto. En el gato, diazepam oral puede causar necrosis hepática idiosincratica y por eso no es recomendado.

Hay varias opciones para control al largo plazo. Tratamiento se considera efectivo si hay al mínimo una reducción de 50% en el numero de ataques durante un tiempo especifico. Terapia medica es un balance entre control de los ataques epilépticos y los efectos negativos de las medicinas.

Existen pocas indicaciones absolutas para empezar anti-convulsantes. Estos son cluster convulsiones, structural intracranial disease, an abnormal neurologic examination and aggression pre- or post-seizure. Otra indicación para empezar medicinas es un intervalo entre ataques progresivamente mas corto – si los ataques están ocurriendo mas frecuentemente, entonces algún tipo de medicina es seriamente recomendado.

Fenobarbital (PB) es un barbitúrico de largo accion con una dosis minima en el perro de 2.2mg/kg PO BID y se tiene que dar a la misma dosis dos veces al dia, lo mas cerca a 12 horas posible. Se puede usar una dosis de carga de 16-20mg/kg IV una vez, seguido por la dosis de mantenimiento 12 horas después. Fenobarbital da control de convulsiones dentro de minutos si se ha dado como carga IV; los niveles in la sangre llegan a nivel terapéutico con la inyección, pero todavía tarda entre 10-14 dias para llegar a estado estable. En los animales viejos o enfermos, la dosis de carga se debe reducir por 25-50% por no sedar el paciente demasiado. Niveles de suero de fenobarbital se mantienen entre 20 y 30ug/mL; a niveles mayores de 30ug/mL, no hay mejor control de convulsiones y solamente hay mas riesgo de daño al hígado. Gatos en general requiren menos fenobarbital para llegar a un nivel terapéutico; yo les doy 8.1mg PO BID (1/2 de 1/4grain tab). PB es metabolizado por el hígado y induce su proprio metabolismo. PB también induce un insoenzyma de fosfatasa alcalina, asi que uno de esperar que el nivel de ALP va a subir en los perros tomando PB. Hepatotoxicidad resultado de PB es casi siempre asociado con un nivel de suero alto, mas de 40ug/mL, por mas de 6 meses. En esos casos, alanina aminotransferasa (ALT) esta mas alto que ALP. El nivel de suero no es temporal si han estado tomando la medicina por mas de 10 dias in >90% de perros. Es recomendado medir niveles de PB y un perfil quimico cada 6 meses. Se sabe que PB interfiere con todas las formas de las tiroides. Los perros parecen tener niveles bajos de T4 total and fT4, pero no son realmente hipotiroides. En cuanto un perro esta tomando PB, no es recomendar hacer análisis de tiroides porque no se pueden interpretar.

Bromuro es una sal haluro que es un anticonvulsivo eficaz en perros; recientemente se ha probado que no es tan eficaz ni tan bien tolerado como PB. No es recomendado usarlo en gatos porque ellos pueden desarrollar complicaciones respiratorias, arriba de que no es muy eficaz. La dosis typica es entre 20-40mg/kg/dia en el perro. El intervalo

terapéutico es de 1 a 3mg/mL. Dosis de bromuro se pueden dar SID o divididos a la mitad y dados BID para reducir complicaciones gastrointestinales. Bromuro no es metabolizado y es excretado por los riñones; se debe evitar en animales con disfunción renal. Debido a la excreción renal, niveles de suero de bromuro son muy sensatos a la cantidad de cloruro en la dieta. Perros tomando bromuro tienen que comer una dieta consistente con cantidades de sal (NaCl) moderadas o bajas en sal. La ingestión inadvertida o acidental de una cantidad grande de cloruro (generalmente como NaCl), causa can cause un aumento rápido en la excreción renal de bromuro y una caída precipitosi en el nivel de suero, asi rápidamente reduciendo el limite convulsivo. Bromuro tiene una media-vida muy larga, ~21 dias, asi que el estado estable no se alcanza por tres meses. Bromuro se puede cargar para obtener niveles terapeuticos rapidamente; esto se puede hacer oralmente con KBr o en la vena con NaBr. Bromuro puede obtener niveles terapéuticos en horas si se da IV o dentro de una semana si KBr es cargado PO, pero no necesariamente es efectivo por un mes si se empieza a dosis de mantenimiento y no llega al estado estable por 3 meses. Debido a la falta de metabolismo de bromuro, si es una buena opción in animales con condiciones hepáticas donde PB y zonisamida se deben evitar. Efectos secundarios comunes incluyen sedación, ataxia, paraparesia, polidipsia y poliuria, y polifagia. Toxicidad de bromuro es casi siempre visto con niveles de sero elevados. Perros pueden demostrar cambios mentales, midriasis, ceguera, ataxia, paresia, disminución de reflejos, disfagia y dolor muscular. Reacciones sospechadas a ser idiosincrásicas al bromuro incluyen cambios mentales y agresión, dermatitis eritematosa y prurito, toz y pancreatitis. Es recomendado chequear niveles una vez al ano si el perro esta bien controllado. Debido a la media-vida tan larga, el tiempo del dia de medicamento y el tiempo de análisis no importan.

Levetiracetam (Keppra) es un anti-convulsivo mas nuevo que se puede usar en perros y gatos. Levetiracetam existe in formas inyectables, liquidas, y en tabletas. Levetiracetam no se ha visto tener ningún mal efecto, pero si puede causar un poco de sedación, in particular cuando se anade a un protocolo con otras medicinas anti-convulsivo. Estudios han ensenado que dosis hasta 100mg/Kg tienen efectos minimos. Se empieza a una dosis de 20mg/kg TID para la formulación normal y empezando a 30mg/kg PO BID para la formulación de lanzamiento prolongado (XR). Las tabletas XR NO se pueden dividir! Si la dosis inicial no llega a dar los efectos queridos, la dosis se debe subir por 25-50%. En mi experiencia, si una reacción appropriada no se ha visto con una dosis a 60-80mg/kg, la droga es considerada no efectiva y se para. Levetiracetam funciona inmediatamente si se da IV y dentro de 2 horas si se empieza a mantenimiento oralmente con 100% biodisponibilidad.

Zonisamida es otra medicina anticonvulsiva que es parte del grupo de las sulfonamidas que se puede usar en perros y gatos. Se empieza a 5mg/kg PO BID, pero se tiene que subir a 10mg/kg PO BID en perros que están tomando PB al mismo tiempo. La zonisamida existe en capsulas de 25, 50 y 100mg y se puede can be hacer un liquido; no existe una formulación inyectable. Como todas las sulfonamidas, es metabolizada por el hígado y puede inducir hepatopatías. Tambien hay reportes dispersos de reacciones sospechadas a ser idiosincráticas incluyendo hepatopatías y desordenes de la piel. Casos raros de neutropenia existen, pero efectos secundarios mas comunes incluyen sedación,

ataxia, vomito y anorexia. Zonisamide es efectivo en 3-5 dias y llega al estado estable en 7-10 dias.

Estimuladores del nervio vagal se han usado en pocos casos con la intención de controlar convulsiones. Los reportes son limitados y el implante es costoso.

Si un perro o gato solamente tiene convulsiones únicas (no multiples) no es necesario tener una terapia de rescate en casa. La administración de medicamentos adicionales en esa ensena puede prolongar la recuperación de la convulsion y probablemente no tiene beneficio. Animales que se sabe que tienen convulsiones multiples (en grupo) son un caso distinto y eso se discuta después.

Droga	Clase	Dosis	Frecuencia	Ruta	Indicacion
Diazepam	**Benzodiazepine**	**0.5-2mg/Kg**	**PRN up to 3 times**	**IV**	**Convulsiones**
Phenobarbital	**Barbiturate**	**M: ≥2.2mg/Kg**	**BID**	**IV, PO**	**Convulsiones**
Bromide	**Halide salt**	**M: 30-40mg/Kg** **L: 500mg/Kg**	**SID** **BID if split**	**PO**	**Convulsiones**
Levetiracetam (Keppra)	**SV2A Ca channel**	**R: ≥20mg/Kg**	**TID**	**IV,PO,PR**	**Convulsiones**
Zonisamide **(Zonegran)**	**Sulfonamide**	**5-10mg/Kg**	**BID** **(Puede sid**	**PO**	**Convulsiones**

Conclusion

El objetivo de terapia anticonvulsiva es reducir la frecuencia y la severidad de las convulsiones mientras minimizando los efectos negativos de las medicinas. Es importante tratar de determinar la causa de las convulsiones. Calidad de vida es una preocupación importante cuando manejando estos casos. La medida mas objetiva que tenemos para vigilar estos pacientes y sus respuestas al tratamiento es la frecuencia de los ataques; por eso, es recomendado que la familia mantenga un calendario de ataques.

Meningitis y encefalitis

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Resumen

Condiciones inflamatorias

Objetivos

1) Categorizar localizaciones de condiciones inflamatorias
2) Listar causas de inflamación en el sistema nervioso
3) Hacer un plan diagnostico y terapéutico para un perro

Las condiciones inflamatorias del sistema nervioso se categorizan basado en las estructuras afectadas. Si es solamente el cerebro, es encefalitis. Si solo las meninges, meningitis. Si solo la medula espinal, mielitis. Y cualquier combinación puede existir, dependiendo de que estructura esta afectada.

Porque muchas de estas condiciones afectan animales jóvenes, es crucial distinguir encefalopatías metabólicas o sistémicas de las neurológicas primarias.

Las causas virales mas comunes incluyen la rabia, la corona/FIP, y el moquillo. Mamiferos infectados con la rabia en general mueren dentro de 7 dias, con un average de 3-5 dias en los perros y gatos. Cuando la coronavirus causa FIP, es casi siempre en gatos jóvenes y pueden desarollar una meningoencefalitis fatal que afecta el sistema nervioso entero. El moquillo afecta a perros jóvenes, y si causa cambios neurológicos, la prognosis depende de la severidad. Algunos perros solamente acaban con un mioclono como cambio permanente. Pueden tener convulsiones, pero no se controlan con anticonvulsivos, no tienden a responder.

Otras infeciones incluyen toxoplasma, mas en los gatos, y la neospora. Neospora en cachorros causa condiciones neuromusculares, pero en el adulto, causa una cerebellitis necrosante.

Varios hongos pueden causar infeciones neurológicas, y la mas común es Cryptococcus neoformans. Este hongo se encuentra en el mundo entero y es neurotrópico. En los perros y gatos, causa una leptomeningitis generalizada. Se puede diagnosticar al ver los organismos en el análisis de fluido rachidico o con un analises de títulos del organismo. Coccidioides immitis también causa una condición parecida y se diagnostica con títulos de suero. La gran diferencia es que Coccidioides tiene una distribución muy regional y solamente se encuentra en los desiertos. Las encefalitis causadas por hongo se tratan con fluconazole que penetra la barrera de sangre del cerebro. Es bien aceptado que las meningitis causadas por hongo requieren tratamiento con un poquito de esteroides, una dosis anti-inflamatoria. Con la presencia de, y entonces la

muerte de, los hongos en el cerebro, hay una reacción inflamatoria severa que si no se controla, causa mas daño.

Causas bacteriales de meningitis o encefalitis son raras. La bacteria es introducida por trauma exterior, como una mordida de perro, o de un abseso local que ha extendido.

Causas inmunológicas de meningitis y encefalitis representan la porción mas grande hoy en dia. Se han hecho varias diagnosis dependiendo de la presencia de necrosis (NME, NLE) o no (GME). Hoy en dia, se juntan todos bajo el titulo MUE – meningoencefalitis de etiología desconocida. No se ha, hasta hoy, identificado una infección en estos casos. Sabemos que las condiciones responden a modulación del sistema inmunológico. En general, perros pequenos y terreros son mas afectados, pero se ve en toda raza de perro. Es una condición fatal si no tratada. Las señales clínicas pueden variar tremendamente dependiendo de la parte del sistema inmunológico afectado. La mayoría de estos pacientes tienen una pleocitosis del fluido rachidico, pero a veces no se le puede hacer el análisis debido a herniación cerebral o presión intracraneal elevada. La resonancia magnética es el mejor diagnostico, usado en combinación con análisis del fluido, cuando posible. La prognosis con todas estas condiciones depende de la respuesta al tratamiento. Mas que eso, todavía no se sabe. Hay una lista de tratamientos documentados, empezando con prednisona y acabando con la radiación. Cualquier droga inmunomoduladora o inmunosopresante que cruze la barrera de sangre craneal se puede usar. La lista incluye ciclosporina, arabinosido de citosina, micofenolato, azatioprina, y lomustina. No hay una protocola perfecta – varias se han publicado. Yo tiendo a modificar mi plan de tratamiento dependiendo de la severidad del caso y las limitaciones del amo, y el mascota. Hay que notar que algunas formas, en particular NME (la de los pugs), puede tener una progresión muy aguda y severa. En general, condiciones necrosantes tienen una prognosis peor que las que no son necrosantes.

Si un perro con encefalitis responde a tratamiento, se deben tratar por minimo 9-12 meses. Si no hay empeoramiento durante tratamiento, es posible que se puedan eliminar las medicinas completamente. Muchos perros requieren medicamento por vida. No tenemos números definitivos para prognosis, pero aproximadamente un tercio de casos se curan, un tercio requieren tratamiento por vida, y un tercio se mueren.

Tratamientos nuevos para condiciones viejas

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Resumen

En los ultimos anos, han habido muchos descubrimientos y nos hemos dado cuenta que, a veces, no sabemos lo que tratamos ni porque. Con esto en mente, a les resumo una serie de nuevas tecnicas para condiciones que considerabamos ya definitivos.

Objetivos

1) Listar tratamientos alternativos para mejorar el recupero neurologico

Herniaciones discales siguen siendo la condicion que afecta la medula canina con mas frecuencia. Historicamente, hablamos de herniaciones Hansen tipo 1, 2 y últimamente 3. Esa terminología no tiene gran impacto clínico y nos hemos enfocado mas en extrusiones vs protrusiones. Podemos decir que, en general, herniaciones discales en los perros son una condición cirurgica. Cuando hay daño suficiente que causa mielopatia, tenemos que dirigirnos hacia las causas de daño medular: contusion, concusión y compresión. De esos tres, el único a que nos podemos dirigir con certeza es a la compresión, entonces al quirófano. En mas de trenta anos de cirugía, los resultados no han cambiado mucho hasta recién. Y peor, que se hace con los casos que no son quirúrgicos?

Varios estudios se han publicado sobre el uso de terapia física como tratamiento principal de perros con mielopatia no quirurgica. Tambien se estan viendo mas publicaciones sobre el efecto de cirugía tradicional combinado con terapia física y como esto puede mejorar la recuperación en varios grupos de pacientes. Perros que reciben terapia física agresiva, diario y hospitalizados, recubren la capacidad de caminar mas temprano, aunque el tiempo a recuperación completa es igual.

La terapia física es el tratamiento recomendado para la mielopatia isquémica y herniaciones discales no compresivas.

Las malformaciones vertebrales afectan las razas de perro “screw tailed” (cola de tornillo) con frecuencia alta. Esto incluye los bulldogs franceses e ingleses, y los terreros Boston. Los pugs a veces caen aquí, pero yo prefiero ponerlos en su propia categoría cuando hablando de la neurología! La generación de la malformación se entiende como un error en el desarrollo, pero no se entiende como causa la mielopatia. Muchas de las malformaciones no tienen impacto clínico, pero cuando si causan mielopatia, existen varias teorías para explicar el mecanismo, pero ninguna se ha probado. Las malformaciones pueden causar una variedad de problemas, incluyendo inestabilidad y compresión, los dos causando isquemia y mas daño a la medula. Varias cirugías se han tratado con resultados variados. Se ha ensenado que perros con malformaciones causando un angulo de Cobb >35^{o} tienen alto riesgo de desarrollar una mielopatia.

Varias técnicas nuevas se han publicado enfocándose en esta condición. Cirugia es probablemente el tratamiento ideal para los perros afectados a una edad joven, pero no sabemos que técnica seria la mejor. Con esta condición, el disco puede lucir anormal, pero estos perros no padecen de una herniación típica. La mayoría de las técnicas quirúrgicas se enfocan en algún tipo de estabilización. Decompresion no es necesario en todos los casos, pero se tienen que evaluar individualmente.

La subluxación atlantoaxial congénita ocurre con mas frecuencia en perros pequenos como el Yorkshire terrier, Pomeranian y poodle de miniatura. Pueden ocurrir en cualquier perro en una situación traumatica, pero eso no es común. Los perros con luxación AA típicamente empiezan a tener problemas desde 4 meses, pero pueden presentar como adultos. Presentan con dolor cervical, ataxia y paresia en las cuatro patas y pueden estar al punto de no poder ambular. A veces se pueden ver cambios medulares: diciendo señales vestibulares. La diagnosis se puede hacer con radiografías simples. No recomiendo que hagan radiografías con flexion si no tienen el animal anestesiado y entubado. La cirugía tradicional usa dos alambres cruzados de C2 a C1. Riesgos con esta técnica incluyen movimiento de los alambres, daño a la medula encefálica y muerte. Una technica nueva usa o tornillos chicos (1.5/5-10mm o 2.0/5-10mm) en el cuerpo de C1 y C2 sin necesidad de cruzar el espacio de la coyuntura y hay menos riesgo de violar en canal vertebral.

Hyperadrenocorticism, Cushing's disease, se clasifica como una condición endocrinológica. En realidad, mas de 2/3 de los casos en perros son debidos a un tumor en la hipófisis. En los gatos, acromegalia acaba en eutanasia debido a la diabetes que es muy difícil controlar. Recientemente, varios grupos han empezado a hacer hipofisectomías para el tratamiento de Cushing's en los perros y acromegalia en gatos. Con esta cirugía, existe la posibilidad de cura. La cirugía es elegante, y tiene el riesgo de complicaciones serias. Si acabas operando un tumor que no es de la pituitaria, la prognosis es peor. Este procedimiento es ofrecido en centros limitados en el mundo, principalmente en la universidad de Utrecht en Holanda, Washington State University y University of Florida en los EEUU, el Royal Veterinary College en Londres y Australia.

Causas y manejo de dolor cronico

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Resumen

El dolor es una sensación compleja y el tratamiento puede ser complicado y difícil. Dolor crónico o neuropatico no responde a drogas de la misma manera que dolor agudo, y es importante considerar terapias apropiadas.

Objetivos

1) Listar causas de dolor neuropatico
2) Listar drogas para el dolor crónico o neuropatico

Nocicepcion es la percepción de estímulos nocivos y dolor es la reacción cerebral, consciente, a la estimulación de varios receptores. Lo que se interpreta, la reacción consciente, tiene que ser transmitida de la periferia hasta el cerebro. Un estímulo nocivo tiene que ser convertido en una potencial de acción en el receptor; este proceso es transducción. Transmisión es el proceso de como la señal se propaga de la periferia a la medula espinal, y de allí se proyecta hasta el cerebro. Al fin, la señal es percibida de una manera consciente. La señal puede ser modulada a varios niveles donde se puede aumentar o disminuir; esto ocurre en la medula y en el cerebro. Hay varias sendas en la medula espinal que existen solamente para transmitir dolor.

No todo estimulo es nocivo, pero en situaciones de heridas agudas y crónicas, un estímulo normal puede evocar una reacción adolorida. Esto se llama alodinia. Hiperalgesia es un aumento en el dolor de un estímulo nocivo y una disminución del límite normal de dolor.

Dolor neuropatico es un estado de dolor crónico que ocurre debido directamente a algo afectando el sistema somato sensorial, sea agudo o sistémico y crónico.

Dolor agudo se ve con frecuencia en un perro con un disco herniado. Esto es una situación complicada porque hay inflamación en las meninges y la medula, y estimulación neural por compresión de la raíz debido al disco herniado. Existen varias drogas con potencial en esta situación. Yo recomiendo una combinación de modalidades incluyendo un anti-inflamatorio, un narcótico, gabapentina y un relajante muscular si indicado. Si hay una compresión severa, drogas pueden limitar o controlar el dolor, pero no es probable que resuelvan el dolor completamente.

Como anti-inflamatorios, yo prefiero empezar con no esteroidales porque tienen menos efectos secundarios diarios. Si uso esteroides cuando indicado. Es importante usarlas a una dosis apropiada – 0.5-1mg/Kg/día equivalente de prednisona.

Tengo opciones limitadas de narcóticos que puedo usar a largo plazo. Tramadol parece tener efecto limitado en el perro y sabemos que no es muy efectivo cuando usado como única droga en perros con osteoartritis. Si veo efecto cuando se usa en combinación con otras drogas. Tramadol funciona como narcótico en varios receptores de opioides, pero también tiene efectos serotoninérgicos y adrenérgicos que se tienen que considerar cuando combinando drogas. Tramadol se debe usar a 2-6mg/Kg q 6-8 horas.

Gabapentina es una droga interesante originalmente desarrollada como anticonvulsivo, pero hoy en día, se usa más que nada para el dolor crónico y neuropatico. En los perros y gatos, es muy bien tolerado y no tiene

gran efecto negativo. A dosis altas en los perros, puede causar sedación. Conozco veterinarios que usan una dosis en gatos antes de una visita a la clínica para "calmarlos." Para el dolor neuropatico, yo empiezo a 5-10mg/Kg q 8 horas. Como punta de referencia, la dosis anticonvulsiva es >20-30mg/Kg q 6 horas.

En varios casos de dolor crónico y neuropatico, se ve que los animales desarrollan un elemento de anticipación de dolor. Por ejemplo, el perro empieza a llorar y gritar cuando uno se arrima pero ni llega a tocarlo. Puedo imaginar que el perro espera que lo toquen y le va doler. En estos casos, la trazodona puede ayudar. Trazodona es un antidepresivo e anti-ansiedad con efectos serotoninérgicos y adrenérgicos. Cuando usado en perros, el rango de dosis es de 3.5-10mg/Kg q12 horas.

Cuando se combinan drogas como tramadol y trazodona, se debe considerar el sindroma de serotonina que puede ser fatal. Unas drogas potentes serotoninérgicas usadas con frecuencia incluyen selegilina, fluoxetina, amitriptilina y buspirona. Debido al riesgo, es recomendado reducir la dosis de una de las drogas serotoninergicas para evitar el riesgo.

El animal mareado

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Resumen
Hay muchas causas para el desequilibrio en un perro o gato. Es muy importante distinguir una lesion central o periférico. Esto tiene un impacto en la lista de diagnosis deferenciales y el plan de tratamiento.

Objetivos

1) Distinguir una lesion periferico o central vestibular
2) Listar causas communes de condiciones vestibulares periferico y sus tratamientos
3) Listar causas communes de condiciones vestibulares centrales y sus prognosis

Problemas vestibulares son común en pacientes felinos y caninos. Es crucial hacer un examen neurológico completo en estos casos para hacer una neurolocalizacion y distiguir central versus periférico; aquí, ceirtas partes del examen neurológico ayudan mas que otros. El poder distinguir central versus periférico tiene gran efecto en la lista de diferenciales, plan terapéutico y prognosis.

El sistema vestibular incluye la oreja, los canales del oído, el timpano, la bula, canales semi-circulares, CN VIII, la medula (CN VIII nuclei) y el cerebelo. ***Notable in gatos es que la bula tiene un septo complete, tiene dos camaras: una ventromedial y una dorsolateral. Tambien es notable que nervios sympaticos al ojo pasan dentro del septo en los gatos, mientras pasan al lado de la bula en los perros. *** Todo afectando CN VIII o la oreja o el oido (los canales, la bula, canales semi-circulares) es considerado periferico. Si esta dentro de la medulla o el cerebelo, es central. Esta distinction clave se puede hacer al saber si la propriocepcion es normal o no; si hay deficits proprioceptivos, la lesión esta afectando la medula y es vestibular central. Solamente porque no tienes defecits proprioceptivos no necesariamente indica que la lesion es periferica, simplemente es mas probable. La excepción grande a la regla de propriocepcion es con lesiones en el cerebelo – eso siempre es central, y no es típico tener déficits proprioceptivos.

Condiciones vestibulares perifericas
Causas comunes de condiciones vestibulares perifericas incluyen idiopatico, infeccioso, inflamatorio, y neoplásico.
Sindrome veistibular periferica idiopatica, “sindrome vestibular de perros viejos,” es una de las causas mas communes de mareo en perros. Esto tipicamente afecta perros grandes y viejos, y puede afectar perros pequenos. Estos perros presentan con un canteado de cabeza severo, nistagmo rápido con la fase rápida lejos del lado afectado, y una ataxia vestibular, si pueden caminar. Perros pueden estar tan mareados que no pueden caminar y dan vueltas; aquí puede ser imposible evaluar propriocepcion. Una sindroma vestibular idiopatica si ocurre in los gatos, y tiene una presentacion distinta. Gatos pueden empeorar sobre un par de días y pueden tardar meses para recuperarse. Los gatos pueden desarrollar polipos nasofaringeos inflamatorios que pueden inducir problemas vestibulares.

Otitis media/interna (OMI) puede causar problemas de balanace; di tienes otitis y desarollas un mareo, la otitis es interna! Vale la pena notar que OMI tiende ocurrir con deficits en otros nervios craneales; en particular paralysis del nervio facial (CN VII) y síndrome Horner's (ptosis, miosis, enoftalmos, elevacion del nictitans) se ven con frecuencia ipsilateral a la infecion. Debido a la anatomía única de la bula felina, la síndrome Horner's puede ser la única señal de otitis. OMI puede ser infecciosa, casi siempre bacterial, y puede ser esteril, como los CKCS con otitis media primaria secretoria o un gato con un pólipo. Si la infección esta dentro de la bula, es otitis media. Si hay cambios neurológicos, es otitis interna porque los receptores neurologicos son afectados. Tratamiento de OMI bacterial es idealmente dirigido al organismo especifico. Pero, cuando no posible, yo empiezo con amoxicilina/acido clavulanico. OMI se debe tratar por un curso de minimo 6 semanas.

Neoplasia en la oreja o dendro del oido puede causar problemas con el balance. Estos tumors son en general del canal auditivo (adenocarcinoma de glándula ceruminosa) o a lo largo de la base del cráneo (carcinoma de células escamosas en gatos).

Condiciones vestibulares centrales
Causas de disfuncion incluyen accidentes vasculares, inflamacion (inmuno-mediado o infeccioso), trauma, intoxicacion, y neoplasia. Eventos vasculares si ocurren en perros y gatos. En los perros, hay una predilecion para el cerebelo. Un accidente vascular en esa area puede causar ataxia del tronco, hipermetria, espasticidad, y nistagmo. Es posible pero no necesario que haya una inclinación de cabeza. Es possible ver deficits proprioceptivos porque la arteria que sirve el cerebelo tambien sirve una parte dorsal de la medula. Es muy importante evaluar perros y gatos por una condicion sistémica. Si existe una condicion sistemica y no se identifica, es porbable que el animal siga teniendo eventos vasculares.

Meningitis/encefalitis/meningoencefalitis inmunomediada puede afectar cualquier parte del cerebro, y prefiere el cerebelo y la medula. Esto se ve mas que nada en perros terreros y pequenos y casi nunca en gatos. Meningitis/encefalitis/meningoencefalitis infecciosa es mas común en el gato que el perro. Toxoplasmosis y Cryptococcosis son dos de los organismos identificados con mas frecuencia; son faciles de diagnosticar en suero. Meningoencefalitis bacterial es infrecuente, y se puede ver como un extension intracraneal de otitis.

Trauma, que suele tener una historia mas obvia, casi siempre afecta la medula y el cerebelo un poco en el perro y gato.

La neoplasia puede ocurrir donde sea. Los tumores mas comun incluyen meningiomas y tumors del plexo coroideo, gliomas se ven en la fosa caudal con menos frecuencia.

Abordaje y diagnosticos
Es indicado hacer examenes generales, ortopedicos y neurologicos completos. Analisis de sangre general es recomendado para eliminar condiciones sistemicas como causas, por ejemplo fallo renal causando hipertensión. Radiografias del torax siempre son indicados en un caso vestibular debido a la nausea y vomito que pueden resultar en pulmonia.

Los estereotipos existen por una razon! Perros viejos (10+ anos) de raza grande desarollan "sindrome vestibular de perros viejos" mientras los perros con una historia muy, muy crónica de

otitis desarollan cambios neurológicos. Con las condiciones centrales, los perros chicos suelen tener encefalitis inmunomediado. En los gatos, otitis media/interna siempre es una diferencial razonable.

La modalidad radiologica major va depender de la localizacion del paciente. Si estas convencido que en animal tiene algo peripheral, y en particular otitis, la tomografía es una buena opción para el oido. Si hay cualquier duda que puede ser algo central, una resonancia magnetica es recomendado.

Terapia
Terapia es sintomatica hasta que haya unda diagnosis difinitiva. Es importante tartar la nausea, si existe. La meclizine funciona, pero solamente existe como formula oral. Muchos pacientes vestibulares estan deshidratados debido al babear o vomitar. Hospitalizacion con fluidos de suero es indicado. Sedacion se puede usar con cuidado, mas que nada en los pacientes que están dando vueltas. Terapia especifica tiene que ser enfocado a la causa. Esteroides se tienen que usar con mucho cuidado en animals vestibulares por el riesgo de inmunosupresión y pulmonía.

Prognosis
La prognosis depende del estado neurologico del paciente y la condicion especifica. Perros vestibulares idiopaticos mejoran dentro de 24-48 horas sin terapia especifica. OMI es mas lento en la respuesta a tratamiento y requiere por lo menos 6 semanas de antibióticos, pero pueden necesitar cirugia. Eventos vasculares varian, pero en general mejoran en dias. Meningitis y la neoplasia requieren tratamiento especifico.

Resumen
Muchos animales mareados no tienen nada en el oido! Gatos con OMI pueden solamente tener la sindroma Horner's. Distinguir si una condición vestibular es central vs periferal es muy importante. Tomografia o resonancia en general es requirido para obtener una diagnosis. Si no se puede, trata lo tratable.

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DEPARTURE/SEPARATION/CONFINEMENT ANXIETY

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Classic signs of "separation anxiety" panic in dogs include distress vocalization [howling, yelping], elimination ["fight or flight" urination and/or defecation], attempts at escape [typically at doors that owners have left through] with resulting destruction, and/or destruction of other locations/objects [digging at walls, chewing at furniture, etc.].

Dogs who feel panic at being left alone do so for typically 3 reasons: 1) They are anxious at watching their owners leave [Departure Anxiety]; 2) They are anxious if they find themselves alone [Separation Anxiety]; and 3) They are alone in a crate or other enclosure [Crate/Barrier Anxiety]. Any of these can be discrete presentations or they can be seen in combination.

Dogs with **Departure Anxiety** tend to show anxiety when they observe the "pre-departure" signals that their owners employ before leaving: putting on certain clothes/shoes, packing a briefcase or handbag, picking up keys, etc. The dog has learned – through classical conditioning – that these actions are associated with the act of being left.

Dogs with **Separation Anxiety** are those who panic as soon as they realize that they are alone. This can be shortly after their owner leaves the house – typically within just a few minutes. Dogs with Separation Anxiety can also panic when their owner is home but not within sight – such as out in the yard, in another room, in the shower.

Dogs with **Crate/Barrier Anxiety** are those who panic because they are confined. These dogs are typically those that present for breaking out of crates and often injuring themselves [broken teeth, torn claws, ulcerated muzzles].

Starting with the Crate/Barrier Anxiety dog, it is the easiest to confirm and treat. Leave the dog out of the crate! Many of these dogs were crated as puppies because they were thought to have "separation anxiety" – perhaps because they eliminated in the house as a result of incomplete house-training. Once the barrier is removed, this group of dogs is no longer anxious when left alone.

For the other dogs, because the behavior that we need to observe is happening out of the owner's sight, it is important to video the behavior. Once there is a record of the dog's activity when alone, we have more information as to the correct diagnosis and treatment plan. For example: If the dog is seen pacing, panting, urinating and defecating a matter of minutes after the owner leaves – that's panic. However, if the dog urinates by the door 3 hours after the owner has left – that could be "I gotta go!" – and is a matter of the dog not yet being completely housebroken.

Getting a complete history from the client is extremely important. For example, for the destructive dog: "What items are being destroyed?" Again, if the video shows that the dog is furiously digging at the door that leads out to the garage – the owner's departure door – then that points to a diagnosis of Departure/Separation Anxiety. However, if the dog is seen scanning the kitchen counters and garbage cans for goodies – then we're dealing with an entirely different problem…

The most common and most erroneous misconceptions that owners have is that their dog is being "spiteful", "ungrateful", and/or "angry" at being left alone. They will often say that their dog *"knows that it did something wrong".* This is NOT the case and it is imperative that owners understand that their pet exhibiting panic associated with a distress response specifically related to being separated from social group members. These animals are in panicked distress, not angry. The dog's apparent "knowing it did something wrong" behavior can be explained, however. In cases where there is destruction and/or inappropriate elimination, the dog is often punished by an angry and frustrated owner. The dog is aware of the owner's anger and of the urine, feces, and destruction. The dog DOES NOT associate the punishment with the act of creating the mess, but the dog DOES associate the punishment with the combined presence of the owner and the mess. So, when these conditions are met: Owner + Mess, the dog will act to appease – crouching down with tail between its legs. Owners mistake this behavior for "knowledge" of an inappropriate act, and believe that the dog is "guilty" or "sorry". These misconceptions can hinder treatment and are counterproductive for a healthy human-animal bond. Also, inappropriate punishment may result in fear-motivated and defensive aggression. Not only is videotaping a great diagnostic tool, but it allows the owner to see exactly what the dog is doing. They can see the "panic". It helps to explain to the owner what is going on, and it is useful in monitoring the effect and extent of treatment.

Diagnosis of Separation Anxiety involves the history of one or more of the "distress behaviors" occurring in the owner's absence and/or excessive excitement behavior when the owner returns. There may or may not be evidence of a strong attachment to the owner. Also, if these behaviors occur when the owner is with the dog, then other differentials must be considered. For example, destruction can be an element of play or exploratory behavior. It can occur in the course of territorial displays at windows and doors, and can also occur during phobic episodes related to noises or storms. Excessive vocalization can be in response to provoking stimuli outside, social facilitation with other dogs, part of a territorial display, or part of play behavior. Inappropriate elimination can be indicative of incomplete house training or urine marking. It can also be a sign of a medical problem or cognitive decline. Knowing when the behavior occurs, again using a videotape, can help to rule out these other differentials.

One should take into account the dog's age when considering a diagnosis. It is important to rule out "normal" puppy behavior: destruction, elimination, etc. Conversely, in an older dog one should consider the possibility of cognitive decline [CDS] – especially if it is a recent behavioral change.

Another thing to consider is "when" the behavior occurs. If the dog is okay for Monday, Wednesday, Thursday and Friday departures but "goes berserk" on Tuesdays – what's going on? It may be that Tuesday is trash pick-up day, or the day when the pool people come. If the behavior is even more random, it's advisable for the owner to keep a log of when the dog exhibits the anxious behavior. Did the dog's excessive salivation coincide with a storm? Did the dog's damage to the blinds occur because of a package delivery? Often, it is not until we start looking for a pattern that we find one…

The goal of treatment is to teach the pet how to be calm and relaxed during the owner's absence. It involves changes in pet-owner interactions, changes in leaving and return protocols, decreasing the anxiety associated with owner departure, teaching the pet how to be left alone, environmental changes and management, and sometimes the use of psychotropic medication.

For the dogs who have distress only when crated or enclosed in a small space, treatment can be very simple and straightforward – let the dog out of the crate/small space.

However, for the dogs who have learned that departures and/or being alone is scary there is more homework for owners. First, owners need to address the actions/cues that predict their departure. This can be done in a number of ways: 1) They can get rid of the cues. For example: briefcases can be packed and put into the car the night before; The car can be taken out of the garage hours before departure so that there is no longer the predictive sound of the garage door going up and down. 2) The dog can be habituated to the cues. This is done by the owner repeating the action over and over – but never leaving. For example: Pick up keys and walk around the house. Pick up keys, go into the kitchen and cook dinner. Pick up keys, sit down and read a book. Over time, the dog will no longer react to the sound of the keys – because it no longer has a predictive quality. During this time, for actual departures, the keys would need to be put into a pocket, etc. so that the dog doesn't hear the sound as the owner leaves. 3) Classical conditioning can be used for good! The negative action [putting on certain shoes] can be turned into a positive one by pairing it with a special treat. So, instead of "See dad putting on loafers and panic because he's leaving!" it becomes "See dad putting on loafers and look for a yummy treat!"

Once the cues are no longer predictive of a departure, owners can start leaving for longer and longer periods of time – teaching the dog that it can be alone.

Teaching the Dog to be Left Alone at Home – This involves the implementation of graduated planned departures GPDs, which use short absences to desensitize the dog to the owner leaving and being gone. Prior to this part of the treatment, the dog must have already been habituated to departure cues and desensitized to approaches to the door, etc.

GPDs are like REAL departures with two exceptions: 1) Initially the absences are *very* short, and 2) As the owner departs, he/she leaves a new and consistent "safety cue" or signal for the dog. Classical conditioning is used such that a neutral stimulus is paired with a conditioned stimulus and results in a conditioned response. In this case, the neutral stimulus, NS = owner departure. The conditioned stimulus, CS = "safety cue". And the conditioned response, CR = good behavior, feeling relaxed. The safety cue can be auditory (bell), visual (a towel or rug that is put down just prior to departure), or a combination of auditory, visual, and olfactory – such as spraying a can of potpourri.

Environmental Changes and Management – Suggestions include: increased play and exercise, "Doggie Day Care", gradual conditioning to crate (can be good with some dogs, disastrous with others…), "mixing up" departure cues, masking departure with noise while dog is busy with toy in another room, etc.

Medications used to decrease anxiety and panic can be very helpful in the treatment of separation-related behaviors. Generally, there are two groups of medications to consider: 1) Long-term, daily-administered medications, and 2) The as-needed medications for departures only.

Pharmacological Intervention – Keeping in mind that the goal is for the dog to not experience anxiety, use of a daily "maintenance" medication along with a fast-acting, short-duration medication may be warranted. Clomicalm™ (clomipramine), a tricyclic antidepressant and Reconcile®, an SSRI are both **FDA-approved for use in dogs with separation anxiety**. It provides the long-term maintenance treatment, and will help to

decrease the dog's overall level of anxiety. Clomicalm™ is administered at 1-2mg/kg BID. It is available in 20, 40, and 80mg tablets. Other of the more common medications that positively affect serotonin are fluoxetine [Prozac®] and paroxetine [Paxil®] – which are selective serotonin reuptake inhibitors (SSRIs). All of these medications are given daily and generally take several weeks to reach peak effects. None of these medications should ever been given together as serotonin syndrome could result.

Xanax® (alprazolam) is a fast-acting benzodiazepine which is given 30-60 minutes prior to departure. It is administered at the dose of 0.02 – 0.05mg/kg, increasing the dose, as needed, due to tolerance. It is available in 0.25, 0.5, 1.0, 2.0mg tablets. Valium® (diazepam) is a longer acting benzodiazepine and can be effective for 6-8 hours. It is dosed at 0.5 – 2mg/kg. As with alprazolam, start at a low dose and work up, if necessary. Another benzodiazepine option is Klonopin® (clonazepam) – the longest-acting of the three. The dose for clonazepam is 0.05 – 0.2mg/kg and lasts 8-12 hours. None of the benzodiazepines are approved for use in dogs, so the client must give consent in writing. The benzodiazepine can be given along with Clomicalm.

There is another anxiolytic medication that can be given alone or along with both the maintenance medications and/or the "as needed" benzodiazepines: **trazodone**. For detailed information about the use of trazodone in dogs with Separation Anxiety, please refer to the complete article in *JAVMA* – Vol 233, No. 12, December 15, 2008 – pp. 1902-1907.

The dog should be weaned off of all medications slowly when the time comes to do so.

Pheromone therapy – Adaptil/DAP® (Dog Appeasing Pheromone) – NOW known as ThunderEase – is reported to "Mimic the properties of the natural pheromones of the lactating female". It may help to decrease the dog's overall level of anxiety and comes in a diffuser, collar, spray and wipes.

HUMAN-DIRECTED CANINE AGGRESSION: WHY DOGS BITE

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DIAGNOSIS AND TREATMENT OF AGGRESSIVE BEHAVIOR IN DOGS

Numerous considerations are involved, such as the human-animal bond, public safety, and euthanasia. When treating aggression in dogs, all of the following should be taken into account: the attitude of the owner, the presence of vulnerable individuals in the household, the size of the dog, the type of aggression, the intensity of the aggression, and special logistical issues for preventing bites (such as doors, fences, gates, collars, muzzles). With the treatment of any aggression, it is important to caution owners of the unpredictability of any attempt to treat. **NO TREATMENT IS 100% EFFECTIVE.** Any dog may bite, whether they have done so previously or not. It is important to obtain "Permission to Treat" from the owner, in writing.

AGGRESSION DIRECTED AT HUMANS

Categories include fear, possessive, territorial/protective, maternal, predatory, and pain. "Dominance" is NOT a cause for human-directed aggression in dogs. Remember the "ritual signals"… If the dog signals with its eyes, ears, head, body, tail and the threatening person doesn't go away, what's left? With some dogs: growling, snapping, and biting. If, at that point the person retreats, the behavior has been negatively reinforced and the dog is more likely to perform that behavior in the future.

FEAR AGGRESSION is the most common motivation for aggression directed at people and it is characterized by aggression coupled with signals of fear and submission: avoidance, ears back/down, tail down, retraction of commissure of lip – "grin", looking away, turning away, and licking lips, yawning. One of the most important components of treatment involves the owner learning to recognize the ritual signals that dogs give PRIOR to growling, snapping, and/or biting. If these signals (the "soft conversation") aren't seen or recognized by us humans, dogs can learn that they need to growl, snarl, snap, or bite ("yelling") in order to make the scary person go away. While there are no medications that are FDA-approved for use in dogs for aggression, anxiolytics can be useful to decrease the dog's level of anxiety and reactivity. Any medication used would be recommended only in conjunction with a behavior modification plan tailored to the specific patient.

POSSESSIVE AGGRESSION

The dog defends specific items (food, bones, chewies, toys, etc.), but otherwise does not exhibit aggression or ritual dominance signals. The behavior is often fear-based. Treatment can be as simple as denying the dog access to certain desirable items. Every dog should be taught a "drop" or "leave it" command! In the meantime, offering a more desirable item for the item the dog has tends to work very well. A yummy treat is better than a paper napkin…. Often there is a play/attention-seeking component to the behavior so walking away from the dog usually results in the dog dropping the illicit item and following the owner. It's important to realize that the

owner isn't "giving in" and the dog isn't "winning". What's happening is that every one wins and no one gets hurt – which should be the #1 goal.

TERRITORIAL AGGRESSION

The aggression can be directed at humans, other dogs, other animals, or a combination of targets. The dog can be territorial of the house, the yard, its crate, its sleeping place, a confined place, the car. It may also protect an individual approach distance – a "mobile territory". The #1 rule with a territorial dog is to not give it a territory to defend. A dog that runs the fence should not be let out in the yard alone. Otherwise, the dog learns that this is the behavior that works for him! Every time he barks and runs the fence, the "intruder" goes away. This is very powerful learning. Treatment involves denying the dog the opportunity to practice this type of behavior. We all get good at things we do day after day after day… The dog can be desensitized and counter-conditioned to people, etc. on the other side of the fence so that the dog responds in a different manner.

PROTECTIVE AGGRESSION

An extension of territorial aggression where the **dog perceives that the owner is threatened** when there is no *real* threat – such as with a stranger at door, when the dog is approached when in a car with the owner, when another dog approaches owner, when a person raises its voice to owner, or when a person hugs the owner. The treatment plan is very similar to that for territorial aggression. In many cases, however – if not all – the dog is actually protecting itself, not the human…

MATERNAL AGGRESSION

This is normal behavior that typically wanes as the puppies mature. Make sure prepartum bitch is familiar with whoever will be caring for her and the puppies postpartum to minimize the likelihood of aggression.

PREDATORY AGGRESSION

Canis familiaris is a predator. This type of aggression results in a number of fatalities each year, in addition to many injuries. Common targets include: joggers, bicyclers, and running children. Risk factors include: a loose dog and any history of predatory behavior. Any dog with a history of predatory behavior needs to be under owner control at all times. Medications that increase serotonin may help in these cases – but need to be part of a comprehensive treatment plan that includes behavioral and environmental modifications.

PAIN AGGRESSION

This is something that we are all likely to see commonly in practice. A dog in pain is likely afraid, so that adds to the possibility for aggression. Try to see things from the dog's perspective… If the dog is acutely painful,

implement analgesia therapy as quickly as possible. For chronic conditions [ear infections, eye diseases, skin allergies] that require long-term and/daily administration of medications it is important that the owner try to make the medicating as "good" a thing as possible. For ear medications, have the owner use the "baby bottle" method to warm the medication and perhaps apply it to a cotton ball first – instead of just pouring the cold liquid into the ear. Pair the medicating with a special treat so that the dog doesn't run and hide every time it sees the "bad bottle". Have the owner engage with the dog at other times – so that the human/animal bond stays strong. The bottom line is to address and treat the underlying disease so that it isn't a lingering issue.

DOMINANCE AGGRESSION is a current issue and ***over diagnosed***. In many cases it is presumed to be the cause of aggression when no diagnostic process has been conducted. Dominance motivated aggression is a **problem of relationships between 2 members of the same species.** Therefore, *it is not possible for it to be the cause of aggression to you during an exam in your clinic"*. Treating a fear-motivated aggressive dog with dominance-based techniques could have devastating consequences, so a diagnosis is imperative! This article discusses the topic of "dominance" in dogs: Dominance in domestic dogs – useful construct or bad habit?

John W. S. Bradshaw, Emily J. Blackwell, Rachel A. Casey; *Journal of Veterinary Behavior* (2009) 4, 135-144.

GENERAL TREATMENT FOR CANINE AGGRESSION

Environmental Modification

Avoidance of triggers known to cause the aggression is of paramount importance. Simple examples include:

Not reaching out/over the dog.

Interacting with the dog only when it's up on all 4 feet – so it can easily move away.

Looking at the dog's body language and respecting what the dog is saying.

Not cornering the dog – up on furniture, under furniture, in its bed, etc.

Avoiding all physical and loud verbal punishment.

Using muzzles can be the closest thing to a guarantee that a dog won't bite that an owner can have. The light-weight, good-fitting basket muzzles are best. The dog can still drink and take treats, it just can't bite. It is very important to make the muzzle a positive thing as soon as you introduce it to the dog – make is a "food cone"! Go slowly and continue to associate good things with every use.

Head collars and harnesses can help in the general GENTLE control of any dog. It is especially important to not use choke, prong or shock collars in aggressive dogs [but again, in ANY dog]. Their use can associate discomfort and pain with the very trigger we're trying to make positive.

Behavior Modification

Desensitization and counter-conditioning (DS&CC) can be done to pertinent stimuli – people that the dog is afraid of and aggressive towards. This is a process that's done slowly – often after weeks or months into treatment.

Classical conditioning can be done early on to teach the dog that previous scary person is predictive of something great: treats! It is very important that you/clients don't feel that the dog is being "rewarded" for its aggressive behavior – he/she is not. What is happening is that the dog is learning new associations. Instead of "see person, feel threatened and react", the dog will start to learn that "see person and look for a yummy treat". Remember: learning through classical conditioning has already happened. Our goal is to use this learning technique to teach the dog something new.

Pharmacological Treatment

Remember that in the overwhelming majority of aggressive dogs, the cause for their behavior is anxiety/fear. Therefore, the goal of any medical therapy is to decrease the dog's overall level of anxiety & reactivity – so that it can learn the new things we're teaching. The **selective serotonin reuptake inhibitors** (SSRIs) and **tri-cyclic antidepressants** (TCAs) help to do this by increasing serotonin. They can take 4-8 weeks to reach peak effects and ideally, the dog should be weaned off of these medications over several weeks/months when the time comes to do so. **Buspirone** (an Azapirone) is a good option – especially for dogs that are more fearful than reactive. If the medication is effective, it is generally used for 3-6 months. That said, some dogs need life-long treatment.

Selective Serotonin Reuptake Inhibitors - SSRIs

Inhibition of serotonin reuptake resulting in increased serotonergic neurotransmission by allowing serotonin molecules to act for extended periods of time. In dogs common uses include anxiety and fear issues. Serotonin is involved in modulation of aggression, therefore, medications which increase central serotonergic activity should produce a decrease in affective aggression and decrease the tendency to engage in sudden outbursts. Side-effects of SSRIs include GI signs – decreased appetite, vomiting, diarrhea/constipation, anxiety, irritability, insomnia, anorexia, and aggression. Contraindications include diabetes mellitus and hepatic disease. *Do NOT use with an MAOI or TCA* as it may result in serotonin syndrome. SSRIs have a slow onset of action and result in neurotransmitter/receptor changes. They are metabolized in liver and excreted through kidneys. They have 1-4 week latency to effect and a long t½. Start at the lower dose and work up to avoid side-effects.

Fluoxetine dose:

Dogs 1.0 – 2.0 mg/kg PO q24h

Paroxetine dose:

Dogs 1.0 – 1.5 mg/kg PO q24h

Sertraline dose:

Dogs 0.5 – 4.0 mg/kg PO q24h

Tri-Cyclic Antidepressants (TCAs)

Uses in Dogs: anxiolytic effect, fears, phobias, aggression secondary to anxiety/fear, lick granuloma, compulsive disorder, urine marking.

TCAs are well absorbed from the GI tract, metabolized in the liver, and eliminated through urine & feces. They are highly lipophilic and can cross the placenta and into maternal milk – therefore, do not give to pregnant animals. They have a very bitter taste.

Common TCAs used: Amitriptyline (Elavil®), Clomipramine (Clomicalm™, Anafranil®),

Doxepin (Sinequan®), and Imipramine (Tofranil®).

The therapeutic effects involve increasing norepinephrine levels which affect general arousal, attention, mood reactivity, and stress response modulation. Increasing serotonin regulates mood states, decreases fear & stress responses, affects feeding behavior, and decreases impulsive behavior. The side-effects include α-adrenergic orthostatic hypotension, dizziness, syncope, sedation, vasoconstriction, smooth muscle contraction. The cholinergic side-effects include dry mouth, dental pathology, stomatitis, mydriasis, decreased tear production, impaired visual accommodation - blurred vision, urinary retention, bronchodilation. The histaminic side-effects include anti-pruritis, sedation, anti-ulcer activity, weight gain. The cardiovascular effects include arrhythmias, sinus tachycardia (NE), ↓ conduction time, heart block, myocardial infarction, stroke. GI effects include nausea, vomiting, constipation, paralytic ileus, anorexia, abdominal cramping, diarrhea. Behavioral side effects include anxiety, restlessness, agitation, sleep disorders, sedation, fatigue, headache, ataxia. Other effects include lowered seizure threshold, altered blood glucose levels, and bone marrow suppression.

The TCAs have 2 – 4 week latency. Stabilize for 1 – 2 months to see true effect. When ready to stop, gradual withdrawal is recommended. Certain conditions require long-term treatment. When withdrawing a TCA, decrease the original dose by ½ for 2-4 weeks. If all is okay, decrease dose by ½ for another 2-4 weeks. If all is okay, decrease dose again either by ½ daily or give every other day. If at any time "undesirable" behavior resumes, go back to last controllable dose. The process should take several months.

The goal is to have the pet off the medication or to be on the lowest possible dose that controls the behavior.

Drug Interactions include anticholinergics, sympathomimetics, cardiac toxicity, MAOIs & SSRIs, thyroid supplements, anti-thyroid agents, agranulocytosis, cytochrome P450 competition, antidepressants, antipsychotics, psychostimulants. See http://medicine.iupui.edu/flockhart/table.htm for more information.

Drug Precautions include glaucoma, urinary retention, cardiac disease, thyroid disease, seizure disorder, adrenal tumors, liver disease, and kidney disease.

TCA Toxicity

The TCAs have a narrow therapeutic index. A 10-day supply for pet could be fatal to adult human!! There is **NO ANDIDOTE** so make sure that drug is kept safely away from pet in child-proof cap.

Clomipramine dose:		**Amitriptyline dose:**	
Dogs	1-3 mg/kg PO q12h	Dogs	1-6 mg/kg q12h

Start low and work up to avoid side-effects

Azapirones – Buspirone – a 5-HT_1 partial agonist – can be used alone or as an "augmenting" agent for SSRIs/TCAs. It is not dependent on serotonin levels. It has direct actions on the receptors so it may be able to "kick start" process. Initially, buspirone slows neuronal impulses which may help the neuron to replace its serotonin. Side-effects are uncommon: agitation and GI effects. It is not sedating and there is no potential for human abuse. It has a relatively fast onset (1-3 weeks). There is no need to ramp up the dose or wean off, and there is no physical dependence. It does not lower the seizure threshold. It can be used in combination with SSRIs and TCAs – if so, decrease the dose of the other drugs accordingly. Buspirone should NOT be given with any of the MAOIs.

Buspirone dose:

Dogs	0.5 – 2.0mg/kg PO q 8-24h

HUMAN-DIRECTED FELINE AGGRESSION: WHY CATS BITE & SCRATCH

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Human-Directed Aggression in the Cat

Categories include: play, fear, petting intolerance, redirected, pain and sexual.

Play Aggression is the most common cause of aggression directed at people, especially in young cats. It is usually, but not necessarily directed to moving stimuli and it may be directed only to some members of the household. In play, the cat approaches victim, crouches in wait, stalks, and chases – with tail twitching and a focused stare. The ears are forward, not back. Play aggression is often seen in the cat that was hand-raised as a kitten – it did not learn how to play appropriately. There may be a history of using hands or feet to play with the cat and there may be inadequate opportunity for acceptable play.

Fear Aggression is also a common cause of aggression directed at people. With fear, the cat's ears are back with the body and tail lowered. The cat tends to avoid the person or persons that the aggression is directed at. The aggression occurs when the cat is approached, reached for, or groomed. There may be a history of poor socialization or feral living. However, it can occur in any cat, any breed, in either sex, and at any age – regardless of neuter status.

Petting Intolerance

Petting intolerance can be seen if the owner initiates petting and/or after a certain amount of petting. The cat will turn around and "attack". This occurs in both males and females at any age and the cause is controversial. It *may* be status related. Cats primarily groom each other on the head and neck, so being groomed or petted on other parts of the body may contribute to this problem. The cat usually signals its "displeasure" by twitching its tail and skin. Its ears are usually back and it may emit a low growl. Watching for these cues and stopping the petting before they occur is key.

Redirected Aggression

This occurs during interference in situations which have caused the cat to become aroused such as a cat fight, a household dog being aggressive to the cat, etc. It involves being denied access to a primary target. The resultant aggression is then redirected onto another target.

Pain Aggression

This is something that we are all likely to see commonly in practice. A cat in pain is likely afraid, so that adds to the possibility for aggression. Try to see things from the cat's perspective… If the cat is acutely painful, implement analgesia therapy as quickly as possible. For chronic conditions [ear infections, eye diseases, skin allergies] that require long-term and/daily administration of medications it is important that the owner try to make

the medicating as "good" a thing as possible. For ear medications, have the owner use the "baby bottle" method to warm the medication and perhaps apply it to a cotton ball first – instead of just pouring the cold liquid into the ear. Pair the medicating with a special treat so that the cat doesn't run and hide every time it sees the "bad bottle". Have the owner engage with the cat at other times – so that the human/animal bond stays strong. The bottom line is to address and treat the underlying disease so that it isn't a lingering issue.

Sexual Aggression

The cat mounts the owner's limb, grabs the skin, initiates pelvic thrusting, and growls. This is not common, but it does occur. It is important to redirect the cat onto a more "appropriate" target – such as a feather toy, catnip-filled mouse, etc.

Medication

Aggressive cats: **Fluoxetine** (Prozac®, Reconcile™)

0.5-1.0 mg/kg/day

Paroxetine (Paxil®)

0.5mg/kg **EOD**

Clomipramine (Clomicalm™, Anafranil®)

0.5mg/kg/day

Fearful cats: **Buspirone** (Buspar®)

2.5-7.5**mg/cat** q 12-24h

Increases self confidence and promotes interaction with people

FELINE ELIMINATION: URINATING/DEFECATING OUTSIDE THE LITTER BOX

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Background

Is this behavior really "Inappropriate"? Ancestral cats did not use plastic boxes filled with pelleted clay material to eliminate in. Nor did they eliminate in caves… The behavior we're talking about is normal for cats but objectionable to their human caretakers. It is a conservative estimate that at least 10% of pet cats at some time exhibit an elimination behavior problem. The incidence probability increases with number of cats in the household. Inappropriate elimination is associated with the highest risk of relinquishment of pet cats to an animal shelter.

Elimination vs. Marking

With **ELIMINATION**, the cat stops using the box and uses target areas of "suitable texture" to eliminate (urination ± defecation). There may be signs of aversion to box and/or litter. The posture is usually squatting and there is a large amount of urine involved. With **MARKING**, the cat continues to eliminate in the litter box. The target areas are those with "behavioral significance". The posture is usually standing with the tail up and twitching. The urine involved is a small amount – not a normal voided amount. It's important to note that by the time the owner presents the problem to you, it may be a combination of both inappropriate elimination and marking – the cat deposits large amount of urine on vertical surfaces.

Medical Causes for inappropriate elimination include any disease causing polyuria, dysuria, diarrhea, or constipation; neurological diseases; and any condition causing pain or discomfort while urinating or defecating (such as a declaw, tendonectomy). Any change in litter post-surgery can be the cause. In elderly cats arthritis, any sight or olfactory impairment, cognitive dysfunction and hyperthyroidism should be considered.

Physical Causes need to be addressed. Does the cat need a haircut? Long hair in the perianal/perineal areas and/or in between the toes may change the tactile sensation.

Behavioral History is very important. Who? What? When? Where? Why? How?

Who? In a multicat household there may be more than one culprit. Confining one of the cats *may* determine who the eliminator is, but if there's an underlying social issue, the confinement may not help. For example, the confined cat may eliminate normally because it is no longer being intimidated. Use of fluorescein (PO or SQ) can be used for urination; crayons for defecation. Be sure to rule out other animals in the household, even the dog!!

What? Urine, feces, both? Is there any marking component?

When? How long has the problem been going on? When does it occur? Is the owner away? Is there any known inciting event? It is important to remember that the initial cause may no longer exist. Is the cat ever "good"? - When confined? When the litter box is first cleaned?

Where? It's important to see a floor plan of the house showing the location of food, water, litter boxes, and of the soiled areas. If the "accident" is close to the litter box it tells you that the cat can get to the litter box but doesn't want to go in. This concentrates the effort on finding a bigger and better litter box. If the "accident" is far from the litter box, there may be a reason… Another cat waiting to attack? A scary child? A dog waiting for the "tootsie roll" to drop? This information concentrates the effort on providing at least one additional litter box in a different location and in dealing with the social dynamics of the household.

Why? With elimination, it's because the cat doesn't like the "toilet" provided or prefers another. With marking there is an underlying anxiety component. In cats with Separation Anxiety, inappropriate urination is the #1 symptom (Schwartz, 2002) The owner's bed is a popular spot. It's important to get information from the owner regarding the litter boxes: How many? How old are they? Where are they located? Type of box – is it open or covered? Type of litter - is it scented or unscented? Is a liner used? The hygiene considerations are Important. How often: Are the boxes scooped? Is the litter changed? Is the box washed? And with what?

How? The cat's behavior in the box can be important. Is there digging, covering? Is there a reluctance to get/stay in? Is there vocalization? Does the cat run out when it's finished? Does the cat stand on the side of the box? Does it run into the box when the litter is fresh?

Elimination – Differentials include substrate aversion, substrate preference, litter box aversion, location aversion, and location preference.

With **Substrate/Box Aversion** the symptoms include perching on the edge of the box, minimal or digging/covering, shaking the paws and/or a hurried exit. Causes include substrate change, box/litter type, poor hygiene, and/or a possible history of a painful event associated with current litter and/or box.

With **Substrate Preference** the cat prefers a specific texture such as carpet, wood floor, linoleum. This could be the result of early learning. There is a multitude of substrates available – but studies show that cats prefer a finely textured clay litter. However, there are individual preferences for texture, granularity, and coarseness. The important thing is to provide a substrate that cat "likes". You may need to be creative and try substrates such as potting soil, newspaper, pee pads, diapers, carpet swatches, and towels. In general, make sure that there are plenty of boxes – the # of cats + one more. The box can be open or covered, but make sure that the cat has easy access into and easy egress out of the box without having to experience an unpleasant encounter with another cat or with a "hungry" dog… It is important to keep the litter box clean by scooping it at least once a day. The litter should be completely changed and the box washed with mild soap and water every 1-2 weeks. It's also a good idea to place the litter box in the cat's core area – where he spends most of his time. Ideally, it should be placed in an area that's quiet and well-lit, away from the food and water.

Location Aversion/Preference is not common. It may not be discovered until the litter box is moved to another location for some reason and the cat continues to eliminate in the former location. There may be anxiety component such as Separation Anxiety – the cat eliminates on the bed while the owner is away, or upon return.

Treatment is highly individualized and consists primarily of environmental modification. The goal is to clean the soiled areas and make them aversive (using upside-down plastic carpet runners with the "nubby" side up, aluminum foil, motion detectors, etc.), and to make the "toilet area" desirable. Provide the cat with a "Litter Box Cafeteria" – new LARGE boxes (open, covered), different litter types, in different locations. The particulars vary in each case and are dependent on the presentation. It is important for the owner to keep a log of which box or boxes the cat uses and also what, if any, inappropriate locations are still being targeted. Any next steps are determined by what the cat does. Most cases of inappropriate elimination are treated and resolved with environmental modification alone and medication is not needed.

Below are examples of large plastic storage boxes. The low-sided option will be good for most cats: –

The high-sided option is especially ideal if the cat in question is a "high-urinator". In any case, the bigger the litter box, the better!

Urine Marking/Spraying is normal feline communication. However, the message of the communication is not entirely understood. Spaying/neutering decreases the incidence of marking by 89% (Hart&Barrett, 1973). Denying access to windows may help, as may motion detectors (CatStop, Scarecrow). Playing interactively is recommended. Feliway™ spray or diffuser may also help. It is an "alleged" synthetic analogue of feline facial pheromone used "To calm the cat in an unknown or stressful environment…" Pharmacological treatment is usually warranted and its use is based on: the cause of the problem (anxiety component), the health of the cat, pertinent underlying social interactions, owner compliance (can the owner medicate the cat 1-2x/day?), and expense. It is important to remember that all use of drugs for elimination and/or marking problems is "OFF-LABEL" and that you must obtain the owner's permission to treat in writing. The "Permission to Treat" form also provides the owner with an explanation of what the drug does as well as a list of possible side effects.

Pharmacological treatment options include the serotonin partial agonists, such as buspirone (Buspar®). Avoid use with aggressive cat as it can make them more assertive. However, its use is great in the "victim". Tricyclic antidepressants, such as amitriptyline (Elavil®), clomipramine (Clomicalm™, Anafranil®), may be effect. It is important to realize that these drugs do have side-effects such as sedation and other anticholinergic effects. The **Selective Serotonin Reuptake Inhibitors**, such as fluoxetine (Prozac®, Reconcile™) and paroxetine (Paxil®) have been shown to be effective in marking cats. Side-effects with this drug class include inappetance and sedation. Less used drugs include the anxiolytics, such as the benzodiazepine Diazepam (Valium®) and the synthetic progestins medroxyprogesterone acetate (Depo-Provera®) and megestrol acetate (Ovaban®, Megace®). Hepatotoxicity has been reported in cats given diazepam, and use of the synthetic progestins has been associated with mammary neoplasia and bone marrow suppression. Consider their use only as a last resort, and/or in refractory cases.

Other Alternatives include various cat enclosures where the cat is "safe" but still has more access to the outdoors. Cat fences can keep your cat safe inside the fenced yard and stray cats out. See Boarding the cat at your clinic can also give the client time to deal with the problem – start the cat on medication, etc. The goal is to give the client an alternative to euthanasia.

For more information on this topic, a good and comprehensive resource is the AAFP/ISFM Guidelines for Diagnosing and Solving House Soiling Behavior in Cats – 2014.

INTER-DOG AGGRESSION: WHY DOGS FIGHT

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INTER-DOG AGGRESSION

The more common categories of Inter-Dog Aggression are Status-Related, Fear, Arousal, Possessive, Protective, Territorial, Redirected, and Predatory. Intact males are generally aggressive to other males, intact males generally show more aggression than neutered males, neutered males are generally aggressive to other males, and females are generally aggressive to other females.

NON-HOUSEHOLD AGGRESSION

Dogs that are aggressive to other dogs - that are not part of the household - are more likely to show predatory behavior and are often more difficult for owners to control. There may be a component of territoriality in these cases. This would be the case if the dog in question was aggressive to dogs that walk by the house, but okay with dogs on walks and/or at the dog park. In any case, it may be the result of improper socialization or an aversive event – such as being attacked by another dog when a puppy, etc.

AGGRESSION BETWEEN FAMILIAR DOGS

This refers to dogs in the same household. In the vast majority of cases, the aggression seen is the manifestation of canid hierarchical conflicts and/or underlying anxiety. In many cases the dogs that are fighting are uncertain of their role in the hierarchy. This type of aggression is most commonly limited to one pair of dogs – even if other dogs are present. It is typically more common between same-sex dogs.

In general, intra-household aggression more severe than aggression between non-housemates and female-female aggression is typically the most severe. When looking at the two dogs that are fighting, physical features do not necessarily determine dominance. But once there is fighting, the larger and stronger dog will typically "win"…

Common household aggression TRIGGERS include times of excitement such as feeding time, walking, and owner arrival. Other triggers include control over resources, physical proximity, confining areas such as doorways, hallways, etc., and/or the owner's very presence – where the dogs may compete for attention.

Generally, the owner tends to support the victim (subordinate) and punish the aggressor (dominant). This can increase the aggression if the victim perceives a "coalition" between itself and the owner – resulting in it reacting more confidently. In many cases, the *owner's presence and behavior exacerbates the instability between the*

two dogs and fights may occur when the owner is present. The behavior may persist in the owner's absence – but most cases present for the dogs fighting *only* when the owner is around.

COMMON TRIGGERS FOR FIGHTS INCLUDE:

Owner interferes when the dogs interact in an attempt to change an established hierarchy

Owner inadvertently or deliberately encourages a subordinate dog to try to establish dominance over the higher-ranking dog

It is important that the dogs be allowed to communicate using their ritual signals – the "soft" conversation – using their eyes, ears, head, body, and tail. A common ritual signal is mounting and it is very often interrupted and/or punished by the owner. If the signaling is interrupted or not allowed in the first place, the "soft" conversation is likely to escalate – to "yelling" – fights. Usually, there isn't a problem between the two dogs as to what the hierarchy is. They understand what the relationship is and signal each other accordingly and appropriately. But if the "normal conversation" is interrupted and/or punished, what's left? Growling. Snapping. Biting.

The onset of household aggression is typically when the younger dog reaches social maturity – at the age of 18 – 24 months old (it can be earlier for females). It can occur is the hierarchy has not been clearly established and is most severe in evenly matched dogs. It can occur when the "dominant" dog is aging or ill. This dog may have increased irritability which can result in decreased tolerance to its housemate. There can also be a "breakdown" in communication as one of the dogs ages [due to loss of vision and/or hearing] and/or experiences cognitive decline. There is an expectation from the other [non-impaired] dog that is no longer being met. This can cause anxiety and resultant aggression towards the dog that's impaired.

The **TREATMENT** of household inter-dog aggression is going to vary with the individual case. But in general, it is a good idea to separate the dogs when they are not supervised. This isn't done so much so that the dogs won't fight when the owner isn't around, but to avoid the dogs coming together in an aroused situation – when the owner comes home. If the dogs are separated, the owner will have more control in bringing them together. Head collars or good-fitting harnesses are recommended – for both dogs – so that the owner can have the dogs together safely, with more control. Basket muzzles may be needed for one of both of the dogs, depending on the degree of aggression. If the dogs involved are intact, spaying or neutering is recommended.

It is important to determine and stabilize the pack hierarchy – the "relationship". Look for general trends. Most relationships are fluid and flexible. The dog that is acting "appropriate" in a given situation is the one that should be rewarded. If there is a clear dominant/subordinate relationship that the dogs agree on, then it should be recognized and supported. The dominant dog should be fed first, given attention first, given access to preferred locations, let inside & outside first, etc. – especially in the beginning of treatment. As the relationship becomes more "normal" and fluid this strict order may be relaxed. The key is to watch the anxiety level of each of the dogs and adjust your behavior accordingly.

Along the same lines, it's important to allow and reward the dogs' ritualized signaling. For the dominant dog these include: eye stare, ears up, tail up, lips up – exposing canine teeth, and mounting. For the submissive

dog these include looking away, ears back, tail down, the "submissive grin" (seeing all of the teeth), and standing to be mounted. The submissive dog may also lick the other dog's muzzle.

Clients often attempt to impose "democracy" to the household – which doesn't tend to work. It is important that the clients understand how canine societies are structured and how dogs communicate. Client education is key! There is a common misconception that the dog that has seniority should dominate the new dog. This just isn't always the case. A dog's social rank is determined by its ability to defend priority access to resources and not by seniority *per se.* An older or sick dog may not be capable of defending these privileges and/or it may no longer want to.

In many situations there are mixed signals. For example:

Dog A is dominant to Dog B

Dog A knows it and Dog B knows it

They signal each other appropriately

Owner reinforces Dog B as dominant

Dog B *knows* that is submissive to Dog A

Both dogs are getting reverse signals from the "BIG Alpha" – which can be a great source of confusion and anxiety…

In general, the aggression typically occurs in situations that involve competition over valuable resources and aims at establishing a dominance-deference relationship.

There may be times when the owner will need to "finish the conversation" for the dogs. For example:

Dog A looks at Dog B

Dog B looks away

Dog A continues to look/stare and starts to growl

Dog A is being inappropriate. Both dogs need to be given a "way out". So at that point, the owner can call one of the dogs over – Dog A – and reward him/her for coming. An alternative would be to shake a bag or can of treats – diffusing the situation so that both dogs can get away from the tense situation.

Another example:

Dog A looks at Dog B

Dog B isn't paying attention to Dog A [this is particularly true if Dog B is a puppy or a dog with physical impairments and/or cognitive decline]

Dog A continues to look/stare and starts to growl

Again, Dog A is being "inappropriate" – but so is Dog B, through no fault of its own. The owner can diffuse the situation by calling the dog most likely to come – again, giving both of the dogs a way out of the tense situation.

MEDICATION may be necessary – especially if one or both dogs are particularly anxious. Anxiety can lead to reactivity and reactivity can result in aggression. Any of the selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, paroxetine or sertraline, or the tricyclic antidepressants (TCAs) such as clomipramine can be used effectively. The goal here is to decrease anxiety and reactivity so that the dogs can start to "listen" again to what the other is actually saying.

When and how should the owner interfere?

Excessive dominance displays – especially if a true fight is likely to occur

Aggressive displays that do not cease when subordinate dog defers

If the subordinate dog does not signal the dominant dog appropriately

The important thing is to diffuse the situation without increasing the arousal. Call whichever dog is more likely to come to you – ideally, the dominant dog. This provides for preferential attention and reinforces owner control.

The problem may not be resolvable with two evenly matched dogs that are strongly motivated to be "alpha". They are likely to fight until one succeeds in injuring the other. In cases like this the owner needs to withdraw privileges from *both* dogs and interrupt dominance displays by *both* dogs. The owner can randomize the order of feeding and handling, and desensitize and counter-condition the dogs to each other's proximity. It is always important to continue to look for ritualized signals and reward them.

The prognosis is poorer is the initiator is younger and/or more able-bodied than the target, if a person has been bitten, and/or is the aggression is truly "unpredictable".

BASIC PRINCIPLES OF BEHAVIOR: HOW DOGS AND CATS LEARN

WHY IS IT SO IMPORTANT?

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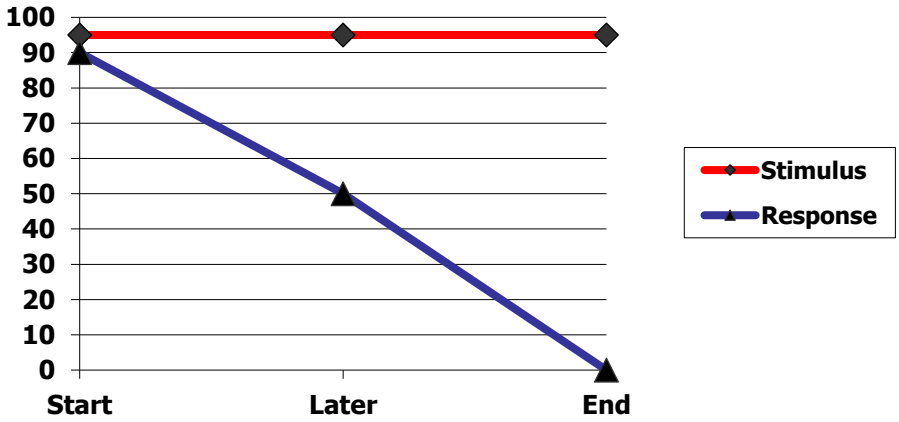
LEARNING is an enduring change in the mechanisms of behavior involving specific stimuli and/or responses that results from prior experience with similar stimuli and responses.

Habituation

A decrease in response as a consequence of repeated exposure to a stimulus – such as the startle reaction to noise. It is typically highly specific to the stimulus that is repeatedly presented such as traffic, sirens, thunder.



The initial response is *innate*, not learned (e.g. startle in response to a loud noise). It is the decrease in the response that is learned.

Habituation ≠ Extinction

In extinction, it is a *learned* response that is lost.

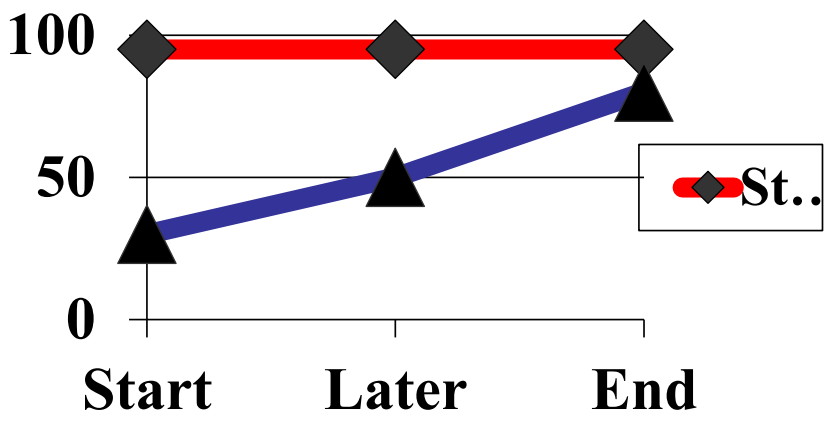
With habituation, the organism ceases to respond to a stimulus, even though it remains fully capable of sensing the stimulus and of making the muscle movements required for the response. The response fails to occur because changes in the CNS block the relay of sensory neural impulses to the motor neurons.

Dishabituation

The habituated response is restored by exposure to a strong extraneous stimulus paired with the stimulus to which the animal has habituated. There is a recovery in the response to a previously habituated stimulus.

Sensitization

An increase in responsiveness produced by repeated stimulation. Sensitization processes generally have temporary effects. The duration is determined by the intensity of the sensitizing stimulus. More intense stimuli produce greater increases in responsiveness, and with more intense stimuli the sensitization effects persist longer.



Habituation/Sensitization

These two effects reflect how an organism ends up sorting out what stimuli to ignore and what stimuli to respond to.

Example: Dog with storm phobia

Dog ignores wind and rain (habituation)

Becomes more reactive to thunder over time (sensitization)

Both habituation and sensitization involve learning about *just one stimulus.*

Classical Conditioning

Also called Pavlovian Conditioning

The simplest mechanism whereby an organism learns about ***relationships between stimuli*** and comes to alter its behavior accordingly – it learns which stimuli tend to go with which environmental events. These systematic studies began with the work of Russian physiologist Ivan P. Pavlov.

<u>The Components of Classical Conditioning</u>

Unconditioned Stimulus (**US**)

A stimulus that elicits a particular response without the necessity of prior training

Unconditioned Response (**UR**)

A response that occurs to a stimulus without the necessity of prior training

Neutral Stimulus (**NS**) and Conditioned Stimulus (**CS**)

A stimulus that does not elicit a particular response initially (NS), but comes to do so as a result of becoming associated with a US (CS)

Conditioned Response (**CR**)

The response that comes to be made to the CS as a result of classical conditioning

Unconditioned Stimulus (US)

→→→ Unconditioned Response (UR)

Neutral Stimulus (NS) + US

→→→ Unconditioned Response (UR)

NS becomes a Conditioned Stimulus (CS)

→→→ Conditioned Response (CR)

Classic Example:

US (food) →→→ UR (salivation)

NS + US →→→ UR

Neutral Stimulus becomes a Conditioned Stimulus

CS →→→ CR

The Response is called a Conditioned Response when it is elicited by the Conditioned Stimulus

Not All Stimuli Are Equal

The number of pairings needed between a CS and a NS depends on:

Intensity of the stimulus

Example: Dog with storm phobia

No previous history of fear of storms

Dog experiences bad storm where lightning strikes nearby and causes tree to fall on dog house

Severe subsequent fear of storms

One pairing was all it took

Relevance of the Neutral Stimulus

How "neutral" is the stimulus?

How well does it pick up the animal's sensual modality?

Example: Dogs and cats have better olfaction than humans do

Need to determine what the triggers are: Visual? Auditory? Olfactory?

Classical Conditioning Example

Fear in a dog

US = being yelled at

UR = fear

NS = sight of owner and/or sound of owner's voice

Various stimuli associated with the owner (NS) become *Conditioned Stimuli* and *come to elicit the Conditioned Response* of fear

Stimulus Discrimination

Only specific stimuli elicit the response – such as:

small women with blond hair

tall men with dark hair and beards

particular person wearing particular clothing

small, white, fluffy dogs

Example: Fearful dog with an unknown history, found as stray by couple that hunted. The dog's subsequent radiographs showed that he had buckshot throughout. The dog typically stayed away of gun case in the house and he was afraid of camouflage clothing. This dog had a **continuum of fear**. The worst: large, tall, bearded strangers wearing camouflage. Next: tall, bearded strangers not in camouflage or some other person wearing camouflage. Next: men in general.

Stimulus Generalization

The response is elicited by a diverse, but related, group of stimuli – such as:

all women

all men

all people

all dogs

Extinction

If the *animal is repeatedly exposed to the CS without further pairing with the US*, then the animal's response to the CS will eventually cease and extinction has occurred.

Example:

Palatable food is paired with bell

Dog salivates after certain # of pairings when there is just the sound of the bell

Stop pairing food and bell

After certain amount of time, dog no longer salivates when it hears the bell

So… **keep the rewards coming!** Otherwise the animal stops the behavior.

Extinction vs. Habituation

Extinction

Loss of a learned response

Habituation

Loss of an innate response

Operant Conditioning

Also called Instrumental Conditioning - Behavior is affected by its consequences. Theory developed by B.F. Skinner – and his "Skinner Boxes".

Instrumental Behavior – is behavior that occurs because it was previously instrumental in producing certain consequences - **"Goal-Directed" behavior**

Operant Conditioning Terms

"Reinforcement" = The probability that the behavior will recur is ***INCREASED***

"Punishment" = The probability that the behavior will recur is ***DECREASED***

"Positive" = The Controlling Stimulus is present or occurs as a consequence of the response occurring. The response produces the stimulus - Appetitive *or* Aversive.

"Negative" = The Controlling Stimulus is absent or is removed as a consequence of the response occurring. The response eliminates or prevents the occurrence of the stimulus - Appetitive *or* Aversive.

4 Possible Combinations:

Positive Reinforcement

Negative Reinforcement

Positive Punishment

Negative Punishment

1. Positive Reinforcement = The probability that the behavior will recur ***increases*** as a consequence of the Controlling Stimulus being ***present*** or ***occurring*** immediately subsequent to the behavior

   If you do X and good things happen, keep doing X

   Example:

   Client with indoor/outdoor cats. All the cat has to do is scratch at the back door – inside or outside – and a human will come and open the door. "If I scratch at the door, good things happen, so I'll keep scratching at the door"

   Say "sit" (Eliciting Stimulus) while holding a treat over a dog's head. If the dog sits (Response), give it the treat (Controlling Stimulus). If it does not sit, do not give the treat

2. Negative Reinforcement = The probability that the behavior will recur ***increases*** as a consequence of the Controlling Stimulus being ***absent*** or ***removed*** if the behavior occurs

   If you do X and bad things go away or stay away, keep doing X

   Example: Dog aggressive to children. Child is causing the dog pain. The dog growls and the child goes away. The *growling is negatively reinforced*

   Example: Cat aggressive to children - same as with dogs. Child causes the cat pain. The cat hisses, growls, or bites and the child goes away. *This aggressive behavior is negatively reinforced*

3. Positive Punishment = The probability that the behavior will recur ***decreases*** as a consequence of the Controlling Stimulus ***occurring*** immediately subsequent to the behavior (Usually referred to as "Punishment")

   If you do X and bad things happen, stop doing X

   Example: Bark Collar "If I bark, I get a gentle spray of nasty smelling citronella in my face, so I'm not going to bark"

For punishment to be effective, ***three conditions must be met***:

The punishment must be immediate

The punishment must be consistent

The punishment must be appropriate for the individual animal

Punishment – Immediate - While the animal is exhibiting the behavior – just *as dog is defecating indoors* - Within 1 second of exhibiting the behavior

Punishment – Consistent - Needs to happen every time the behavior occurs. If punishment occurs only under some circumstances, animals often discriminate the circumstances in which the aversive stimulus does not occur.

Punishment – Appropriate - The punisher should be strong enough to interrupt the behavior, but not excessive as to cause fear. "Remote" punishers tend to work best. It is important to remember individual differences. For some dogs, a simple "no" is enough. For other dogs, a loud "no" with an additional gentle holding on of the scruff is needed. The same thing goes for cats. For some cats just the presence of a water bottle is enough to deter them. For others, the water bottle is just another game.

If the 3 necessary conditions are not met, use of "punishment" is unlikely to be successful.

Start with the strongest punishment that you are willing to use.

When punishment works, the bad behavior stops!

Use of the aversive stimuli typical of punishment introduces the risk of causing fear-related problems.

Don't do what doesn't work!

Punishment – Effective Use

Human-directed play aggression in cats

Housetraining in dogs

Punishment – Ineffective Use

Dog getting into the garbage at night or during the day when no one is around. The "punishment" is often administered several hours later. Owners think the dog "knows it's been bad"

Why?…. What is ***really*** going on?…

Classical Conditioning

The dog gets yelled at and/or hit →→ Fear

The frowning owner + garbage on the floor change from being a NS to being a CS eliciting the fear response

Dog lowers ears and tail and runs away – these are appeasement behaviors. The owner thinks dog "knows it did wrong".

Dogs only know what they've been taught! What we think we're teaching and what your pet is learning can be two entirely different things!

4. Negative Punishment = The probability that the behavior will recur ***decreases*** as the consequence of the Controlling Stimulus being ***absent*** or ***removed*** if the behavior occurs (Usually referred to as "Time Out")

   If you do X and a good thing doesn't happen or stops happening, don't do X

   "If you poke your sister again, you won't get any dessert"

   Not commonly used in veterinary behavior

   Social isolation (time out) is effective in certain cases

Operant Conditioning - Common Errors

Punishment ≠ Negative

Punishment = behavior decreases

Negative = CS* absent or removed

Confusion of terms “negative” and “aversive”

Operant Conditioning - Schedules of Reinforcement

A program that determines how and when the occurrence of a response will be followed by a reinforcer. The delivery of a reinforcer may depend on: the occurrence of a certain # of responses, the passage of time, the presence of certain stimuli, and/or the occurrence of other responses.

Continuous

The required number of responses is “1”

Every occurrence of the instrumental response results in the delivery of the reward

Example: Dog gets a treat **every time** he sits on command

Continuous Reinforcement is the *most effective method when an animal is first learning a new behavior*.

Variable Ratio

A different number of responses is required for the delivery of each reward.

Example: Trainer requires the dog to sit 4 times before he gives the first treat, 2 times for the second treat, 1 time for the third treat, and so on.

If an animal is on a steadily increasing variable ratio schedule, the *behavior tends to become very persistent*

Variable Ratio - Uses:

any behavior we wish to become persistent

sit, stay, heel

Variable Ratio - Problems:

Nuisance behaviors such as barking and jumping up

These behaviors are reinforced by giving attention some of the time

Reinforcers and Motivation

The animal’s motivation affects how fast and how well learning occurs. A hungry animal responds better to food rewards than a satiated animal. Animals perform better for highly palatable food treats than for low palatability food treats:

roast beef > hard dog treat > cheerio

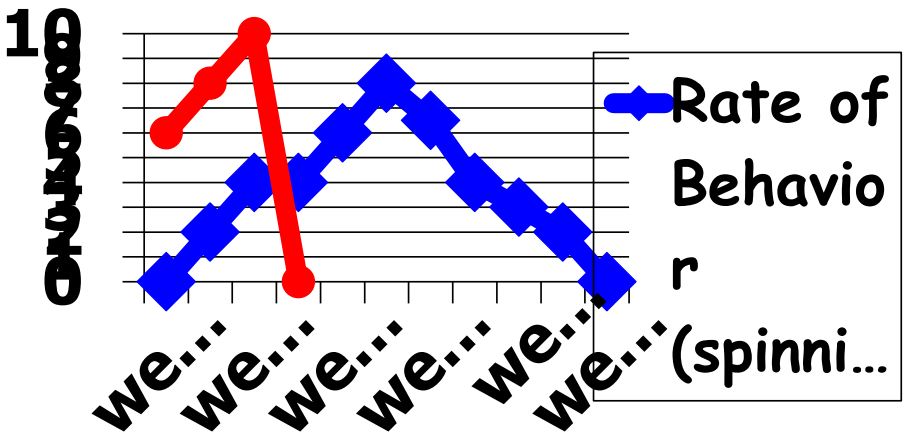
Secondary Reinforcers and Punishers

Due to Classical Conditioning, a Neutral Stimulus can come to have a similar rewarding or punishing value as an Unconditioned Stimulus. A clicker can be associated with food treats; the sound of keys being picked up can be associated with being left alone.

In General… because of Classical Conditioning:

Animals trained using appetitive techniques tend to have relaxed and friendly attitudes – ears up, focused, "happy". Conversely, animals trained using aversive stimuli tend to have fearful or anxious attitudes – head down, tail down

Extinction of a Learned – Motivating – Behavior



With EXTINCTION there is typically what's called the "extinction burst" – where **the behavior gets worse** (increases – such as between week 4 and week 7 in the above graph) **before it gets better**. This occurs when you only ignore the behavior – not giving the individual something else to do. With "response substitution" this phenomenon is less likely to occur.

Learned Helplessness

Interference with the learning of new instrumental responses as a result of exposure to inescapable and unavoidable aversive stimulation

Experiment:

Normal, naïve dogs, are put into a situation where shock is signaled. The dog learns to escape the shock at first, then avoids the shock. He learns that the signal predicts the shock.

Dogs that previously have been exposed to unavoidable shock act in a quite different manner. They fail to learn to avoid and they fail to learn to escape. They simply sit and take the shock. The dog has learned that there is no consequence to its behavior. There is no benefit to trying to get away. "Life is horrible…" The dog shuts down.

Learned Helplessness - Clinical Relevance

Improper use of punishment

Continuous use of shock

Dominance training

The α-roll

Flooding

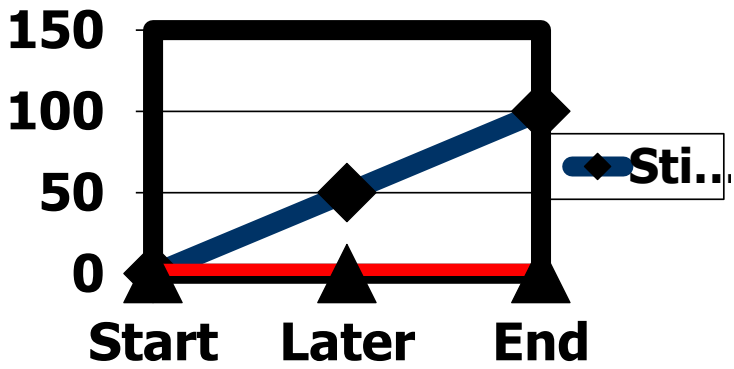
Animals with a history of chronic, inescapable abuse are typically withdrawn and present with abnormal behavior. They may not play and sometimes they don't seem to respond to rewards. Getting them "back" will take time…

Flooding

Term used for the deliberate exposure of the animal to a stimulus until the response extinguishes or the animal habituates. Once a flooding session is initiated, exposure to the stimulus must continue until the response ceases – otherwise the behavior may be reinforced. Animals with strong fears may injure themselves, other animals or people in the vicinity, or damage their surroundings.

Desensitization

Expose animal to low-level stimulus. The stimulus elicits a low-level response that can be easily interrupted/diverted. ***Gradually*** increase the intensity of the stimulus - ideally without eliciting the response.



Counter-Conditioning

Response Substitution - A response is elicited that is ***behaviorally*** and ***physiologically*** incompatible with another response. Fido cannot be anxious and relaxed at the same time. Reward Fido for relaxation. Counter-Conditioning reverses the animal's previous response to a stimulus.

For example: an animal may be conditioned to be relaxed in the presence of a stimulus that initially elicited withdrawal reactions – such as approaches by strangers

Desensitization and Counter-Conditioning Applications:

Fear of people

Fear of noises

Fear of thunder storms

Aggression to people or other animals

Fear of being alone

Barking

Eric Garcia

Aproveche Instagram para impulsar su práctica veterinaria

Eric Garcia

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"Look at Instagram as your opportunity to share exclusive behind the scenes access to your veterinary practice." – *Eric D. Garcia*

The social media sites with the highest traffic in 2017 aren't just getting millions of views; they're receiving *billions of them.* That's right, as of May 2017, Facebook is averaging *almost two billion visitors per month.* The exact figure, according to online source Statista, is 1.94 billion.

When I first started talking about Facebook and using their platform as a focal point in my presentations, they had just broken 500 million users back in 2010-2011. Since then, they've catapulted to the top of the index when it comes to heavy-hitting social networking platforms with the largest global impact, achieving an almost unfathomably large user base in the process.

YouTube comes in second with about one billion monthly visitors, but guess which social media site comes in third? If you guessed, Instagram, you'd be right; coming in on the heels of YouTube with 700 million monthly users.

Instagram however, which centers around posting, liking and commenting on pictures and short video, has a key difference from other social platforms like Facebook and YouTube that I often discuss.

Instagram is a platform that may already extensively showcase your veterinary practice… *even if you've never set up an account.*

In fact, there is a very good chance that your practice is already on Instagram (also known as *Insta* for short) because of geolocation tagging that exists as a major function of the platform. This *location* feature within Instagram, allows people to share and post their location, wherever they are. Check it out for yourself, visit Instagram.com or download the Instagram app. To easily look up your location page, simply type in the name of your practice. You'll see a listing come up, like this one:

This listing at the top with the little pin and your address is the location that Instagram has already created for you.

Very few practices know that this location listing exists. It's like both Google and Yelp, where the listing was created *for you* by using a database of businesses. The biggest differentiating factor is that, with Instagram location tagging, you can't leave reviews and you can't claim your listing (at this time).

People are social by nature, so when pet owners are sitting in the waiting room, right after the veterinarian leaves the exam room, they might just take out their phone and start posting!

In fact, they probably are.

This is how the conversations about your practice on Instagram starts in the first place. After all, *who can resist a selfie with their beloved pet?*

What this ultimately means for you is that if you haven't started using Instagram to interact and engage with pet owners who are already posting about your veterinary practice, you're missing a major opportunity!

Your veterinary practice can immediately tap into its existing user base by liking and commenting on photos, and by posting your own. This can serve as the perfect opportunity to offer pet care tips, send a quick thank you, offer condolences for a pet whose final moments are posted to Instagram by the pet owner (it happens often) or anything else that truly lets the client know that they are appreciated. If you haven't set up your account yet, it's certainly not too late. Currently, there are close to 6 million posts that use the hashtag #dogsofinsta and almost **55 million** using the hashtag #catsofinsta (yes, let the rivalry continue).

A hashtag, by the way, is just a way to tag your photos. Hashtags categorize or describe the picture or details at hand. So, when I post a picture with Elvis and Penny, tagging #dogsofinsta is an easy way to reach more viewers and gain more likes.

To get started, you'll need a practice owned smartphone (or iPod Touch). Then you'll need to download the Instagram app, even though you can browse photos through the Instagram website, you'll need to have the app downloaded and logged in to post photos or short videos to your own account.

Now, without further ado (and if you promise not to use too many hashtags), let's start using Instagram to interact with pet owners in fun and meaningful ways.

Get started by taking these simple steps:

(1) Download the latest version of the app to avoid bugs and ensure you have the best version possible at your disposal. Make sure you use a practice owned device, and pick a user handle. Your handle is your social media short name and should contain the keywords of your veterinary practice name. My handle is @*EricGarciaFL* and I use it consistently across social media channels to make sure veterinary practices and pet owners can find me easily.

(2) Switch your account to a business profile by following these simple steps (https://www.facebook.com/business/help/502981923235522). This is important because it will unlock a full range of advertising and analytics options that are otherwise unavailable. Don't forget to include a bio, your website, your practice phone number and a nice, high-resolution logo.

(3) Now, download the free Perch App (perchapp.com), which will automatically notify you via email and/or push notification when a pet owner or client tags your location on Instagram. Since you can't control whether your veterinary practice is listed or what people post with *their* location tag, the Perch App keeps you a step ahead by notifying you instantly when a post is made.

(4) Finally, it's time to start posting! Look at Instagram as your opportunity to share exclusive behind the scenes access to your veterinary practice. Post compelling pictures of your hard-working team and the occasional selfie to let pet owners know who's behind the camera (as if I needed to convince you to take another selfie!) As long as they sign a photo-release form, you can even post pictures of pet owners and their pets. In general, have fun with it and don't look too surprised when you see new likes flooding in almost instantly after posting! One of the most fun parts of Instagram is the immediate feedback you'll get after a great post.

(5) Finishing touches on a great post can include hashtags that appropriately describe your local area, theme or mood. For example, #Happy #TampaBay #DogsofInsta (with emojis optional) might be the perfect addition to a post with you and your dog's outside on a sunny day.

By creating an Instagram account, converting to a business profile and using Instagram just like pet owners do, you'll tap into something very special. People share photos of their pets and themselves not because they must, but because of the incredible joy that these pets bring and the fun of it all!

The more you tap into this feeling and share this bond with those coming to your practice, tagging pictures and commenting along the way, the more you'll see that your pet family is even bigger than you first thought it was.

Now that's something worth posting about.

Follow me on Instagram at @EricGarciaFL!

Cómo involucrar a los dueños de gatos en el cuidado de por vida

Eric Garcia

Simply Done Tech Solutions, LLC

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“Time spent with cats is never wasted.” - Sigmund Freud

The unique relationships we form with animals is something of a spiritual experience. The way that they can sense our emotions, or that we can read their moods just by looking at their eyes, all hints at a connection that’s extraordinary.

But despite our love of animals and pets, some are represented constantly across websites, social media channels and presentations, while others are left behind. I’ve found that practices rarely post about cats, both within social media and across their marketing efforts as a whole.

When I’m consulting with veterinary practices across the world, I’m combing through everything I see to get a holistic impression. This includes everything from the learning about marketing materials in their waiting room, to their website, Facebook Page, brochures, etc. I’ve noticed that kittens are sometimes used in picturesque settings (yes, that picture of a basket of kittens in a sun-drenched field is oh so realistic), but cats as a whole are mostly neglected.

While this presents an issue, it also presents an opportunity.

To take a more comprehensive look at this, let’s begin with some impactful data directly from the American Association of Feline Practitioners (AAFP). The AAFP has found that 50% of cat owners report they didn’t seek to own a cat, but instead their cats “found them.” 69% of those responding to the same survey state they paid nothing for their cats.

This means that the majority of cat owners received little to no instruction on proper veterinary care for their cats, so while we’ve bonded with our cats early and often, we may lack professional insights into how to best care for these lovely animals.

I believe that many who own a cat can relate. One day, you’re leaving some extra cat food outside for an occasional visit, and soon enough, you’ve bonded and you’re the proud parent of a cat!

With this being said, where do first time cat owners go to learn more about the best way to care for their new feline friend? Well, of course they turn right to the Internet. While this used to make me cringe a bit (considering the amount of unvetted blogs and forums circulating about), I'm happy to report that an increasing number of online searches tend to endorse quality information that the majority of veterinarians would recommend.

This is thrilling for somebody like me, who loves when proud pet owners have access to the information they need! This being said, the Internet (I won't call out any specific social media network by name…except for YouTube) is still absolutely ripe with horrible advice on cat care.

As veterinary professionals, it's up to us to represent all sorts of pets and to provide equal representation. This is also effective for marketing to more people, and for showcasing our commitment to all species of animals we care for. I challenge you to become more pro-active about sharing the stories of cats in your practice to ensure they are properly represented.

You can start off small, by sharing just a few pictures or an anecdote. During my routine social media audits (a process that helps me quickly hone-in on the strengths and weaknesses of existing social media strategy) I actually look to see the last time your practice shared content about a cat. Content that I routinely audit looks a lot like this:

- Dog Post (Monday)
- Dog Post (Tuesday)
- Dog Post (Wednesday)
- Dog Post (Thursday)
- Dog Post (Friday)
- Cat Post (Saturday)
- Dog Post (Sunday)

You get the picture. Not only does this content become redundant, but it underrepresents two specific groups: cats and consequently, cat owners. I'd like to see certain themes that show more interest in cats, like "Featured Feline Friday," which gives practices the chance to share something about cats that will resonate with cat owners directly on an on-going basis.

Looking again at some crucial data from the AAFP, their statistics show that 51% of clients believe cats are "low-maintenance" while a whopping 70% do not believe that cats regularly hide symptoms. 81%, yes 81% of cat owners in this poll believe that their cats are in excellent health and are self-sufficient.

Now we're beginning to see that the underrepresentation also creates an environment where misinformation can too easily spread and become the "norm" of what's largely believed. I'm confident when I say that it's rare to find a veterinarian who believes that cats don't hide symptoms! A lot of this misinformation comes from pet owners going to the wrong sources for info, like a pet store employee or their local Facebook group instead of a tried-and-true veterinary professional.

The AAFP also notes that "veterinarians estimate that 50% of cat owners consider a trip to the veterinarian to be stressful, versus 20% of dogs." ***Now we've got a scenario where cat owners don't believe their cats hide illnesses and also believe their cat hates going to the vet.***

Do we see a troubling trend emerging here?

Yes! So how do we overcome it?

What's the best way to inform pet owners that cats do indeed hide illness and that yes, our veterinary practice can provide care that truly accommodates the needs of their feline friend?

We need to tell the stories of the cats we see in our practices! Not just telling but showing too. These narratives are crucial to connecting to the hearts and minds of pet owners!

Read on to learn how to tell these stories and how to adhere to industry-standard best practices along the way:

Remember first and foremost, permission is required from a cat's owner and/or caregiver before sharing any of their information. This consent must be written.

(1) Find a cat you've seen recently at your practice.

(2) Secure written permission to share a story about the cat.

(3) Briefly, gather information including the following:

a.) What illness was the cat brought in for?

b.) How did you help to discover the cat was ill?

c.) How did you help to treat this cat from a veterinary perspective?

d.) How is this cat doing today?

When you combine these elements, you're ready to begin telling the story itself, which may look something like this:

Example:

Gazpacho, a 4-year-old calico, came into All Animal Clinic, a Cat Friendly Practice®, after her caregiver, Emily, noticed that she had not been eating a lot lately, and had started hissing and avoiding being petted. Dr. Gray carefully examined Gazpacho using feline-friendly handling and discovered that she had severe dental issues. So, we worked with Emily to take care of Gazpacho's painful mouth. While we had to do a few tooth extractions, we were also able to clean and do preventive treatments. After a short recovery time, we are happy to report that Gazpacho is feeling much better. She is eating well again and since she is no longer in pain, she is no longer hissing or avoiding being petted. Keep your cat's mouth healthy and pain free with regular check-ups at All Animal Clinic. Our staff use gentle, feline-friendly handling to help keep your cat calm.

Why is this story so impactful? Again, let's look at the data! According to the AAFP, 56% of clients report that they would bring their cat to the veterinarian more frequently if they knew this could prevent problems!

This data shows us that increased information, including storytelling and specific examples, would likely lead to increased engagement from cat owners.

To take things even a step further, I recommend that practices consider becoming a Cat Friendly Certified Practice, which really takes the commitment to delivering remarkable feline care to the next level. While I'm not a veterinarian, I know there's more we can be doing to create a better experience for cats.

I also think it's equally important (whether you decide to become certified or not) to proactively share the things your practice does to make visits for cats easier.

This could mean using pheromone diffusers or sprays to create comfort for a cat while explaining how this works and why it's important. Then and only then can you show me the cat cuddled up and content inside a blanket!

The same goes for sprinkling cat nip on a blanket in the exam room. Explain to me that cats prefer a blanket over a cold, sterile table and that the cat nip is just the icing on the cake to enhance the experience further. Do you use feline-friendly handing techniques or have a cat friendly waiting area? Great, tell me more and show me too with pictures or even video!

Without this type of content being shared regularly both via social media and on your veterinary practice's website, getting cats to come back to your practice is a lost cause.

But if you're willing to engage in thoughtful ways and go the extra mile to care for these beloved felines, well, they'll be beating a path to your door in no time at all.

Share your story, and the rest will follow.

TELL YOUR STORY

People are often under the impression that social media is only for peer-to-peer interactions. This, however, couldn't be further from the truth. Facebook is a platform that's become as universal as the water cooler itself. Successful veterinary practices around the *world leverage Facebook as a place to tell their unique story.* Your veterinary practice has a story and details that make it entirely unique: the year it was founded; your founder (or two, or more); your **Cat Friendly Practice®** designation; and your practice style and perspective.

Use social media to tell your story! It is a perfect platform where you can capture and captivate your audience. Tell your followers about success stories at your practice such as:

- How and why you chose to become a **Cat Friendly Practice®?**
- How being a **Cat Friendly Practice®** has improved visits for cats and their caregivers?
- What differences your practice has made today in the lives of cats and other animals?

Sharing this kind of information with your followers in a story format fosters community, trust, interactions, and keeps your trusted cat clients coming back to you. Stories like these are also known as:

Case studies – a story particular to a specific cat client, place, and time.

Case studies are crucially important for a variety of reasons, but primarily to help your audience know about the stellar care your **Cat Friendly Practice®** provides!

When you are creating your case study, be sure to provide your audience with:

- The reason the cat came in to receive veterinary care.
- Details regarding the type of care you provided for the cat.
- How being a **Cat Friendly Practice®** improved the veterinary visit and overall care for the cat and the caregiver.

- An update on how the cat is doing today.
- A photo, or quick video of the pet.

When you provide this level of in-depth information on a cat, you tell the story of your patient and demonstrate that you can deliver the same quality of care to any prospective client. You can to forge an immediate bond with cat caregivers who appreciate your attention to detail, and the accountability needed to provide optimal care for their cat.

Your followers and their friends want to hear of your successes, which will brighten their day and instill them with confidence about your **Cat Friendly Practice®.** In exceptional circumstances, news coverage has even come about after particularly sincere and uplifting stories. This results in tremendous positive publicity, and simultaneously helps you to market your services to a wider audience. This wider audience can soon grow and enhance your veterinary practice online, and in your local community.

Case studies are also a great opportunity to educate your clients. By highlighting a particular health concern (like lily toxicity in cats), you can spread important information in your success story that will resonate with cat caregivers. These posts can be timed for specific times of year (the “chocolate holidays,” the start of flea season, holiday dangers) to help your clients stay aware of how to best care for their cat, and to keep your practice at the top of their minds.

GET PERMISSION

Yes, you should receive permission from the cat caregiver to share their story, pictures, or a video of their cat on social media or elsewhere. This is an important thing to note and emphasize, as some members of your staff may be appointed to collect signed photo/video release forms, to ensure that you’re permitted explicitly to share various types of media.

Most cat caregivers don’t hesitate at the opportunity to share the joy of their cat with the world and online but receiving permission firsthand is definitely a must.

Sample topics for case studies can include:

- Dermatology: Before and after skin cases
- Dental: Before and after dental care with photos
- Surgical Case Examples
- Laser Therapy Cases

By using Facebook with photos and videos to create and communicate compelling stories, you can enhance your marketing efforts, stay on the cutting edge, and attract more clients to your **Cat Friendly Practice®.**

APPRECIATE CAT OWNERS

In a world that's moving so quickly, who really has the time to say "please" *and* "thank you"? We might think that our world is so filled with stimuli, that nobody would hear it if we said, "Thank you", just a little more often.

It may feel like these tiny, syllable-sized gestures are antiquated or meaningless in our modern-day environment. However, this couldn't be further from the truth. In fact, those precious two little words might be more important now than ever before. Scarcity solicits demand, right? As **Cat Friendly Practices®,** we might be busier than ever before, but our need to express gratitude is also more prominent than ever.

Our need to express a heartfelt, "Thank you", has never been more relevant or imperative, than it is right now.

Despite what you might have been told, this simple phrase is emblematic of a whole lot more. It can make or break a friendship or even a relationship with one of your clients. In feline medicine, we are so intent on acquiring new business, that often times we do not designate enough attention to telling our existing clients how much we appreciate them, or thank them for coming in. Now, why would we work so hard to build our **Cat Friendly Practice®**, market effectively, and provide stellar service, only to stop short of giving thanks to our clients?

With a few simple phrases you can help retain your clients, but even more importantly, create an ongoing, genuine bond of solidarity and trust. I recommend that you make saying the following few sentences a habit. You'll thank me later:

"Thank you for bringing your cat in to see us. Thank you for being a wonderful cat caregiver, and most of all, thank you for choosing to trust our ***Cat Friendly Practice®*** *with your cat's health care needs."*

This type of response to a new or established client may only take seconds to say but can make a world of difference. Of course, it's got to be genuine, even when you're busy and the phone is ringing again. You can't overlook the importance of sincere gratitude as a cornerstone of building any healthy relationship.

The central point here is this; *the effort really matters, because we really matter.* Simply taking time out of each day to thank your clients and letting them know explicitly of your appreciation and their importance can be surprisingly rare.

I used to work closely with a widely respected veterinarian, Dr. Eddie Garcia (no relation, I promise) who would call each and every one of his clients within 72 hours of their initial visit. He would do this with no ulterior motive or hidden reasoning. He would simply call to say, “Thank you for visiting our practice. If there is anything, we can do for you, we are only a phone call away.” He strongly encouraged both positive and negative feedback, in whatever form it came. He would use this feedback to learn about the wants, needs and fears of his clients, and thank them for it - even if their visit was sub-par, as well. I can hear you asking, “Wouldn’t this level of openness leave him vulnerable to hours of time-consuming critique?” While that’s a fair question, the kicker is this:

- *A majority of phone calls were left on an answering machine (well, voicemail box nowadays).*
- *People were so excited about the calls that they called him back simply to express their gratitude.*
- *Dr. Garcia boasted a 90% success rate of retaining upset or displeased clients*.

I watched Dr. Eddie Garcia make these types of phone calls every day for over 10 years (watch him in action). *Yes*, he really made these calls each and every day, and *yes*, they really did make a difference.

Calling both new and existing clients is equally important and can’t be emphasized enough.

Whereas most of the time clients might simply express their grievance or general feedback to a spouse (if anyone at all), Dr. Garcia used their direct feedback to forge a bond, improve his practice, and retain his clients in a single call. You can do the same.

When I used to ask Dr. Garcia what motivated him to go above and beyond to make these phone calls, he had quite a simple explanation: to stay true to his mission. In his mission, he outlined that his veterinary practice, “will meet and exceed expectation”. These phone calls were his little way of making sure that he exceeded his client’s expectations of what an attentive and caring veterinarian looked like. And it did.

From phone calls to automated “Thank You” emails, there are plenty of ways to effectively implement gratitude into your **Cat Friendly Practice**®. Here is a 3-step-solution to implementing ‘Thank You’ into your practice today:

3 Steps to Saying Thank You at your Cat Friendly Practice®

(1) Implement a protocol to have your team members print two reports at some point, consistently, each day. These should consist of two parts:

1) New client report from the day before.
2) Appointment schedule report from the day before.

(2) Decide in your practice who the appropriate person is to make the call. I usually recommend that associates call their own clients in order to create a genuine bond. If associates do not have the time to do so, the practice owner or medical director may make the call. I've recently heard the idea of practices delegating this responsibility to a receptionist or technician. The reason they do this is because they've expressed that cat caregivers are more likely to share a negative experience with the receptionist vs. the owner or associate. Choose the person who you feel would be great at taking on this type of task.

(3) Begin by calling all new clients and only choosing 3-5 existing clients from the appointment schedule report from the previous day. You don't need to call back every existing client to say thanks but spot-check and call a few.

**Optional Recommended Step*

You may also choose to include an automated 'Thank you' email to supplement the phone calls. This email can add a wonderful touch to a follow-up phone call and coincides with my line of thinking:

You can never be too thankful.

I hope that these tips will help you implement new and improved techniques for your cat caregiver experience now and into the future.

Consigue que los clientes digan que sí a tus recomendaciones! Cómo construir una estrategia de contenido atractiva

Eric Garcia
Simply Done Tech Solutions, LLC
Tampa, Florida, USA

TELL YOUR STORY

People are often under the impression that Facebook is solely about peer-to-peer interactions. This, however, couldn't be further from the truth. Facebook is a platform that's become as universal as the water cooler itself. Successful veterinary practices around the *world leverage Facebook as a place to tell their unique story.* Your veterinary practice has a narrative; a year it was founded, a founder (or two, or more) and a style and perspective that makes it entirely unique.

Use Facebook to tell your story and not only capture, but captivate your audience!

Tell us about your success stories: the pets that you care for and the difference that you've made today. All of these things foster community, trust, interactions, and keep your trusted pet owners coming back for more.

These success stories are technically known as:

Case studies – a story particular to a specific pet, place and time.

These case studies are of crucial importance for a multitude of reasons, but primarily because they help your audience to see firsthand the type of stellar care that your veterinary practice provides!

In a particular case study, be sure to provide your audience with:

- Why the pet came in to receive veterinary care
- What you did to provide care for the pet
- How the pet is doing today

- A photo, or quick video of the pet!

By providing this level of in-depth information on a pet, you tell the story of your patient and ensure that you can deliver the same quality of care to any prospective pet owner who needs it. You'll be able to forge an immediate bond with pet owners who appreciate your attention to detail, and the accountability needed to provide optimal care for a pet.

People want to hear of your successes, which will brighten their day and instill them with confidence about your veterinary practice. In exceptional circumstances, news coverage has even come about after particularly sincere and uplifting pet stories. This results in absolutely tremendous publicity, and simultaneously helps you to market your services to a wider audience. This wider audience can soon grow and enhance your veterinary practice online, and in the local community.

Case studies are also a great opportunity to educate your clients. By highlighting a particular toxicity (like xylitol, grapes, or lily toxicity in a cat) you can spread the important information in a success story that will resonate with pet owners. These posts can be timed for specific times of year (the "chocolate holidays", the start of flea season, holiday dangers) to help your clients stay aware of how to best care for their pet, and to keep your practice at top of mind.

GET PERMISSION

Yes, you should receive permission from a pet owner to share their story, pictures or a video of their pet on Social Media or elsewhere. This is an important thing to note and emphasize, as some members of your staff may be appointed to collect signed *Photo/Video Release Forms*, to ensure that you're permitted explicitly to share various types of media.

Most pet owners don't hesitate at the opportunity to share the joy of their pet with the world and online, but *receiving permission firsthand is definitely a must.*

Sample topics for case studies can include:

- **Dermatology:** Before and After Skin Cases

- **Dental:** Before and After Dental Care (Photo)

- **Surgical Case Examples**

- **Laser Therapy Cases** (Pets can often improve a limp in a matter of weeks after laser therapy)

By using Facebook, photos, and videos to create and communicate compelling stories, you can enhance your marketing efforts, stay on the cutting edge, and attract more pet owners to your veterinary practice.

About the Author: Eric Garcia is an IT expert. Digital marketer. Industry thought leader. When it comes to helping veterinary practices streamline their technology and attract and retain clients, Eric Garcia has a proven track record of educating the industry and producing results. Eric is an IT and Digital Marketing consultant working exclusively with veterinary practices. In addition to a long list of satisfied clients, Garcia's work has been recognized throughout the industry. He speaks regularly at conferences all throughout the world. **Facebook:** facebook.com/EricGarciaFL **Instagram:** @EricGarciaFL

Puedes ayudar con mi aullido?!:cómo manejar a los haters, bullies y más en línea

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As with most industries over the past few decades, the veterinary field has gone virtual — and with benefits ranging from online pharmacies to simpler appointment scheduling and telehealth visits, to online advertising, and of course, greater access to client feedback thanks to social media, there's a lot to be grateful for.

But this level of access also leads to much simpler (and more anonymous options) for leaving hate. Negative comments or constructive criticism is one thing: cyberbullying is another.

20% of the American Veterinary Medical Association (AVMA) members have reported encountering some form of cyberbullying from vicious reviews to threats of physical harm.

As a world and as a profession, we've forgotten the Golden Rule, and it's time we face this problem before it causes any more harm to our field.

Here are some tips I shared at the virtual 2020 PSIvet Business Symposium, to help you determine what you should do if you or your practice start to encounter online harassment:

● **Leave private hate private.** Facebook groups and other niche forums can both bring about a great sense of community and (unfortunately) an even greater sense of entitlement. It's amazing what people feel confident to say with their real photos and names attached to their profiles — and it only gets worse when there's greater anonymity. Somehow typing a rude response feels like less of a risk than insulting someone in person, but whether you feel tempted to argue their point or defend your practice on any of these forums you're better off leaving it alone. They did not write this comment to you — you are not going to change their mind. You're better off leaving the debate to other people within the private group - and chances are they'll move onto another topic by the time you've formulated your response anyway. The more attention you give the hate (through comments or replies) the more you can unintentionally add fuel to an already dying flame.

● **Take a moment before engaging with negative reviews.** When a client has lashed out online, you are better off giving them anywhere from 24-72 hours to cool down before you reach out personally. This means pulling out their pet's medical records, picking up the phone, and seeing what you can do to help them in person first, before settling for responding to their comment online. If they are unavailable, then your first step is to publicly apologize for their experience and note that you haven't been able to get a hold of them. This way they (and anyone else who sees the negative comment) will know that you and your practice are trying to make things right. Apologizing isn't about admitting that you or your practice is in the wrong: it's about expressing empathy and acknowledging the client's perspective — you cannot fix a situation without first acknowledging their feelings. Although it's tempting to share your side of the story in your apology, avoid discussing anything about their pet's case online — especially if it's on a public forum. There is still client confidentiality at risk, and you could get reported to your state board. Yikes.

> **Sample Reply to a Negative Review**
>
> "We're sorry for your experience. We have not been able to reach you by phone. We would like to make this situation right with you. Please call our medical director at (xxx) xxx-xxxx."

● **Report slander and false reviews.** There's a difference between an angry (but honest) client review and a false one. The good news is that with Google and Yelp and other public reviews, there are actual guidelines in order to protect businesses like yours. If a review is fake, false or misleading, or otherwise in violation of the review's host site, you can send requests for their removal and get them taken down.

Here are some simple steps you can take to get false reviews taken off Google and Yelp:

Google

- Log into Google My Business at **google.com/business.**
- Select "Reviews" from the menu.
- Find the review in question. Click the 3-dot menu, then select "Flag as inappropriate."

Yelp

- Claim your business page at **biz.yelp.com**.
- Locate the review in the "Reviews" section of your business account.
- Click the 3 dots and click "Report Review."
- Choose the reason for removal from the dropdown list.

- Grounds include containing false information, threats, lewdness or hate speech, not describing a personal customer experience, and being posted by a competitor or ex-employee.

● **Overwhelmed? You don't have to go it alone.** It can be emotionally draining and generally exhausting to find yourself and your place of work under attack. The good news is that AVMA has its own cyberbullying hotline to help veterinary professionals of all types with immediate support and a free counseling session to help get your practice's reputation back to what it used to be. Simply call (626) 531-1140, and you'll have a safe space to discuss your concerns and your side of the story without ticking anyone off or violating confidentiality guidelines.

● **Stop vet-on-vet harassment.** Unfortunately, not all cyberbullying comes from clients. Whether it's coming from competitions veterinarians or unhappy staff, veterinary professionals should know better than engaging in unnecessary online harassment campaigns — especially when they consider that the veterinary field is already a profession that is prone to suicide. When you have a problem with another vet, you can do much better than calling each other out in negative ways on social media. We all have bad days: venting to a friend is a much better idea than spilling all of your problems on Twitter or Instagram. And if you're upset about something unfair or unjust happening in your profession, write to your state board or national governing bodies, or write an article or create a series of podcasts — make something positive for change instead of giving into simply complaining for sympathy points or petty revenge.

● **And finally, skip social media with your breakfast.** One of the number one rules of the internet is "don't read the comments" but you can extend that to mindless scrolling on social media, too. Of course, as a business, you do need to respond to legitimate criticism and reviews but if you want to be happier, start your day without checking social media. You'll be glad you did.

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Ya programó su próxima cita? construir estrategias de retención de clients

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THE DIGITAL MARKETING REVOLUTION HAS ARRIVED

The days of print-heavy advertising dominated advertising campaigns are over. The old scenario used to mean creating an advertisement that was clean, clear and direct; paying a lump sum or quarterly fee to get the ad in circulation and hoping for a successful campaign that picks up business in some way or another. If you wanted to get fancy with it, you could target a few specific locations with growing populations, or take out a double-page advertisement to ensure your advertisement was as visible as possible.

Now, physical advertisements are sometimes looked at as cumbersome by newer consumers and younger demographics, while more people are using their iPhones and computers to shop and search for businesses and new products each day.

While print media still plays a role, more and more consumers and clientele are adapting to the digital world and moving their attention to Google, Facebook, Instagram and the web as a whole.

This means that if you're still using the same techniques for marketing that you were a few years ago, you may be missing out on a huge array of new clients! These potential clients aren't hiding; they're just waiting to be attracted by the right advertisement or promotion to bring them in! More often than not, you can target these new clients effectively by using the right approaches to marketing on the web.

In fact, popular search engines like Google, along with your veterinary practice's website, are the two primary sources of New Client Referrals. This is a trend that doesn't seem to be slowing down anytime soon and is impacting the way that successful veterinary practices do business.

The good news is that even if you did have success with older forms of marketing, the room for you to grow and capitalize on new techniques is greater than ever. There are tools in place to ensure that your marketing is as effective as possible, and that your Return On Investment (ROI) is robust enough to ensure that the campaigns are worthwhile. When it comes to measuring the performance of digital marketing campaigns, your techniques can be boiled down to a science, where the better the execution and measurement, the more success you'll have.

Here are some proven tips and tools that can enhance your current marketing efforts and ensure that you have the right tools in place to have profoundly successful campaigns when it comes to marketing your veterinary practice:

TIPS & TOOLS FOR SUCCESS

It's important to ensure that your client management software doesn't count "no show" clients as new clients. Why? This can throw off your measurement of revenue and growth, when the best digital marketing campaigns will only use data that's truly effecting your veterinary practice.

I recommend looking at New Client Revenue as opposed to just looking at New Client Numbers. After all, it's the revenue that these clients generate within the first twelve months of doing business with a veterinary practice that will help to determine if the veterinary practice has received return on the respective marketing tools used. Unless a certain amount of revenue and return is reached, you won't be able to justify certain marketing channels that may be consuming more resources than they are generating, or are keeping your margins paper-thin.

Additionally, you have to be diligent about making sure that the figures reflected in your software are true to what's occurring day to day. For example, sometimes your management software might say that you've received a new client, when in reality you have not! This can commonly occur when an account is created for a client in advance of their appointment, but the client cancels or is a no show. If this occurs, you should make the adjustments to reflect the most accurate information possible. A simple error during this stage can throw off your projections for revenue and your new client data as a whole.

ENSURING YOUR RETURN

It's important to have certain parameters in place to ensure that your efforts are a success. If you spend $500 USD on a campaign and it returns $750 USD, is this considered a success? What about the time and expenses required to measure and implement the campaign in the first place?

As a rule of thumb, **I recommend a *minimum* of doubling your return on.** While looking for higher return is a great place to aim, you want to at least double your return to constitute the expense in the first place. Anything lower puts you at risk for losing your money toward ineffective marketing, and anything greater means that you are on pace for a truly successful campaign. I'd also recommend keeping a close eye on your returns and the techniques used to achieve them; this way you can refine and enhance your return with even more robust margins in the weeks and months to come, capitalizing on the successes you've already established.

If in fact you do achieve a low return on an investment, this doesn't mean that you need to scrap the campaign altogether. For example, what's the best course of action if you achieve a return of $750 USD on a $500 USD investment in a local magazine advertisement? In this situation, you can keep a close eye on this and either consider canceling your renewal or renew but keep a very close eye on the success of the campaign. You may decide in this particular case, the margins are sufficient, but that if improvement is not achieved within a certain amount of time, it's time to pivot and try another avenue altogether.

NEW CLIENT SOURCES

Something else that's extremely important to be mindful of is tracking your new client sources. The most common New Client Referral sources are as follows**: Search Engines, Website, Social Media, Community Based Print Advertising, Existing Clientele** (word of mouth) and **Community Events.** = Tracking your new client sources is an imperative step to success.

While this may seem like a lot of elements to account for, remember that each insight gained allows you to enhance your future marketing efforts. While perusing the data at first may seem overwhelming or even unnecessary, **it is this data that is key to driving your most successful marketing efforts yet.**

TRACKING COUPONS

Coupons are a time tested and effective way to measure the overall effectiveness of your existing marketing campaigns. For example, if you're advertising in a local magazine, try adding a promotion

for a “Free Nail Trim” directly onto the ad. Then, tally how many people come in with the coupon to start to boil down the figures on the success of the campaign. On each coupon, you’ll want to specify the source by creating a **Coupon Code** that should be specified with a phrase. You may also wish to hand out promotional coupons at events sponsored or participated in by your veterinary practice, so you can see which events are worthwhile and bring in new clientele directly to your veterinary practice.

Some potential strategies for creating coupons include offering free services like grooming or nail trims, offering a free gift with a paid service. There is room to experiment with which promotions attract clients and are in high-demand, and by tuning into this feedback you’ll stand the most to gain overall.

Remember, it’s important to add a tracking code for each event and specific campaign so that you can measure the success of the campaign.

One of the most important takeaways, is learning how to move away from the “feeling” of success and toward the actual “execution” of success. For example, an event can feel like a true success after some positive interactions and feedback from attendees. But you can only know if the event is creating substantial ROI (Return On Investment) by implementing tools that measure your success in more tangible terms. Data is most certainly your friend when it comes to the world of digital marketing! In fact, the more data you use to implement your next marketing moves, the more you’ll be moving toward the science of profitability.

TRACKING CLIENT RETENTION

It’s also imperative to track your client retention, even while implementing the aforementioned marketing campaigns. Attracting clients is extremely important, but are they still visiting your veterinary practice 12 months later? To track client retention effectively, try pulling a report of clients who came to visit 18-24 months ago. Have those clients come back in for a repeat visit since then?

For example, if 18-24 months ago, you received 150 new clients total, but only 75 have come back in to visit your veterinary practice for repeat visits, this means that you have a retention rate of 50%.

If you want to improve business for your veterinary practice over the long-haul, set a goal of achieving client retention that’s 5-10% higher than where you’re at right now. Tracking client retention in this way will help you to determine which marketing efforts work better at attracting long term clients versus short term clients. While you do want to bring new clients through your front door, attracting clients that stay with you over a long period of time will yield far higher returns than clients that visit once and do not come back. If in fact you spent a substantial amount of marketing dollars to bring in that one-time client, you could be looking at low-margin profit, or even a loss.

FINDING THE RIGHT APPROACH FOR YOUR VETERINARY PRACTICE

While there are proven techniques that help to transition digital marketing away from a shot in the dark and instead toward more of a science, these techniques and your approach toward them will require examination and levels of refined implementation over time. A strategy that works effectively with a print magazine one year, could decline the next, especially if the circulation of the magazine decreases or more people begin to transition to reading a different magazine altogether.

The more you begin to clue into the world of digital marketing, successful approaches and the necessary adjustments needed, the easier it becomes to capitalize on successes and shed old ways of doing business that are no longer effective.

When you begin to implement the right combination of marketing techniques, accompanied with effective ways of measuring them, well, that's when you really start to get your veterinary practice purring the way it should.

Let's do this! Our last event is up next. I'm so proud of you.

About the Author: Eric Garcia is an IT expert. Digital marketer. Industry thought leader. When it comes to helping veterinary practices streamline their technology and attract and retain clients, Eric Garcia has a proven track record of educating the industry and producing results. Eric is an award-winning Global IT and Digital Strategist working *exclusively* within the veterinary field. In addition to a long list of satisfied clients, Garcia's work has been recognized throughout the industry. He speaks regularly at conferences all throughout the world. **Instagram:** @EricGarciaFL **Facebook:** facebook.com/EricGarciaFL **Twitter:** @EricGarciaFL

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Antibody Testing in Clinical Practice

Indications for Point-of-Care Testing

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In veterinary medicine, the concept of measuring antibody as a means of assessing the need for, or the response to, vaccination is still relatively new. Initial interest in patient-centered testing seems to have started over concerns that the 3-year booster recommendations for core vaccines had not been validated. More recently, clientele concerned about risks associated with pet over-vaccination have prompted veterinarians to offer serological testing in lieu of routine vaccination. As demand for antibody testing of individual patients increased, more laboratories began offering serological testing for vaccine-preventable diseases. In addition to laboratory-based testing, point-of-care antibody test kits are now available that offer results within 25 minutes at reasonable cost.

As the demand for patient-centered antibody testing continues to emerge in companion animal practice, more *indications* for patient testing have also emerged, along with questions regarding testing interpretation and patient management.

It is the purpose of this webinar to address 3 of the most fundamental questions pertaining to the use of antibody testing in clinical practice:

- **ARE ANTIBODY TEST RESULTS VALID?** Does a "positive" test result actually correlate with protection?

- **WHAT ARE THE INDICATIONS FOR TESTING?** The AAHA Canine Vaccination Guidelines have identified 12 indications…representative examples will be described.

- **INTERPRETATION of results?** When testing is indicated, how should the individual patient be managed if the test result is "positive" vs. "negative"?

ARE ANTIBODY TEST RESULTS VALID?

Making rational, patient-centered clinical decisions based on serological (antibody) test results depends on understanding a few "must know" facts. Consider the following points:

1. **The only *true* test of protective immunity involves exposure (challenge) to a virulent pathogen** in which non-vaccinates (controls) are infected and manifest clinical illness while vaccinated animals remain healthy after a significant challenge dose. Licensing of animal vaccines is based on this premise.

Serological studies conducted in conjunction with "challenge" studies have consistently demonstrated exceptional correlation between antibody level and protection *for canine distemper (CDV), canine parvovirus (CPV), canine adenovirus (CAV), and feline parvovirus (FPV, or panleukopenia).* See references: 3,4,5,6,8,10,11, and 12.

2. "POSITIVE" vs "NEGATIVE" Test Result…*this is important.*

- A "positive" antibody test result means that the patient's sample has sufficient antibody to meet or exceed a defined "positive" reference threshold or control established by the laboratory or the manufacturer of the test kit.

> ***To be clear…***
>
> …consider a patient sample submitted to a commercial laboratory is returned with results for canine parvovirus antibody reported as: **1:1600 "POSITIVE"**
>
> By using the term "positive", the laboratory is *only* stating that the level of antibody detected in that sample met or exceeded their reference threshold for positivity. The laboratory does not, and will not, make a *clinical interpretation* of what the "positive" test result means in the individual patient.
>
> That's the clinician's responsibility….

- A "negative" test result only indicates the patient's sample either did not have a detectable level of antibody or that the level present was below a defined threshold. Note…a *"negative" test result does not necessarily define "susceptibility"* (see INDICATIONS & INTERPRETATION below).

3. Some antibody test results correlate with PROTECTION…some do not…

Commercial laboratories offer serological testing for several bacterial, fungal, and viral pathogens.

"Positive" antibody test results have a significantly different meaning depending on the pathogen (or vaccine) that induced the antibody. THINK **PIE** when interpreting a "**positive**" test result:

PROTECTION or…INFECTION or…EXPOSURE

For example, as described above, a "positive" antibody test result for CDV, CPV, CAV, and FPV correlates exceptionally well with *PROTECTION*…that fact is well established.

In practice, a "positive" Leptospira antibody testing is used as a diagnostic tool to identify *INFECTION.* Leptospira antibody does NOT correlate well with protection following either vaccination or natural infection. Other factors, such as cell-mediated immunity, are primarily involved. The same is true of Feline Immunodeficiency Virus (FIV)…a cat having a "positive" FIV antibody test is deemed infected…not protected.

On the other hand, a "positive" antibody test result for *Ehrlichia spp.* or *Anaplasma spp.* only correlates with prior *EXPOSURE*…results do NOT correlate with either protection or infection. The same is true for canine influenza virus…a "positive" CIV antibody test denotes prior exposure. CIV antibody levels become positive *after* the short-lived viremia (2-4 weeks) is over. Furthermore, a CIV antibody-positive patient is still susceptible to infection if re-exposed …antibody does not correlate with protection.

4. The Testing "Platform"…a technical point. Antibody testing can be performed *quantitatively* (laboratory-based titer) or *qualitatively* (point-of-care, in-clinic test kit):

a. ***Quantitative* Testing**…aka 'titers'…refers to laboratory-based, end-point testing methods (sometimes referred to as "gold standard tests" because all other testing methods must be correlated with titer results) used to determine the relative concentration of antibody, expressed as a ratio, that has been produced in response to a specific antigen. Patient samples must be sent to a laboratory and results are usually available within days. NOTE: the amplitude of the titer is not a correlate of the degree of immunity. A dog with a high "positive" parvovirus antibody titer is not more immune, or better protected, than a dog with a low "positive" parvovirus antibody titer.

b. ***Qualitative* Testing**…refers to "point-of-care" testing methods (or, test kits) practical for use within a veterinary practice. Depending on the test, results can be obtained in as little as 10 to 30 minutes. Test kits licensed for use in dogs and cats reliably distinguish "POSITIVE" results from "NEGATIVE" results.

> The **VacciCheck**[1] point-of-care test kit provides "semi-quantitative" results. Although results are not read as end-point titers, the test kit utilizes a graduated (gray-purple) color scale to determine the relative amount of antibody present compared to a "positive" reference (control) color for each antigen (CDV-CPV-CAV) tested. The color scale is scored from zero (0) to six (6). Scores ranging from 2 to 6 represent a protective level of antibody.

A "positive" antibody test result, whether performed by quantitative testing, "semi-quantitative" testing, or qualitative testing, is interpreted the same way…a "positive" is a "positive".

WHAT ARE THE INDICATIONS FOR TESTING?

The online version of the AAHA Canine Vaccination Guidelines[1] includes a menu option entitled "Antibody Testing for Vaccine-Preventable Diseases". The purpose of the section is to provide veterinarians with various scenarios (12 are listed) for which serological testing (CDV, CPV, and CAV) of an individual dog would be indicated. Several of these indications are also applicable to the cat.

For each *indication*, recommendations on patient management are offered for a "positive" test result as well as a "negative" test result.

Listed below are representative indications for assessing serological responses in patients vaccinated against canine distemper virus, canine adenovirus, and canine (and feline) parvovirus. Refer to the AAHA Canine Vaccination Guidelines (online) for additional testing indications.

1. Assess antibody response following administration of the *Primary (initial) Core Vaccine series* in young dogs:

For various reasons, clients of young dogs/cats may request antibody testing *in response to vaccination*. A common example being the client who desires to transport puppies/kittens for sale or show purposes following completion of the initial series of core vaccines. Antibody testing can be conducted as early as 2

[1] Available as an open, on-line educational resource for veterinary medicine: *Search*: AAHA Canine Vaccination Guidelines

weeks following administration of the last dose in the initial series (although 2 to 4 weeks following the last dose is commonly recommended).

Interpretation: If the last dose is administered at 16 weeks of age, blood can be collected as early as 18 weeks of age and tested for the presence of antibody.

If results are "positive" for antibody, the patient is immunized (protected)…a booster dose of the core vaccines is recommended 1 year later.

If results are "negative" for antibody against any virus, the patient is considered *susceptible.* A booster dose of vaccine should be administered as soon as practical. A combination vaccine can safely be administered even if the antibody level against one virus is "negative" while other results are "positive".

Sustained, interfering levels of maternally derived antibody are the most likely reason vaccination fails to immunize a young dog or cat. Therefore, it would not be unreasonable to recommend an additional test, 2 weeks following administration of the additional booster dose, to verify the patient has seroconverted and is protected.

2. Identification of genetic "non-responders" to canine parvovirus

With the introduction of canine-origin parvovirus vaccines in the early 1980s, veterinarians soon recognized that well vaccinated dogs, particularly among certain lines of Doberman pinschers and Rottweilers, became infected and died following exposure to canine parvovirus. Ultimately, vaccination failure in these dogs was attributed to a highly specific genetic mutation that resulted in a low, or no, antibody response following administration of modified-live parvovirus vaccine. Interestingly, antibody responses to canine distemper and adenovirus were protective. The term "genetic non-responder", or "genetic low-responder", is used to describe the affected animal.

Today, genetic non-responders (and low-responders) have been recognized throughout the world and are *not* limited to Doberman pinschers and Rottweilers. (In the author's recent experience, confirmed genetic non-responders have all been pure-bred dogs…little ones and big ones). It is presumed that feline genetic non-responders (to feline panleukopenia virus [feline parvovirus]) also exist.

Interpretation: Testing for canine or feline parvovirus antibody is the only means of identifying a genetic non-responder.

If the results for parvovirus antibody are "negative" 2 or more weeks following administration of the last dose in the initial series, the patient should be re-vaccinated against parvovirus as soon as practical and scheduled for a follow-up antibody test. A second "negative" test result, obtained 2 to 4 weeks after administering an additional (booster) dose of vaccine, indicates that the patient is likely a genetic non-responder. Administration of additional doses of parvovirus vaccine are not expected to immunize. The seronegative patient must be considered *susceptible* if exposed to parvovirus.

3. Antibody testing of adults in lieu of administering a booster.

In the previous 2 examples, antibody testing was performed to assess a patient's response to vaccination. In the next 2 examples, antibody testing is performed to determine *the need for re-vaccination.* Clients who are concerned about risks associated with 'over-vaccination' may request antibody testing in lieu of re-

vaccination. In addition, veterinarians concerned about the need to administer routine booster doses of vaccine in geriatric patients may elect to recommend antibody testing in lieu of re-vaccination.

Interpretation: The adult dog/cat that has a history of prior vaccination, "positive" antibody test results are expected for each of the viruses, even in patients that are significantly overdue for a scheduled booster. "Positive" test results indicate that the patient does have protective immunity and that re-vaccination is not necessary.

On the other hand, antibody testing of previously vaccinated adults will occasionally yield a "negative" antibody test result for one (or more) of the viruses for which vaccine was previously administered. It happens… antibody is a protein and blood levels will diminish over time in the absence of exposure (or re-vaccination).

In contrast to the previous two examples, in which a "negative" test result indicates *susceptibility…*a "negative" test result in the adult, previously vaccinated dog or cat likely does NOT correlate with *susceptibility…see the BOX below.*

Does a "positive" antibody test result today assure the patient will be protected tomorrow? … or a year from now? …or 3 years from now?

In a way…YES…it does. A "positive" antibody test results for CDV, CPV, CAV, and FPV not only correlates with protection, but indicates that the patient has produced long-term immune (B-cell) "memory". This "memory" (clones of B-lymphocytes residing in germinal centers of lymphoid tissue) enables the patient to "remember" specific (disease-producing) antigens (viruses)….often, for years… depending on the antigen. If the patient is exposed to virulent virus, the patient rapidly (within days) develops a "secondary" (anamnestic) antibody response, even if the antibody level has declined to a level below the "positive" threshold on a test. In effect…the patient's immunity will be "boosted" by that exposure.

That's why a "negative" antibody test result in a dog that has previously been vaccinated against distemper, parvovirus, or adenovirus, does NOT necessarily correlate with *susceptibility*.

4. Assessment of patients having a history of a vaccine adverse reaction or immune-mediated disease.

Serious adverse reactions following vaccination are uncommon in both dogs and cats. Among the contingent of patients with a history of having recovered from a known, or suspected, vaccine adverse event (reaction)…or, are known to have been treated for and recovered from an immune-mediated disease (eg, hemolytic anemia or thrombocytopenia), evaluating the level of antibody becomes an important alternative to re-vaccination.

Interpretation: Patients having a "positive" test result can avoid re-vaccination and the potential risk for eliciting an acute-onset reaction or re-activating an immune-mediated disease.

If, on the other hand, a patient has one or more *negative* test results, the decision whether or not to administer vaccine becomes more complicated, because:

…among previously vaccinated adults, immune "memory" is likely sustained and is expected to provide a rapid, protective response if exposure to virulent virus occurs even in the absence of detectable levels of antibody.

…among young animals, especially if having experienced an adverse reaction prior to completing the initial 3 or 4 dose vaccination series, a "negative" antibody test likely correlates with susceptibility. The decision to vaccinate, or not, becomes a clinical decision that must take into consideration not only the owner's concerns, but the potential risks associated with administering a dose of vaccine vs. the risk of not immunizing the animal.

LIMITATIONS to ANTIBODY TESTING for CORE VACCINES

Seroconversion, the antibody response, from a seronegative state to a seropositive state, that follows vaccination can be determined for each of the core vaccines administered to dogs and cats. However, the development of antibody does not always equate to **protective immunity**.

Feline Calicivirus (FCV) & Feline Herpesvirus (FHV)

- "Positive" antibody test results for feline herpesvirus (FHV) and feline calicivirus (FCV) vaccination *do not correlate well with protective immunity*. For this reason, serology is not generally recommended to assess protection following vaccination or to determine the need for re-vaccination.

- Assessment of **cell-mediated immunity (CMI)** is a better correlate of protection against FHV-1 than serology. However, CMI tests are complex and not routinely performed as a clinical service to veterinary practices.

- The so-called "gold standard test" (quantitative titer) used to measure FCV antibody has been judged only as *fair to good*. For this reason, antibody testing for FCV antibody is generally not recommended.

Rabies Virus

- Rabies virus neutralizing antibody (RVNA) testing is available through a limited number of certified laboratories only. Point-of-Care test kits are not available. One point all veterinarians should note: a "positive" RVNA titer result is NOT *a legal index of immunity in lieu of revaccination*.

- The interpretation of an RVNA, as would be performed on dogs or cats being exported to a rabies-free country or region of the world, is that the "positive" animal has been "adequately vaccinated"…*that's it!* Do not submit serum for RVNA titers as a means of confirming protective immunity against rabies.

WELLNESS and ANTIBODY TESTING

In clinical practice today, the concept of "wellness" and "wellness testing" continues to evolve in a variety of ways that provide measurable, long-term health benefits to the individual dog and cat. It's not surprising that "wellness" programs are being integrated into the curriculum at veterinary schools and individual State Veterinary Medical Associations continue to promote wellness exams and testing to the pet-owning public. With the increased acceptance and practice of "wellness exams" in human medicine, increasing numbers of pet owners accept this approach to preventive health care offered by individual veterinary practices.

Parameters for pet wellness testing have not been strictly defined, but reasonably include a physical examination & history (lifestyle assessment), heartworm testing, complete blood count, biochemistry profile

(especially in geriatric patients), urinalysis, etc. As the emphasis on intervals for administering core vaccines continues to shift from "annual boosters" to triennial boosters, or longer, the concept incorporating antibody testing as part of a pet wellness program becomes increasingly practical.

Concluding Comments

Point-of-care testing for antibody to CDV, CPV, CAV, and FPV represents a relatively new clinical resource in veterinary medicine that enables the clinician to assess patient risk against the most serious (core) infections. The application of this technology in practice requires an awareness of the indications for testing *and* the knowledge to properly interpret test results. Given the high degree of correlation between a "positive" antibody test result (whether using quantitative, semi-quantitative, or qualitative testing platform) and protection, serological testing offers veterinarians a relevant, reliable tool for making informed decisions relevant to managing individual patients in the clinical setting.

Additional Reading

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TABLE 1. Serological Testing for Vaccine-Preventable Core Diseases[2]

[2] NOTE: laboratory results reported as "positive" or "negative" only imply that the antibody being measured was either present ("positive") or was not present ("negative") relative to a threshold defined by that laboratory. Commercial laboratories typically do not make a clinical interpretation of the results. That's the clinician's responsibility. Furthermore, the reference range for titer results reported by one laboratory should not be compared with the reference range for titer results from a different laboratory as testing methods used by different laboratories can, and do, vary.

Virus	Interpretation of Test Results
Rabies Virus	Rabies virus neutralizing antibody (RVNA) levels are available through certified laboratories only. "Positive" test results are only indicative of prior (recent) vaccination and are not to be interpreted as an index of protection.
CANINE	
Adenovirus	In-clinic titer test results correlate *well* with gold standard testing (VN).
Distemper virus	In-clinic titer test results correlate *well* with gold standard testing (VN).
Parvovirus	In-clinic titer test results correlate *well* with gold standard testing (HI).
FELINE	
Calicivirus	The correlation between gold standard testing (VN) and protection is only *fair*.
Herpesvirus	The correlation between gold standard testing (VN) and protection is only *fair*; cell-mediated immunity is a *better* correlate of protection.
Parvovirus (Panleukopenia)	In-clinic titer test results correlate *well* with gold standard testing (HI).

TABLE 2. In-Clinic Antibody Titer Test Kits

	TiterCHEK (Formerly *Witness*) CDV+CPV	**VacciCheck Antibody Test Kit (CDV+CPV+CAV2)**
Manufacturer	Zoetis (zoetisus.com)	Biogal Galed Laboratories (*biogal.co.il)*
Canine Antibody	CDV and CPV only	CAV, CDV, and CPV
Feline Antibody	Not Available	Feline Parvovirus (FPV)
Sample	Serum or plasma (can use hemolyzed sample)	Serum, plasma, or whole blood (can use hemolyzed sample)
Test Time	15–20 min (minimum)	21 min (minimum)
Results	Qualitative: Positive or Negative	Semi-Quantitative: utilizes a graduated color scale to determine the relative amount of antibody present compared to a "positive" reference (control) color.

CAV = canine adenovirus; CDV = canine distemper; CPV = canine parvovirus; DOI = duration of immunity; FCV = feline calicivirus; FHV = feline herpesvirus; RVNA = rabies virus neutralizing antibody; FPV = feline parvovirus (panleukopenia); Ig = immunoglobulin; MDA = maternally-derived antibody; VN = virus neutralization test; HI = hemagglutination inhibition test.

CHRONIC COUGH IN THE DOG

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Chronic bronchial disease (CBD) is a general term used to describe a complex, progressive respiratory syndrome characterized by excessive mucous secretion within airways *and* thickening (hyperplasia of smooth muscle and epithelium) in the bronchial tree and frequent coughing. Cough is often described in the veterinary literature as one that persists at least "2 consecutive months" (cough duration is derived from the human literature and often extrapolated to veterinary medicine…I personally am not certain this is an accurate extrapolation).

What is accurate is the fact that the term chronic bronchial disease implies that the coughing episodes occur exclusive of other bronchopulmonary disease, e.g., cardiac disease, neoplasia, and infection (bacterial, mycotic, viral). In veterinary medicine, however, it is impossible to disregard the impact that secondary infections have on the progression and severity of clinical signs associated with chronic bronchial disease, particularly those associated with acquired bronchial disease and tracheal collapse. Interestingly, scientists addressing chronic bronchial disease in humans have attributed the underlying cause to one or a combination of 3 factors: age, inhaled particulate material (especially smoke from tobacco), and bacteria (…*not* pneumonia). As outlined below, clinicians, and their clients, who are willing to manage a pet with chronic bronchial disease must accept the premise that treatment is aimed at long-term control, not cure…*with expectations for quality outcome at reasonable cost*.

NEW: recent (not yet published) studies (U of Missouri) provide insight into at least one pre-disposing cause of chronic bronchial disease in middle-aged to older dogs…acute canine infectious respiratory disease syndrome (CIRD)…aka, "kennel cough". The role of vaccinating dogs, especially young dogs, against *B bronchiseptica* and parainfluenza virus may have significant health implications later in life.

For the client, **chronic bronchial disease** is a diagnosis very much worth the effort to manage.

Physical Findings

***Chronic* cough** is the hallmark clinical sign in dogs with advanced bronchial disease. However, CBD can be associated with severe, acute-onset paroxysmal coughing episodes which, in some cases, may results in emergency presentations associated with acute-onset respiratory distress…a good example of "acute-on-chronic" disease. Collapse/syncope are occasionally reported by clients who are faced with observing acute episodes in an affected pet.

In our experience (NCSU), acute respiratory distress associated with CBD is likely to be accompanied by *acquired* airway (not necessarily *tracheal*) collapse. While the disease is most common in dogs over 5 years of age, younger dogs can be (albeit rarely) affected. Among dogs, *clinical signs associated with* CBD appear to be most prevalent (most severe?) in small and toy breed dogs, such as, miniature/toy poodles, Pekingese, Yorkshire terriers, Pomeranians. At least one author has suggested a hereditary predisposition to CBD in dogs. It is perhaps more appropriate to consider these breeds (uniquely?) at risk of developing severe clinical signs of bronchial disease, since CBD clearly occurs in mixed breed and large breed dogs as well as smaller breeds. Compromised airway integrity of toy dog breeds (chondrodysplasia), possibly an inherited problem, may further complicate the clinical course of CBD in the older dog. *Obesity* and *advanced dental/periodontal disease* are commonly reported findings among small and toy dog breeds with CBD and are often cited as contributing factors in the clinical patient (more on that later).

Detection of abnormal respiratory sounds (rales/wheezes/crackles) during thoracic auscultation can occur in dogs with CBD, but these are NOT consistently reliable indicators of CBD. The ability to elicit coughing by simple manipulation of the cervical trachea is an inconsistent finding in dogs with CBD and should NOT be considered to be a diagnostic criterion.

Careful thoracic auscultation, in a quiet room, can provide important physical evidence contributing to to the diagnosis of CBD and associated collapse of intrathoracic airways. Auscultation, especially during coughing episodes, can be particularly revealing. Toward the end of the expiratory phase of a cough, airway collapse may be audible as a distinct, abrupt thump, often referred to as an end-expiratory click or "snap." The sound is generated as the main bronchi (and possibly the intrathoracic trachea) collapse and literally interrupt the expiratory phase of a cough.

In affected dogs, coughing paroxysms can lead to substantial airway collapse (during exhalation), inability to eliminate CO_2, culminating in respiratory distress and syncope. Affected dogs may die subsequent to airway obstruction and respiratory arrest during an acute episode of paroxysmal coughing.

Laboratory Findings

Conventional hematology and biochemistry profiles are unlikely to contribute to the diagnosis of CBD but are still indicated to assess the presence of underlying disease.

The diagnostic value of fluid samples collected during transtracheal wash/aspiration (TTA) are, in the author's opinion, significantly limited. While properly performed bronchoalveolar lavage (BAL) may yield higher quality samples (compared to TTA), there are significant limitations to the procedure: eg, technique used and experience of the individual performing the procedure, patient size, bronchospasm, secondary airway infection, etc. Cytologic assessment of BAL samples may be useful in ruling out other chronic

pulmonary diseases. But is not considered to be either consistently reliable or a high yield procedure in the diagnosis of CBD.

DIAGNOSTIC CONFIRMATION

Thoracic Radiography: In the early, non-obstructive stages of CBD, a generalized interstitial lung pattern is usually present, although bronchial changes predominate. Thickening of bronchial walls, indicated by the "doughnut" appearance of end-on bronchi, and "tram lines," the longitudinal shadows associated with thickened bronchi, can be seen. Bronchial calcification alone, commonly seen as a normal age-related change in old dogs, should NOT be interpreted as bronchitis.

As CBD progresses, there is a tendency for the small airways, bronchi and, eventually, the intrathoracic trachea to collapse during exhalation, particularly during the expiratory phase of cough. The prevalence and severity of tracheal collapse appears to be most severe in adult, miniature, and toy dog breeds. Although chondrodysplasia and trachealis muscle dysfunction have been implicated in the pathogenesis of tracheal collapse, the functional diameter of the small airways in dogs with chronic bronchitis is also an important cause of bronchial and tracheal collapse, particularly in older dogs.

Acquired airway collapse is a significant and complicating factor in dogs (especially small breeds) with CBD. Acquired changes in intra-thoracic airway aerodynamics lead to lower intra-thoracic airway pressure during exhalation (cough) and can lead to rapid, intermittent, but total, collapse of the airway, especially at the level of the carina (tracheal bifurcation). These can be heard during auscultation as the expiratory phase of cough (end-expiratory 'snap') is abruptly interrupted. (video of acquired airway collapse will be shown during the presentation)

Bronchoalveolar Lavage and Culture: Cytology of specimens collected during BAL may contain only mucous and normal respiratory epithelium in spite of the severity of the patient's clinical signs. Neutrophils, eosinophils, macrophages, lymphocytes, goblet cells, and even bacteria may be seen. However, in our hands, the diagnostic value of cytologic examination of tracheobronchial washings collected during tracheal aspiration or bronchoalveolar lavage is limited.

Bronchoscopic Exam: In the dog, direct visualization of the trachea and right and left main bronchi using a flexible endoscope is a valuable diagnostic procedure (although cost and operator experience are limiting factors in clinical practice). Compared to the lower airways of normal dogs, the primary and secondary bronchi may appear irregular in contour, can have a mottled white and pink color, and often contain visible accumulations of thick mucous that cling to the bronchial walls and trachea, sometimes even 'stranding' across the lumen of the airway.

TREATMENT OF CHRONIC BRONCHIAL DISEASE

The Acute Exacerbation ("Acute-on-Chronic")

It is possible for dogs with CBD to present with acute-onset respiratory distress, cyanosis, and syncope, especially following or during an episode of paroxysmal cough. Affected dogs characteristically have dramatic bronchial and intra-thoracic tracheal collapse during expiration. Oxygen should be administered by face mask at the earliest possible opportunity, and an intravenous catheter placed in any available vein. Sedation with morphine (dogs only--0.5 mg/kg, SQ or IM) or diazepam (dogs @ 5 to 20 mg IV or cats @ 5 mg maximum, IV) is indicated in the conscious, anxious patient. The patient is given a single dose of methylprednisolone (1-2 mg/kg, IV). It may be safer to actually anesthetize particularly anxious patients with an intravenous, short-lived anesthetic (eg, propofol), intubate, then administer oxygen through an endotracheal tube. When the patient has been stabilized, thoracic radiographs should be obtained as soon as possible to determine the integrity of the lungs and airways. Even in extreme cases, it has generally not been helpful to suction mucous from the airways. Restriction to airflow in comatose patients is attributable to airway thickening and collapse rather than mucous accumulation.

Long-Term Management

Corticosteroids. Dogs with CBD derive significant benefit from the short-term administration of anti-inflammatory doses of corticosteroids. Orally administered corticosteroids not only have a rapid, anti-inflammatory effect and serve as a potent antitussive. Rapid resolution of cough is expected following onset of corticosteroids. This is true in patients with acute and chronic disease. Even when evidence of tracheobronchial collapse and/or pneumonia exists, ***short-term*** corticosteroids (up to 5-7 days) have an important role in managing the affected patient. Oral prednisolone is given at doses ranging from 0.2 to 0.5 mg/kg, twice daily in both dogs and cats. Once stable, most dogs can be effectively managed with a single dose given on alternate days.

The goal of corticosteroid therapy is *not* long-term management. The clinician should strive to administer the least effective dose possible for the shortest period of time needed to control the clinical signs. Exacerbation of cough is expected in the future. Therefore, it is preferred that steroids be administered selectively in these patients. I prefer to use steroid therapy in these patients as short-term rescue treatment.

(administration of corticosteroids via the respiratory tract can be accomplished with a Metered-Dose Inhaler [MDI]. MDI's have been modified for use in dogs as well as cats. Treatment with an MDI can be difficult. I see little to no benefit in the use of a MDI to administer corticosteroids over oral administration).

Antimicrobials. The role of *long-term antimicrobial therapy* appears to be underappreciated (at least in the veterinary literature) in managing patients with CBD. Although bacterial *infection* (pneumonia) is seldom

recognized as a co-factor in dogs with CBD, many pulmonologists (human medicine) consider "low-grade" bacterial colonization within the small airways to be a key factor in the pathogenesis of CBD. Although relatively uncommon, opportunistic infections (pneumonia) involving normal respiratory flora can become life-threatening in dogs with significantly compromised respiratory defense mechanisms, particularly tracheobronchial collapse and diminished mucociliary transport. The role of *B. bronchiseptica* as a complicating factor in the pathogenesis of CBD must not be underestimated. When in vitro culture and sensitivity results are not immediately available, the clinician is justified in prescribing antimicrobial. In the author's experience, antimicrobial therapy plays a critical role in the long-term management of CBD in dogs.

Several antimicrobial agents are available for use. Those most commonly prescribed are listed below:

DOXYCYCLINE 5 mg/kg, orally, q12 h; alternatively: 10 mg/kg orally, once daily);

AZITHROMYCIN (5 mg/kg, orally, once daily…recommended because of the compliance associated with once daily administration in dogs);

ENROFLOXACIN (2.5 to 5.0 mg/kg, orally, once daily) *caution when using with methyxanthine (aminophylline or theophylline) bronchodilators. …see below.*

Administration: For example, azithromycin would be prescribed for 14 to 21 days (5.0 mg/kg, once daily) for a patient with CBD. Following treatment, it is not uncommon for the patient's clinical signs to resolve for several weeks, or even months, followed by a gradual redevelopment of cough. In this case, the treatment regimen with azithromycin can be repeated with similar results expected. If an individual patient does become less responsive to therapy, another antimicrobial can be selected and administered in the same way.

Bronchodilators. The methylxanthine bronchodilators, theophylline and aminophylline (theophylline ethylenediamine), are often described as the preferred treatment for long-term management in dogs (extended-release theophylline, initially 5.0 mg/kg, orally, q12h; with gradual increase up to 10 mg/kg). NOTE: USE OF THEOPHYLLINE WITH a FLUOROQUINOLONE antimicrobial (eg, Baytril®) CAN CULMINATE IN TOXIC ACCUMULATION OF THEOPHYLLINE…it is therefore recommended to reduce the theophylline dose by 30% if used concurrently with a fluoroquinolone. Alternatively, beta-adrenergic bronchodilators (terbutaline and albuterol) can be used (small dogs: 0.625 to 1.25 mg [total dose] orally, q12h) (larger dogs: up to 2.5 to 5.0 mg/kg, orally, q12h). In my experience, the long-term benefit derived from bronchodilator therapy varies considerably among individual patients.

Antitussives. Cough suppressant therapy has limited value as a first-line drug in the management of CBD. Over-the-counter products (e.g., dextromethorphan) are simply not effective. Narcotic cough suppressants such as hydrocodone can be prescribed for their antitussive affect in dogs, but the risk of sedation and (client) abuse has to be considered. Clearly narcotic antitussive agents should not be used alone in the management of CBD.

Aerosol Therapy. The greatest benefits to aerosol therapy are derived in patients with severe, acute-onset signs, an excessive accumulation of bronchial and tracheal secretions, and those with secondary bronchial infections. Treatment, if needed, entails aerosolization of 5 to 7 mL of sterile saline (with or without antibiotics added to the solution) at least 3 to 4 times daily. Each treatment requires 15 to 20 minutes.

PROGNOSIS

In the stabilized, non-acute dog with documented CBD, even when airway collapse is determined to involve both bronchi and the entire intrathoracic trachea, the client should understand that, although the prognosis is fair to good, the goals of treatment are control and long-term management, not cure. Left untreated, CBD could progress to bronchiectasis and, although uncommon in dogs, emphysema (chronic obstructive pulmonary disease or COPD). The objective of therapy, therefore is to delay progression of the underlying respiratory disease. Treatment is life-long. However, the results can be rewarding and excellent quality of life can be achieved for years.

Vaccination. Administration of intranasal or oral vaccine containing *Bordetella bronchiseptica* antigen has **no role in the treatment** of chronic cough in the dog. Vaccine is appropriate only when used to mitigate the consequence of exposure to *B. bronchiseptica* and/or parainfluenza virus and should only be administered to healthy dogs. There are no studies to support therapeutic administration of either the intranasal or the parenteral vaccine.

However, vaccination of dogs with CBD against *B. bronchiseptica* is indicated for any patient at risk of exposure to populations of dogs. However, it is my recommendation that if *B. bronchiseptica vaccination is indicated, neither the IN or ORAL vaccine should be used in patients with CBD.* Reason: ALL Intranasal and ORAL *B. bronchiseptica* vaccines contain attenuated (live) bacteria, sometimes in combination with a modified-live parainfluenza virus vaccine (IN). Post-vaccination replication of the vaccine antigen on the respiratory mucosa could infect the respiratory mucosa and actually precipitate an acute respiratory event.

ADDITIONAL READING

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2023 VACCINES & VACCINATION

Products, Protocols, and Controversies

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Each year this 'Vaccines & Vaccinations' manuscript is updated to reflect current changes in the Canine and Feline Vaccination Guidelines, as well as to provide additional updates on companion animal vaccines and vaccination protocols. This manuscript addresses an international perspective on best practice guidance for companion animal vaccine selection and administration.

In September 2020, the American Animal Hospital Assoc. (AAHA) joined with the American Assoc. of Feline Practitioners (AAFP) in releasing the latest update to the Feline Vaccination Guidelines….then, in 2022, AAHA released an updated version of the Canine Vaccination Guidelines….and, as happens when writing such documents via "committee", controversial issues arise. There is no exception with the latest Guidelines.

Throughout these notes, I will occasionally include recommendations that vary from those listed in published Vaccination Guidelines. These comments, identified by a

Text-Box, are for your consideration only but do represent the opinions of experts in the field of immunology, internal medicine, and immunization.

In the face of the COVID-19 pandemic, demand for veterinary health care has been high…but, anecdotal reports suggest increasing numbers of dogs/cats presented to veterinary hospitals today are "overdue" for a routine booster, especially for the non-core vaccines. The notes that follow include guidance on vaccination management of the *overdue* patient (dog and cat). These comments are derived from personal conversations I've had with representatives of individual manufacturers pertaining to individual products.

Reminder: Vaccination Guidelines for the Dog and Cat are recommendations only; they are NOT requirements. In practice, vaccination protocols for individual animals will (and should) vary from published recommendations based on the clinician's assessment of health issues, age, risk assessment of the individual animal, etc. The reader is reminded that requirements for rabies vaccination are NOT flexible…*veterinarians are expected to practice within the context of applicable State/local/provincial statutes as they pertain to rabies and rabies vaccination.*

NOTE: *Published vaccination recommendations for the dog and cat are based, whenever possible, on the results of current scientific studies. However, scientific studies are not always available to support all recommendations. In these notes, as is the case with published Vaccination Guidelines, recommendations are based on credible science, expert opinion, as well as current knowledge of immunology and infectious disease. In addition, readers may notice variances between recommendations put forward by vaccine manufacturers and published Guidelines. Variances found in TABLES 1 & 2 have been reviewed by academicians as well as vaccine manufacturers; recommendations outlined below are considered to be safe, effective, and consistent with best immunization practices today.*

TABLE 1: VACCINATION of PUPPIES & ADULT DOGS

CORE Vaccines	Administration	Booster Recommendations
Combination product administered as: **Distemper Virus** (MLV *or* Recombinant) **+ Parvovirus** (MLV only) **+ Adenovirus-2** (MLV only) (Several vaccine options are available that include combinations of core and non-core vaccines)	Beginning as early as 6 weeks of age, administer sequential doses of a combination vaccine at an interval of 2 to 4 weeks until at least 16 weeks of age. NOTE: recommending a single dose at 8 weeks; and 12 weeks; 16 weeks of age is common practice throughout North America and represents an excellent primary series. **NOTE:** ***a minimum interval of 2 weeks between any 2 doses of vaccine is strongly recommended*.** **NEW:** 4th Dose Option: In areas where the risk of exposure to distemper and (especially) parvovirus is high, an additional (4th) dose is recommended at 18 to 20 weeks of age to assure minimizing the risk of vaccine interference by maternally derived antibody (MDA).	Administer a single dose (of a combination product) within 1 year following the last dose in the initial series. Administer subsequent boosters every 3 years (or longer). **NOTE**: MLV Parainfluenza virus (CPiV) vaccine, commonly available in combination with distemper-parvovirus-adenovirus vaccine, provides limited protection against CPiV. Intranasal (mucosal) vaccination against CPiV is recommended (see below). The rCDV vaccine is minimally interfered with by maternally derived antibody and offers the opportunity to immunize puppies against CDV earlier than MLV Distemper vaccine.

Rabies Virus (Killed only) 1-Year & 3-Year Labeled vaccines are available. (NOTE: MS and WV do not recognize use of a 1-Year labeled Rabies Vaccine: The CA only permits the use of rabies vaccine that has been authorized by the State.	A single dose of rabies vaccine is administered at not less than 12 weeks of age. Most, but not all, States permit administration of the initial rabies vaccine dose at any time between 12 and 16 weeks of age. Although Rabies vaccination of dogs is NOT required in all States, veterinarians are strongly encouraged to recommend vaccination of ALL dogs seen by the practice. \	Schedule a second dose to be administered not later than 1 year following administration of the 1st dose, *regardless of the dog's age at the time the initial dose is administered.* Then…every 3 years thereafter, *depending on the product label*. NOTE: some jurisdictions within States still require annual rabies vaccination for dogs. If a 3-Year labeled rabies vaccine is administered as the 1st dose, a second (booster) dose must be administered with 1 year following administration of the 1st dose, *regardless of the dog's age at the time the initial dose is administered.*

NON-CORE Vaccines	Administration	Booster Recommendations
INTRANASAL (IN) administration only ***B. bronchiseptica*** (avirulent live bacteria) Bivalent products are available that include: **Canine Parainfluenza Virus** (MLV) Trivalent products are available that include: **Canine Adenovirus-2** (MLV)	Administer a single dose by the intranasal route at 12 or 16 weeks of age. IN vaccine may be administered as early as 3 to 4 weeks of age as maternally derived antibody does not interfere with the local (mucosal) immune response. (Early vaccination is generally limited to use in puppies housed in a high-risk environment, eg, animal shelter)	Where risk of exposure is sustained, administer a single dose 1 year following the last dose administered then annually thereafter. IN vaccination with *B. bronchiseptica* + CPiV is preferred over parenteral vaccination for either *B bronchiseptica* or CPiV. > Expect protection within 3 to 7 days following administration of a single IN dose. > Based on challenge studies in dogs, the duration of immunity has been shown to be 12 to 14 months following a single inoculation.
ORAL **administration only** (monovalent) ***B. bronchiseptica*** (avirulent live bacteria) **or** ***B. bronchiseptica*** (avirulent live bacteria) + **MLV CPiV** ***(New: Sept 2022)***	Oral: Administer a single initial dose into the buccal pouch administered as early as 8 weeks of age. Oral: A single dose is administered as a spray into the oral cavity as early as 7 weeks of age.	Where risk of exposure is sustained, administer a single dose 1 year following the last dose administered then annually thereafter. > Based on challenge studies in dogs, the duration of immunity has been shown to be 12 to 14 months following a single inoculation. > NOTE: the combination oral *B bronchiseptica* + CPiV has not been studied independently of the manufacturer. The Duration of Immunity has not been established (per the manufacturer).

PARENTERAL **administration only** (monovalent) ***B. bronchiseptica*** (cellular antigen extract-inactivated)	Initially, 2 doses (required) are administered subcutaneously 2 to 4 weeks apart, beginning as early as 8 weeks of age. The manufacturer recommends an annual booster thereafter. Administration of a parenteral *B. bronchiseptica* vaccine with or subsequent to administration of an intranasal *B. bronchiseptica* vaccine has not been definitively shown to enhance protection in challenged dogs.	This vaccine, which has been available in the US for several years, is now being promoted as a "Booster Shot", presumably for dogs that received an initial oral or intranasal dose. There are no studies available that support this regimen. Duration of immunity for the parenteral *B bronchiseptica* vaccine is not known. Mucosal (IN or oral) administration of vaccine induces a local IgA antibody response (at the site of infection) and is considered to provide superior, longer-lasting protection compared to the parenteral vaccine.
NON-CORE Vaccines	**Administration**	**Booster Recommendations**
Leptospira spp. (killed) 4-serovar **NOTE**: *use of a 2-serovar Leptospira vaccine is no longer recommended.*	Primary (initial) vaccination: 2 doses, 2 to 4 weeks apart, are required. **NOTE**: Small Breed Dogs (<20 pounds): delaying initial doses until 2 weeks after completion of the CORE vaccine series has been recommended as means for mitigating risk of an acute adverse reaction (eg, angioedema).	Where risk of exposure is sustained, administer a single dose 1 year following completion of the *2-dose primary vaccination*, then every year thereafter. (The 4-serovar Leptospira vaccines have been subjected to additional removal/filtration of reactogenic excipients. Reports from practitioners suggest the 4-seorvar vaccines are significantly less reactogenic compared to the 2-serovar vaccines.)

Incorporation of *Leptospira* vaccines as part of the CORE protocol is being recommended by several academic internists on the basis that infections are more common that realized and testing limitations.		(the 2-serovar leptospira vaccines are discontinued.)

Borellia burgdorferi (Lyme Disease) 4 types of vaccine are currently available: - Recombinant (OspA) - Chimeric/Recombinant (OspA + chimeric OspC) - Killed, whole-cell (OspA) - Killed, whole-cell (OspA + OspC)	Primary (initial) vaccination: 2 doses, 2 to 4 weeks apart, are required regardless of the dog's age and regardless of the type of vaccine selected. **NOTE**: Small Breed Dogs (<20 pounds): delaying initial doses until 2 weeks after completion of the CORE vaccine series has been recommended as means for mitigating risk of an acute adverse reaction (eg, angioedema). If exposure risk is high and delaying vaccination is NOT an option, it is reasonable to administer Lyme Disease vaccine in conjunction with core vaccines. Use of a recombinant vaccine is recommended to mitigate risk of an acute adverse reaction.	Where risk of exposure is sustained, administer a single dose 1 year following completion of the *initial* 2-dose vaccination, then every year thereafter. > OspA antibody is widely regarded as the primary protective antibody and is the focus of the human Lyme Disease vaccine currently in clinical studies in the US. > OspC antibody has not been shown to provide protection independently of OspA antibody. > OspC antibody is known to be particularly short-lived (weeks only) vs. OspA antibody (~13 months).

NON-CORE Vaccines	Administration	Booster Recommendations
Canine Influenza Virus (**H3N8**) (killed) *Surveillance studies on H3N8 suggest that this strain of CIV has self-eradicated. Vaccination is not recommended (RBF)* -and- **Canine Influenza Virus** (**H3N2**) (killed)	2 initial doses, 2 to 4 weeks apart are required. The manufacturer recommends annual boosters where the risk of exposure is sustained.	Where risk of exposure is sustained, administer a single dose 1 year following completion of the *initial* 2-dose vaccination, then every year thereafter. *Sporadic cases were confirmed in several Gulf Coast states during 2022. The virus life-cycle is limited to 3-4 weeks. Infections are typically self-limiting.*

NOTE: Canine coronavirus vaccination provides minimal to no protection and is not recommended.

NOTE: *Crotalus atrox* (Western Diamondback rattlesnake) vaccine should only be used in dogs with a defined risk for exposure. Follow the manufacturer's recommendations for dosing: (www.redrockbiologics.com)

NOTE: An attenuated (MLV) Measles Virus (MV) vaccine (in combination with distemper virus vaccine) is available for administration to young dogs **(between 6 and 12 weeks of age…NOT older than 16 weeks of age**) to protect against canine distemper virus (CDV). In dogs, measles virus vaccine induces heterotypic immunity regardless of maternal antibody presence. Measles Virus vaccine **must** be administered by the **IM route (1.0 mL)**. The recombinant canine distemper virus vaccine also immunizes puppies dogs against distemper virus despite the presence of maternal antibody (without age and administration restrictions) and is therefore recommended over the combination Distemper-Measles Virus Vaccine. (personal opinion RBF)

PUPPIES & ADULT DOGS OVERDUE for VACCINATION

NOTE: Studies focused on dogs that are overdue for routine vaccination have not been published. Recommendations that follow are based largely on expert opinion and recommendations from vaccine manufacturers.

PUPPIES: CORE Vaccines (excluding rabies). Puppies that are overdue during the initial vaccine series (CDV-CPV-CAV):

Puppies should NOT receive a dose of a combination core vaccine at intervals of less than 2 weeks (to avoid cytokine interference). There are NO maximum interval limitations because a *single dose* of a core (CDV-CPV-CAV) will immunize in the absence of maternal antibody (dogs ≥ 20 weeks of age).

Conventional Practice: administer 2 doses, 2-4 weeks apart, for puppies between 16 and 24 weeks of age at the time of initial presentation. A single booster, administered 1 year later, is recommended, then every 3 years or longer thereafter.

PUPPIES: OVERDUE for the initial RABIES Vaccination: State (or Local) and Provincial law dictates when a dog is overdue for the initial rabies vaccination. Throughout the US, a dog that receives a dose of rabies vaccine PRIOR to 12 weeks of age is not considered to be "currently vaccinated". Regardless of a dog's age at the time the initial rabies vaccination is administered, a booster dose is required within 1 year.

(For State-level requirements see: www.rabiesaware.org)

Dogs Overdue for Vaccination (continued)

PUPPIES: NON-CORE Vaccines. **Puppies that are overdue for re-vaccination during the initial vaccine series:**

Parenterally administered non-core vaccines are inactivated (killed) and 2 initial doses (priming dose + immunizing dose) are essential to induce lasting protective immunity. The 2 doses should be administered not less than 2 weeks apart and not more than 6 weeks apart. If the interval exceeds 6 weeks, it is recommended to re-administer 2 doses, 2 to 4 weeks apart.

Intranasal and oral vaccines only require a *single dose* to prime and immunize. Administration of 2 consecutive doses, 2 to 4 weeks apart, is not required.

ADULT DOGS: CORE Vaccines (excluding rabies). Adult dogs that are overdue for a CORE vaccine booster:

Administer a single dose of a combination core vaccine *regardless of the time elapsed since the previous dose was administered.* Administering 2 doses of a core vaccine to an adult dog that is overdue for a booster is not necessary.

ADULT DOGS: NON-CORE Vaccines. Adult dogs that are overdue for a NON-CORE vaccine booster:

Minimal data are available on which to base booster recommendations for an adult dog that is overdue for a booster dose of a non-core vaccine. Recommendations listed are based on discussions with immunologists and manufacturer's representatives and may vary (slightly) depending on the individual product.

Overdue for Lyme Disease and/or parenteral *Bordetella bronchiseptica* booster: dogs that are within 13 months of a previous dose of vaccine for Lyme Disease may receive a single dose. Dogs exceeding a 13-month interval should receive 2 consecutive doses 3 to 4 weeks apart. There are NO PUBLISHED DATA regarding recommendations for re-vaccinating dogs overdue for a parenteral *B. bronchiseptica* vaccine as the duration of immunity is generally considered to be < 1 year. 2 doses, 2 to 4 weeks apart is a reasonable recommendation for any dog overdue for a parenteral booster against *B. bronchiseptica.*

Overdue for Leptospira booster: dogs that are within 13 to 16 months of a previous dose may receive a single dose. Dogs exceeding a 16-month interval should receive 2 consecutive doses 3 to 4 weeks apart.

Overdue for intranasal or oral Bordetella booster: administer a *single dose* regardless of the number of years that have lapsed since the last dose was administered.

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Overdue for Canine Influenza Virus booster: the H3N8 CIV vaccine is NOT recommended (see comments in the table above). Dogs that are within 18-months of a previous dose of the H3N2 strain of CIV, *and are known to be at risk for exposure,* may receive a single dose. Dogs exceeding an 18-month interval should receive 2 consecutive doses, 3 to 4 weeks apart. (NOTE: this recommendation has not been scientifically established).

ADULT DOGS: Overdue for RABIES.

Where required, there is NO tolerance for a dog that is overdue for a rabies booster…a dog must be considered "overdue" and "not currently vaccinated" if just one (1) day beyond the labeled duration of immunity (1-Year or 3-Year). (EXCEPTION…*if a 3-Year labeled rabies vaccine is administered as the INITIAL dose, the dog is considered to be "currently vaccinated" for a period of 1 year only* (as determined by State and local regulations/statutes…not immunology).

RABIES Re-vaccination: Most States follow the recommendation published in the *2016 Rabies Compendium* which states: administer a single dose, after which the dog will be considered *immediately* "currently vaccinated" (…and no longer "overdue"). This is regardless of the time that has lapsed since the last dose was administered. HOWEVER, the duration of immunity, following re-vaccination of the overdue patient, may be determined by State, Provincial, or local regulations/statutes. (For UNITED STATES requirements see: www.rabiesaware.org)

NOTE: the *Compendium on Animal Rabies Protection and Control*, as published by the Natl Assoc. of State Public Health Veterinarians, Inc., is NOT a legal or statutory document. State and local regulations/statutes will vary from recommendations outlined in the *Rabies Compendium.*

TABLE 2: VACCINATION of KITTENS & ADULT CATS

CORE Vaccines	Administration	Booster Recommendations
Combination vaccine for parenteral (SQ) administration: **Panleukopenia (MLV)** **+ Herpesvirus (MLV)** **+ Calicivirus (MLV)**	3 doses of a parenteral vaccine are recommended between 8 and 16 weeks of age.	Administer one booster dose of a combination vaccine 1 year following completion of the initial series; then administer subsequent boosters every 3 years thereafter. (**NEW**) Current feline Guidelines state: "Consider [revaccination] at 6 months of age"…rather than the conventional

NOTE: Feline Injection-Site Sarcoma (FISS): A combination, killed virus (adjuvanted) vaccine is currently available for parenteral administration of care vaccines in cats. However, many authors and academicians concur with recommendations of the *WSAVA and European Advisory Board on Cat Diseases (2015) which recommend veterinarians avoiding use of killed (adjuvant-containing) vaccines in cats.* (RBF) All MLV and recombinant feline vaccines are adjuvant-free *unless combined with a killed vaccine*.	**Example:** 8 weeks; and 12 weeks; and 16 weeks of age. *… an additional dose at 18 to 20 weeks of age* should be recommended where risk of exposure is considered high.	recommendation to administer the first booster 1 year following the last dose in the initial series. HOWEVER… *The "6-months of age" booster recommendation is based on only 2 studies (both from 2012) suggesting one-third of kittens vaccinated at 16 weeks of age will experience maternal antibody interference with vaccination.* NOTE: it is the author's personal opinion that this recommendation is NOT warranted due to: 1) the lack of sufficient studies documenting maternal antibody interference, and, 2) the absence of reports suggesting that vaccinated cats fail to be immunized and are becoming infected following completion of the primary series.
MUCOSAL **Administration Only** **Panleukopenia (MLV)** **+ Herpesvirus (MLV)** **+ Calicivirus (MLV)** -and- **+ Herpesvirus (MLV)** **+ Calicivirus (MLV)**	Administer a single dose of vaccine at 12 weeks of age. The entire 0.2 mL/dose product is administered onto the nose web. The 0.5 mL/dose product is administered via 1 drop onto each eye and the remainder onto the nose web. Cats vaccinated prior to 12 weeks of age should receive a second dose prior to 16 weeks of age.	The duration of immunity for the mucosal vaccines has not been established. It is recommended that cats receive a single dose annually if a mucosal vaccine is used. Parenteral (MLV) panleukopenia vaccine is recommended over intranasal vaccine. **NOTE:** Following administration of an intranasal herpesvirus-calicivirus vaccine, some kittens may experience post-vaccinal sneezing (sometimes requiring treatment).

(Vaccine is available as either a 0.5 mL/dose or 0.2 mL/dose)		

CORE Vaccines	Administration	Booster Recommendations
- **Recombinant Rabies (rRabies)** Available as 1-Year & 3-Year labeled vaccine. **Adjuvant-free** -or- **- Inactivated (killed) Rabies** Available as 1-Year & 3-Year labeled vaccine. **Adjuvanted.**	A single dose of rabies vaccine is administered at not less than 12 weeks of age. Most, but not all, States permit administration of the initial rabies vaccine dose at any time between 12 and 16 weeks of age. Although rabies vaccination of cats is NOT required in all States, veterinarians are strongly encouraged to recommend vaccination of ALL cats seen by the practice.	Schedule a second dose to be administered not later than 1 year following administration of the 1st dose, *regardless of the cat's age at the time the initial dose is administered.* Then… every 3 years thereafter, *depending on the product label.* If a 3-Year labeled rabies vaccine is administered as the 1st dose, a second (booster) dose must be administered with 1 year following administration of the 1st dose, *regardless of the cat's age at the time the initial dose is administered.*
NON-CORE Vaccines	**Administration**	**Booster Recommendations**
- **Feline Leukemia Virus (rFeLV)** (Recombinant viral-vectored vaccine) **Adjuvant-free** -or- **- Feline Leukemia Virus** (killed vaccine) **Adjuvanted** -or- - **Subunit (recombinant) FeLV** Inactivated vaccine **Adjuvanted**	Recommended as CORE for all kittens (due to the high degree of susceptibility if exposed): Administer 1 dose as early as 8 weeks of age followed by a 2nd dose AT LEAST 3-4 weeks later. (Avoid intervals less than 3 weeks)	Manufacturers recommend annual re-vaccination for adult cats at risk of exposure. (NOTE: Adult cats enjoy "age-related resistance" to FeLV infection beginning around 6 to 8 months of age. It is difficult [although not impossible] to infect an adult cat with FeLV. Therefore, some authors recommend re-vaccination every 2 years for adult cats considered to be at (very high) risk for exposure, ie, they fight…but, not very well.

Chlamydia felis (former names: *Chlamydia psittaci* and *Chlamydophila felis*) (Available as either: Avirulent live, adjuvant free vaccine, or killed, adjuvanted)	2 initial doses 3 to 4 weeks apart, if indicated.	NOTE: *indications for use of this vaccine are limited. Clinical signs associated with infection are generally limited to conjunctiva …parenteral vaccines confer limited protection at the level of the conjunctival mucosa.* Duration of immunity has not been established. *Among infected cats, topical antibiotic treatment is effective.*

Feline non-core vaccines (cont)

NON-CORE Vaccines	Administration	Booster Recommendations
INTRANASAL **Administration Only** Feline *Bordetella bronchiseptica* Avirulent Live Bacteria- (non-adjuvanted)	A single intranasal (IN only) dose (0.2 mL total volume) onto the nose web. Administer as early as 4 weeks of age, if indicated.	The manufacturer does not stipulate booster recommendations. NOTE: *<u>indications for use of this vaccine are limited</u>.* While clinically *significant B. bronchiseptica infections in cats are uncommon, most (all?) occur in kittens.*

Virulent Systemic (VS) Calicivirus (May also be referred to as: "hypervirulent calicivirus") Killed [adjuvanted] virus; contains 2 strains ("dual-strain") of calicivirus. Currently available in combination with other killed (adjuvanted) feline virus vaccines.	Administer 2 initial doses subcutaneously, 2 to 4 weeks apart, if indicated. Only recommended for use in housing environments where cats have a high risk for exposure to infected cats or where a history of virulent systemic calicivirus has been documented.	The manufacturer recommends annual vaccination where exposure risk is sustained. Disease prevalence is considered low, even within high-density housing environments (eg, shelters). NOTE: *this vaccine is not recommended for routine use.*

FELINE VACCINATION (notes)

<u>NOTE</u>: Unless specifically indicated for intranasal administration, all feline vaccines should be administered by the SQ route.

<u>NOTE</u>: The Feline Infectious Peritonitis (FIP) vaccine (intranasal only) is ***not recommended*** due to lack of demonstrated efficacy. The World Small Animal Veterinary Association (Vaccine Guidelines Group) does not recommend administration of the FIP vaccine; this author does NOT recommend use of the FIP vaccine. *There's a trend here!*

<u>NOTE</u>: The FIV Vaccine has been discontinued in the US and Canadian markets.

NOTE: The risk of administering an attenuated virus vaccine to a healthy FeLV or FIV infected cat has not been studied…the risk that an FeLV or FIV-infected cat might develop a significant adverse event (reaction) subsequent to administration of a MLV vaccine has never been demonstrated and today is NOT considered a reason to avoid use of MLV vaccines in accordance with routine protocols. Current Feline Vaccination Guidelines (2020) *no longer recommend against* vaccinating FeLV or FIV "positive" cats with MLV vaccines.

KITTENS & ADULT CATS OVERDUE FOR VACCINATION (Revised)

Studies focused on cats that are overdue for routine vaccination have not been published. The following recommendations represent expert opinion and are intended to provide a practical approach to immunizing cats when conventional vaccination recommendations have not been followed.

KITTENS: CORE Vaccines (excluding rabies). Kittens that are overdue for re-vaccination during the initial vaccine series (FVR-C-P *and* FeLV):

Kittens should NOT receive a dose of a combination core vaccine at intervals of less than 2 weeks (to avoid cytokine interference). There are NO maximum interval limitations because a single dose of a core **MLV** vaccine (FVR-C-P) will immunize in the absence of maternal antibody (cats ≥ 20 weeks of age).

Cats Overdue for Vaccination (continued)

Conventional Practice: administer 2 doses, 2-4 weeks apart, for kittens between 16 and 24 weeks of age at the time of initial presentation. A single booster, administered 1 year later, is recommended, then every 3 years or longer thereafter.

FeLV is recommended as CORE for Kittens: 2 doses of FeLV are required to immunize whether using a killed (which is adjuvanted) or recombinant (adjuvant-free) vaccine. There are currently NO established recommendations for the management of kittens that are 'overdue' for their 2nd (required) dose of FeLV. (Serologic testing for FeLV antibody is NOT a valid assessment of immunity OR response to vaccination). If the 2-dose vaccination interval exceeds 6 weeks, conventional recommendations suggest re-vaccination with 2 doses, 2 to 4 weeks apart.

Recommendations are different if using inactivated (killed) core vaccines. I recommend against the use of inactivated (killed) core vaccines (all of which contain adjuvant) for kittens and cats. (RBF)

KITTENS: OVERDUE for the initial RABIES Vaccination: State (or Local) and Provincial law dictates when a cat is overdue for the initial rabies vaccination. Throughout the US and Canada, a cat that receives a dose of rabies vaccine PRIOR to 12 weeks of age is not considered to be "currently vaccinated". Regardless of a cat's age at the time the initial rabies vaccination is administered, a booster dose is required within 1 year.

(For State-level requirements see: www.rabiesaware.org)

KITTENS: NON-CORE Vaccines. Kittens that are overdue for re-vaccination during the initial vaccine series:

Bordetella bronchiseptica vaccine is avirulent-live and administered by the intranasal route (IN) only. A single dose will immunize a kitten. That's why they aren't 'overdue' for a 2nd dose. Maternally derived antibody does NOT interfere with IN vaccination.

Chlamydia felis vaccination requires administration of 2 *initial* doses, 3 to 4 weeks apart, regardless of the vaccine administered (MLV or killed). Recommendations for kittens that are overdue for the 2nd dose are not published. If the 2-dose vaccination interval exceeds 6 weeks, conventional recommendations suggest re-vaccination with 2 doses, 3 to 4 weeks apart.

ADULT CATS: CORE Vaccines (excluding rabies): Adult cats that are overdue for a CORE vaccine booster:

Administer a single dose of a combination core vaccine *regardless of the time elapsed since the previous dose was administered.* Administering 2 doses of a core vaccine to an adult cat that is overdue for a booster is not necessary.

ADULT CATS: NON-CORE Vaccines: Adult cats that are overdue for a NON-CORE booster:

Minimal (to no) data are available on which to base booster recommendations for an adult cat that is overdue for a booster dose of a non-core vaccine. Recommendations listed are based on discussions with immunologists and manufacturer's representatives and may vary (slightly) depending on the individual product.

Overdue for *Bordetella bronchiseptica* booster: NOTE: the manufacturer does not stipulate booster recommendations for this vaccine…much less for cats that are 'overdue'. Recommendation: administer a single dose, regardless of the time lapsed since the last dose was administered…but ONLY if really deemed necessary…(I do NOT recommend the use of this vaccine in adult cats…RBF).

Overdue for *Chlamydia felis* booster:

Administer a single dose of an MLV (attenuated) vaccine, regardless of the time lapsed since the last dose.

Administer 2 doses of an inactivated (killed) vaccine, 3 to 4 weeks apart, to a cat that is more that 12 months since the last dose was administered.

(NOTE: the ability of either vaccine to protect adult cats has not been established…I do NOT recommend the use of *C. felis* vaccine in adult cats. (RBF)

Overdue for FeLV booster: this is complicated…compared to kittens, adult cats (by 6 to 8 months of age) are significantly tolerant of FeLV infection. For this reason, differences of opinion exist with respect to *conventional booster intervals* (annual vs. biennial). If recommending revaccination to an overdue (more than 2 years since the previous dose was administered) cat, it would be reasonable to recommend 2-doses, 3 to 4 weeks apart, be administered. Thereafter, administer a single dose every 1 to 2 years as determined by life-style and risk for exposure.

ADULT CATS: Overdue for RABIES booster.

Where required, there is NO tolerance for a cat that is overdue for a rabies booster…a cat must be considered "overdue" and "not currently vaccinated" if just one (1) day beyond the labeled duration of immunity (1-Year or 3-Year). (EXCEPTION…*if a 3-Year labeled rabies vaccine is administered as the INITIAL dose, the cat is considered "currently vaccinated" for a period of 1 year only.*

RABIES Re-vaccination: Most States follow the recommendation published in the *2016 Rabies Compendium* which states: administer a single dose, after which the cat will be considered *immediately* "currently vaccinated" (…and no longer "overdue"). This is regardless of the time that has lapsed since the last dose was administered. HOWEVER, the duration of immunity, following re-vaccination of the overdue patient, may be determined by State, Provincial, or local regulations/statutes. (For State-level requirements see: www.rabiesaware.org)

NOTE: the *Rabies Compendium*, as published by the Natl Assoc. of State Public Health Veterinarians, Inc., is NOT a legal or statutory document. State and local regulations/statutes may vary from recommendations outlined in the *Rabies Compendium.*

Update on FeLV and FIV

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The feline retroviruses, FeLV and FIV, today are well recognized as the cause of immune-suppressive disease in cats throughout the world. Clearly among the most complex infections affecting the cat, a retroviral infection demands an immune response that is robust and sustained if the infected cat is to survive long-term. Both innate immune responses (neutrophils, macrophages, and antigen presenting cells [APCs]) as well as adaptive immunity (B-lymphocytes and T-lymphocytes) are critical factors…all of which make the outcome of exposure difficult to predict.

Generally, FeLV causes the most significant clinical infection, compared to FIV. FeLV is an *oncogenic* retrovirus and, unlike FIV, is capable of transforming infected cells into malignant cells (integrational mutagenesis occurs in around 10% of FeLV infected cats). In the past, FeLV was considered the most common cause of death from infectious disease. Today, however, the incidence of FeLV-related disease has clearly declined significantly from what it was just 20 years ago. While vaccination accounts for some of that decline, the ability to perform rapid, accurate retrovirus testing of cats is recognized to be the principal reason behind the global decrease in FeLV incidence.

Age-Related Resistance: It's important to note that susceptibility to FeLV infection is greatest (infection risk is actually very high) during the first 6 months of a cat's life. After that, "age-related resistance" makes *clinical* infection (viremia, immunosuppression, and viral shedding) unlikely…this has been attributed to maturation of the immune system in an adult cat and production of one (or more?) of the interleukins as well as decreased numbers of FeLV binding sites on adult cat monocytes. In the immunologically naïve kitten, exposure to FeLV seems most likely to result in infection and development of progressive disease and death.

Consider this: the majority of the adult cats you have ever diagnosed with FeLV infection were likely infected as kittens.

NEW: recent advances in diagnostic technology (for **FeLV proviral DNA**) have revealed significantly new and important information concerning FeLV infection: *while a POSITIVE FeLV test (SNAP or IFA) correlates strongly with active infection…a NEGATIVE test does NOT necessarily indicate the cat is free of infection…read on.*

Susceptibility to infection by the Feline Immunodeficiency Virus (FIV), on the other hand, does not change with a cat's age. Risk among adults is similar to that in kittens. Furthermore, FIV infection is not associated with the same spectrum of clinical consequences seen in FeLV-infected cats. Although FIV does cause an acquired immunodeficiency syndrome, one that shares many similarities with HIV infection in humans, the prognosis of FIV infection is generally going to be better than that of FeLV, especially when level of medical care the cat receives during the course of infection is high. Opportunistic infections are common, but FIV-infected cats tend to live longer (given the opportunity to do so) than FeLV-infected cats. Many FIV-infected cats are known to die of age-related causes *not* directly linked to their retroviral infection. And…as such, FIV has not had the impact on the feline population that FeLV has. You can see why the FIV vaccine had little, to no, impact on survivability.

FeLV and FIV: The Diagnostic Paradigm Shift

Advances in scientific technology are wonderful things…they can also be frustrating. And such is the case with FeLV diagnostic testing. As those of us who have practiced veterinary medicine for a while know, one of the most significant diagnostic technologic advances introduced over the last 20 years has been the ENZYME-LINKED IMMUNO-SORBENT ASSAY, or **ELISA,** eg, the well-known IDEXX "SNAP Combo Test" or commercial microwell test kits. The ability to perform in-hospital testing (and do it in about 8-minutes) for both feline leukemia virus (FeLV) **antigen** and feline immunodeficiency virus (FIV) **antibody**, is clearly among the most important value-added laboratory services offered by veterinarians today. For FeLV…a POSITIVE Antigen (p27) test result is (appropriately) interpreted as an "active infection"; while a NEGATIVE test result is often interpreted as "*NOT* infected". *However,* all is not what it appears…advanced technology is changing our understanding of FeLV pathogenesis, which may change our recommendations for cats with a NEGATIVE test result, and may even impact vaccination strategies for cats deemed to be at risk.

Here's what's going on…the "advanced technology" of which I speak centers around several studies that have employed molecular diagnostic technology (PCR-based) to gain greater "resolution" into the consequences of FeLV exposure in cats. In particular, the ability to detect **FeLV *proviral DNA***[3] has allowed the opportunity to look for infection in places not "visible" to IFA or conventional ELISA test technology. Historically, it has been stated that most cats, following FeLV exposure and infection, mount a robust immune response and eliminate the virus (NEGATIVE SNAP test result); a smaller percentage would develop persistent infection, develop clinical illness, and frequently die from complications linked to profound immune suppression (POSTIVE SNAP test result).

It's the cat with the NEGATIVE (by IFA or ELISA) test result that's at issue here. With the ability to now look into cells, particularly bone marrow lymphocytes, it is apparent that cats having a NEGATIVE IFA or ELISA test may, in fact be POSITIVE. Based on the ability to detect FeLV proviral DNA of challenged, IFA and ELISA Negative cats, "regressive" (aka, latent) FeLV-infected cats can now be identified…the so-called

[3] **Proviral DNA:** feline retroviruses are RNA viruses. The use of the term "DNA" in reference to FeLV may be confusing. However, during retrovirus infection, through production of the unique enzyme reverse transcriptase, FeLV is able to duplicate its own single-stranded viral RNA making a double-stranded provirus…referred to as "proviral DNA"…which integrates into the infected cat's genome.

"hidden virus" residing in healthy appearing cats. And it happens more often that we realized in the pre-proviral DNA days.

As will be described in the lecture, investigations into FeLV pathogenesis using PCR technology have revealed better understanding on the consequences of FeLV exposure. *Generally* (subtle variations occur), exposure takes on 1 of 4 defined pathways:

1) **abortive** infection; the immune response rapidly neutralizes virus and eliminates the infection (these infections may actually occur commonly following natural exposure)…but, for the clinician, the incidence of abortive infections is 'moot'; it's unlikely you would ever detect this cat in practice as they become negative for p27 antigen; negative for proviral DNA, and negative for culturable virus.

2) **progressive** infection; most often occurring in young cats/kittens, progressive infection is associated with persistent viremia (beyond 16 weeks), rapid onset of clinical signs, immune suppression and frequently death (this is the sick cat with a POSTIVE IFA or SNAP test result).

3) **regressive** infection; this is what makes FeLV infection challenging. Following a short period of viremia (generally 3 to 6 weeks but less than 16 weeks, FeLV will 'infect' cells (especially bone marrow lymphocytes)…during that process, the viral RNA is released into the cytosol of the cell where the unique enzyme (characteristic of retroviruses), called Reverse Transcriptase, allows single-stranded RNA to transform into complementary DNA…this is ***proviral DNA***. And…this is this the origin of the latently infected cat. as proviral DNA then enters the nucleus of the cell and actually integrates into the cat's genome…where it can either sit…for years…or begin to produce new FeLV RNA (possibly detectable by PCR as ***viral RNA***). Conventional IFA and SNAP tests are negative…and…affected cats are NOT shedding virus….usually. Reactivation can occur…years after the initial infection.

4) **focal** infection: although believed to be uncommon, FeLV may sequester, latently, within selected tissues/organs (eg, kidney, GI tract, bone marrow). Testing blood by IFA or SNAP test will be negative.

It's the apparent incidence of **regressive FeLV infection** that will continue to challenge all of us…ie, what are the clinical consequences of latency in a SNAP negative, healthy cat. Based on information available today, the odds favor the cat…there is a good chance the cat will remain healthy, may eventually clear the proviral DNA, and they are NOT shedding FeLV as long as the virus remains as proviral DNA (latent). Some, however, don't do as well…a small number of **regressive infections** will **re-activate**…this is the adult cat…with a history of having been healthy and FeLV negative for some time (years even). And despite the fact they may have never encountered another cat throughout life…they appear to develop disease spontaneously and may become **progressive** (IFA or SNAP positive, sick cat)**…or…**they may develop complications of their infection, including solid tumors (FeLV is an *oncogenic* retrovirus)…and may become IFA or SNAP negative!

In accordance with current retrovirus management guidelines, it is still recommended that the FeLV and FIV status of **all** cats seen by the practice be established *and* that all cats be tested (and determined to be NEGATIVE) *prior to vaccination*. The point here is that there's no value in administering vaccine to an FeLV (SNAP) positive cat. However, the commitment to perform routine screening of cats for retroviral infection raises important issues pertaining to interpretation of test results and follow-up actions needed to further manage those households with confirmed FeLV and/or FIV positive cats. Current testing recommendations outlined by the AAFP's Advisory Panel on Retrovirus Management have recently been updated and be reviewed/downloaded at:

www.catvets.com

(Search: *Practice Guidelines*: 2020 Retrovirus Management Guidelines) (see REF #3)

Fundamental to the proper use of the SNAP (ELISA-based) testing for the diagnosis of FeLV and FIV infected cats is an understanding that FeLV tests are designed to detect circulating (not intracellular) p27 **antigen** while FIV tests detect the presence of **FIV antibody.**

In clinical practice, these facts have important implications. For example, the FeLV test can detect FeLV virus in the blood (serum or plasma) of kittens, even as young as 1-day of age; a **positive** test is consistent with **infection**. It is important to note that FeLV tests designed to detect the presence of virus in tears and/or saliva are also ELISA-based tests.

Saliva and tear tests should **not** be used for routine screening of individual cats. It should also be noted that **neither** maternal antibody nor prior FeLV vaccination interferes with the SNAP or IFA test results. **Figure 1** will be used during the lecture to explain some of the fundamental issues behind interpreting test results in cats at various stages in the course of FeLV infection as well as provide an update on new information concerning pathogenesis of the infection and the meaning of a Negative test result.

In contrast to FeLV, ELISA-based FIV tests are **not** considered to be reliable in kittens less than 6 months of age for at least 2 reasons:

1) Since antibody response to FIV infection requires weeks or months to become detectable, a **negative** test result could occur in an exposed, infected kitten that has not seroconverted…

2) also, uninfected kittens from FIV-infected queens may test **positive** (antibody) as a result of having acquired maternally-derived (colostrum) FIV antibody; detectable levels of maternal FIV antibody can persist until around 6 months of age. NOTE: vaccinated queens that become seropositive are also able to transfer maternally derived antibody to healthy, non-infected kittens resulting in a FALSE POSITIVE test result.

Among healthy cats with a positive ELISA test for either FeLV or FIV, follow-up testing is recommended. The clinician should repeat the **ELISA test in 1 to 2 months**. As noted in **Figure 1**, re-testing 1-2 months following a POSITIVE test result is justified in healthy cats considering the possibility that the

infection may become regressive and the cat will subsequently develop a NEGATIVE test result. (The consequences here are that the cat may still be infected…ie, with latent proviral DNA hidden away in bone marrow lymphocytes).

Among the retrovirologists in veterinary medicine, it is agreed today that the FeLV Ag test (NOTE: FeLV Ab titer is *not* a reliable diagnostic test), as performed on the SNAP test, is a reliable (highly specific test) for infection. While at one time it was said that the indirect fluorescent antibody (IFA) test was necessary to "confirm" FeLV infection, that is no longer the case. Today, the IFA merely corroborates positive results on the SNAP test.

On the other hand, the SNAP Test for FIV antibody is **not** a confirmatory test. Confirmation of infection is predicated on a positive Western blot assay. In contrast to FeLV, the FIV-infected cat may live for years with its infection; early detection and treatment of associated illness will enhance longevity and quality of life.

POINT OF FACT: any cat having an FeLV POSITIVE test (SNAP) result is considered to be shedding virus, regardless of its health status. A cat that has an FeLV NEGATIVE test (SNAP) is not viremic and is not considered to be shedding virus. A cat having a "positive" test result for FIV, and confirmed by Western Blot, still must be assessed for prior FIV vaccination history before it is possible to confirm the diagnosis and establish risk. At this time, there is NO TEST that is considered to be consistently reliable in distinguishing *infected* from *vaccinated* cats.

Here's the problem…all cats vaccinated with the current killed FIV vaccine are expected to develop FIV antibodies following administration of the first dose. Antibodies are known to persist for at least 1 year (much longer, actually). Vaccine-induced antibodies interfere with all commercially available FIV Ab tests in the North America, UK, and Europe.

- SNAP® FeLV Antigen/FIV Antibody Combo (IDEXX Laboratories)

- PetCHEK® FIV (IDEXX Laboratories)

- All commercial Western Blot immunoassays

NOTE: Generally, a *NEGATIVE* FIV Antibody test result may still be reliably interpreted as negative for exposure and active infection.

FeLV Vaccination

Today, there is good evidence to support the fact that the prevalence of FeLV within the US cat population has declined over the last decade. Two factors are most likely to have played a major role in this decrease: vaccination and (especially) testing for FeLV antigen (allowing identification/ removal/isolation of infected cats). However, results of a recent survey of >18,000 cats in the US suggest that the prevalence of FeLV is still relatively high, around 3% of all cats (feral and non-feral). Clearly the need for routine testing and vaccination of susceptible cats is justified.

In accordance with AAFP Feline Vaccination Advisory Panel (2020), FeLV vaccination is highly recommended in kittens/young cats (because of the high degree of susceptibility among kittens vs. adults). A reasonable vaccination schedule would be:

Two initial doses (required) **one month apart** is recommended…**NOT EARLIER**. The initial dose can be administered as early as 8 weeks of age (I personally prefer administration at 12 and 16 weeks of age.)

Subsequent vaccination would depend on the assessment of risk for the individual cat:

The adult cat, worthy of annual (or biannual) boosters is characteristically the one that likes to go out at night, likes to fight, but doesn't do it well. You know the cat I'm referring to.

Of the various FeLV vaccines available today, 2 are killed, whole-virus vaccines, one is a subunit vaccine, and a fourth is a novel recombinant (rFeLV) vaccine. Any claim of FOCMA antibody and "anti-tumor" effects associated with a vaccine are NOT VALID.

The ONLY FeLV vaccine that does NOT contain an adjuvant is the recombinant (rFeLV) vaccine available as a 0.5 mL dose. The recombinant FeLV vaccine immunizes by its ability to deliver 2 discrete FeLV genes that express 2 immunogenic proteins (antigens): p27 (*gag*) and gp70 (*env*). Furthermore, the gp70 gene in the vaccine has been genetically modified such that both innate (NK cells) and adaptive (CD8+ and T-cell) immune responses are enhanced

All killed and sub-unit vaccines do contain an adjuvant and are licensed for parenteral administration as a 1.0 mL dose. None of the licensed vaccines interfere with the either the IFA or ELISA (SNAP) test platforms.[4]

[4] FeLV-FIV Combo Test, Idexx Laboratories, Westbrook, ME (USA)

FIV Vaccination

This vaccine is discontinued in most countries.

VACCINATION….

1) …causes FALSE POSITIVE test results with all FIV tests on the market;

2) …may cause False POSITIVE test interference up to 7 years post-vaccination, and…

3) …there is no way to distinguish an INFECTED cat from a VACCINATED cat.

In addition, a vaccinated, seropositive queen will pass antibody to kittens (presumably through colostrum). FIV testing of kittens that nursed from FIV seropositive cats is likely to result in a false positive test until around 5 to 6 months of age.

"Multiple studies have shown that cats infected with FIV have low levels of morbidity and mortality with appropriate husbandry and disease management." (see REF: #3 below) Cats vaccinated against FIV have not been shown to enjoy a significantly extended life span compared to cats living with long-term infections.

Treatment of FeLV/FIV

Over the past decade, a number of studies have been published that address a wide variety of treatment modalities for retrovirus-infected cats targeting cancer (FeLV-related), hematologic disorders (anemia, leucopenia), antiviral chemotherapy, immunomodulator therapy, and antibody therapy.[6] While it is possible to manage lymphoid tumors and hematologic disorders, the outcomes are expected to be transient as complications associated with the persistently infected and viremic cats unfold. Despites several attempts to treat the viremia, no modality has demonstrated sustained beneficial effects. Reference 3 (below) details several options for the management of FeLV-infected, as well as FIV-infected, cats.

Prognosis

Overall, when supportive care is provided, FeLV-infected, viremic cats have a poorer prognosis than FIV-infected cats. That said, it is not unreasonable for some clientele to maintain FeLV + cats (several in the same household) and report long-term survivals despite evidence of active viremia and shedding. A positive test (IFA or ELISA) for FeLV is not necessarily associated with impending death or poor quality life.

Additional Reading

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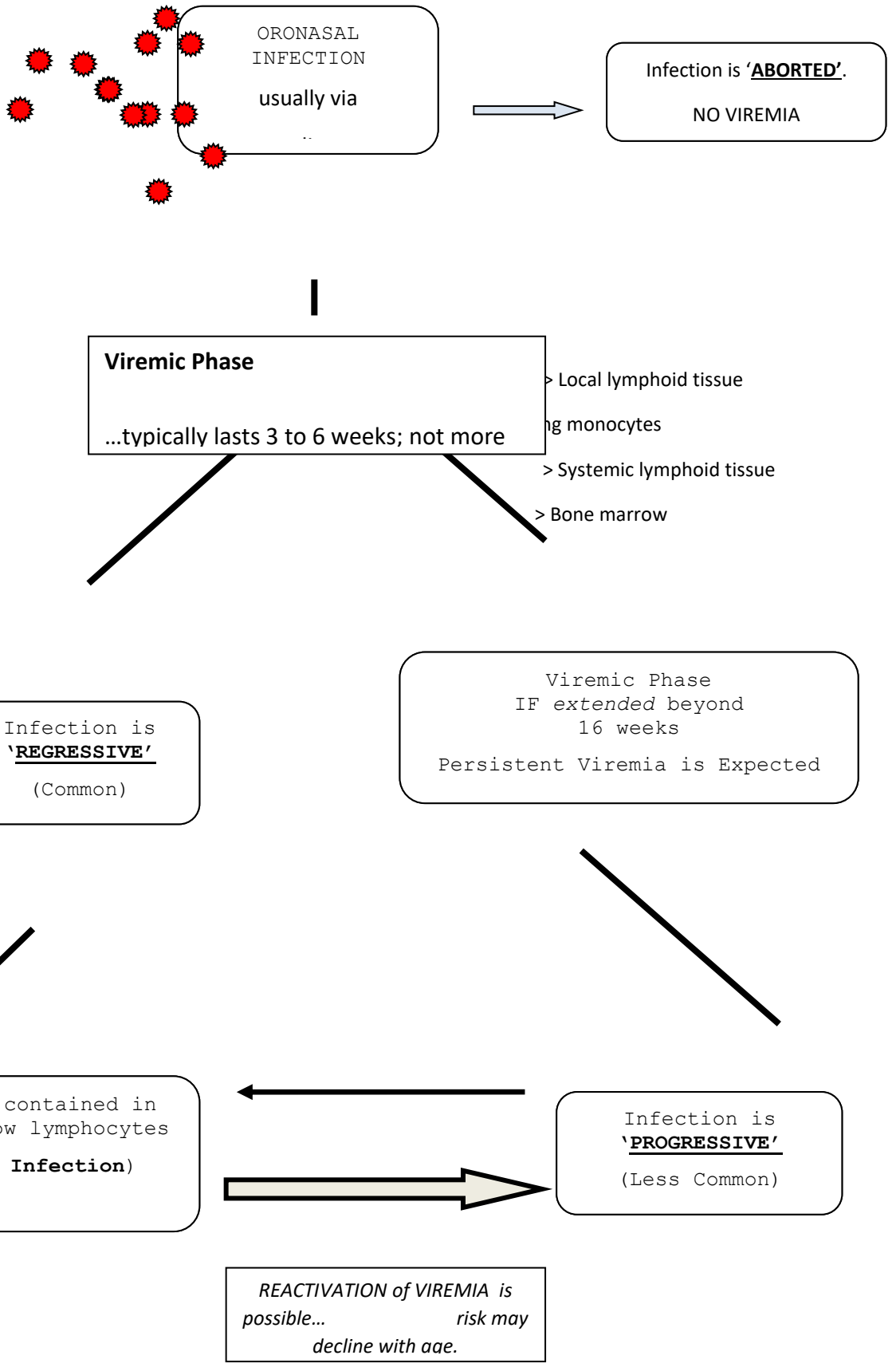
Reviewed/Updated: January 2023

Figure 1: FeLV Testing in the Clinical Setting



Well Cat

Sick Cat

FELINE INFECTIOUS PERITONITIS (FIP)

More Complex than We Thought

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As long as we've known about, tried to diagnose, and attempted to treat feline infectious peritonitis (FIP), it remains elusive! But, some very novel, yet effective, treatment options are altering the landscape on the management of FIP. This complex disease affecting kittens and adult cats throughout the world is attributed to a mutation of the ubiquitous Feline Enteric Coronavirus (FECV) into a virulent coronavirus biotype called the Feline Infectious Peritonitis Virus (FIPV). But that's the "easy part". For the clinician, the clinical challenges remain: risk factors, diagnosis, prevention (vaccine?), treatment, and prognosis. For the client of an infected cat…the challenge becomes one of quality of life and, not unreasonably, cost. New and effective treatment options, becoming more available at reasonable prices, represent the latest "must know" news for practicing veterinarians….

EPIZOOTIOLOGY

While it is presumed that 100% of cats/kittens are infected with FECV, 11% of cats are believed to experience the mutation from FECV to FIPV. The worldwide lethality of FIP ranges from 0.3% to 1.3% of all cats. Under the worst conditions, the morbidity (clinical illness) due to FIP is around 3-4% in multiple-cat households. (**NOTE:** that compares to 28%-30% for FeLV endemic households). Nonetheless, the disease we call FIP is highly lethal and carries a poor prognosis for survival once clinical signs develop.

The incubation period for FIP is variable, ranging from days to months (years?). 50% of cases of clinical FIP are seen in cats < 7 months of age. 70% of cats with FIP are < 18 months of age. 95% of cats with FIP are < 7 years of age. We have diagnosed fatalities caused by FIP in kittens as young as two months of age.

FIP infection in adult cats must be regarded as a chronic FIPV infection that has persisted for months or years before causing clinical signs. This may account for the fact that clinical signs attributed to FIPV are occasionally recognized in adult cats 10 years of age and older *despite an excellent history that the cat has lived indoors as the lone cat in the household for all of its life!*

THE CLINICAL DISEASE

Generally speaking, FIP occurs in two distinct forms: an effusive form characterized by peritonitis or pleuritis, or both, and a non-effusive, or dry, form that causes granulomatous lesions in major organs, such as lymph nodes, kidneys, the eyes, and the central nervous system (CNS).

Effusive FIP is characterized by a widespread vasculitis that is responsible for the outpouring of protein- and fibrin-rich fluid. Although antibody titers do not correlate with immunity, titers will rise simultaneously with the development of lesions of effusive FIP. The presence of effusion in cats with FIP has been attributed to a *strong* humoral immune response to the virus, but a *weak* cell-mediated immune (CMI) response. NOTE: immune-mediated vasculitis is the fatal lesion associated with FIP.

The non-effusive form of FIP, clearly the most difficult to diagnose, is characterized by a rather significant pyogranulomatous reaction in localized tissues (liver, spleen, abdominal lymph nodes) but can also be highly selective in its tropism (nervous system or the eye). Again, antibody is not protective. An "intermediate" CMI and humoral response is responsible for the lack of effusion.

Cell-mediated immunity does not always lead to complete elimination of the virus. Apparently, virus can persist in the body of some cats for an indefinite period of time. With advancing age or drug-induced immunosuppression (FeLV infection or steroids), the FIP infection may again become active.

TRANSMISSION of FECV

The route by which FECV is spread is via the fecal-oral route (esp, queen to kitten). Transmission in utero has been suggested; however, this route has not been definitely proven. Fecal shedding of FECV is common and poses the greatest opportunity for transmission in catteries, foster/rescue environments, and shelters. It appears that close, sustained contact between cats (esp. a carrier queen and her kittens) is required for effective transmission of the virus. NOTE: the virus appears to remain infectious for up to 7 weeks in a dry environment….it's more resilient than originally thought. Therefore, cluster households where breeding is prevalent (lots of kittens) pose the greatest risk of transmission of FECV.

IMPORTANT: FCoV is commonly found in individual as well as households of cats; up to 90% of healthy cats living in a household can be found to have FCoV (fecal shedding).

Most common household detergents rapidly inactivate the virus and disinfectants; Clorox bleach diluted in water (1 part bleach to 32 parts water) is preferred.

The clinical disease we call 'FIP' is results from:

1) exposure to and infection with FECV (which is very common… possibly impacting 100% of kittens)…*and,*

2) mutation of the "very common" FECV into a virulent coronavirus called the FIP virus (FIPV). The mutation is significant as the tropism of the virus changes from lower intestinal epithelial cells (FECV) to peritoneal macrophages (FIPV).

IMPORTANT TO KNOW: this mutation IS UNIQUE TO EACH CAT…mutated FIPV does not appear to spread among cats)...*and, THEREFORE, the disease we call FIP IS NOT REGARDED AS CONTAGIOUS.*

3) a genetic predisposition of the individual cat to develop disease once the mutation occurs has been described…but this point has not been conclusively proven. (Persian and Burmese appear to be at the top of the predisposed breeds list).

TRANSMISSION OF FIPV: [NOTE to the Reader: FIPV is a mutated variant of FECV that is unique to the individual cat and is **rarely** subject to shedding or transmission]

DIAGNOSIS OF CLINICAL FIP

Clearly, the effusive form of FIP is far easier to diagnose than the non-effusive form. Once a pleural or peritoneal effusion develops, gross and microscopic examination of the fluid is usually sufficient to make a clinical diagnosis. In the non-effusive form, the disease is far more difficult to diagnose because of the virus's ability to localize in discrete organs and the absence of obvious clinical signs.

Hematology and Biochemistry: In both the effusive and non-effusive forms of FIP, the total white blood cell (WBC) count is typically elevated with an absolute neutrophilia and a normal to low lymphocyte count. Cats with concurrent feline leukemia virus (FeLV) infection may have profound panleukopenia. In most cases of FIP, a mild to moderately severe anemia exists.

Fluid Analysis: Peritoneal and pleural effusions (**when present!**) are characteristic and essentially diagnostic. The fluid is light to dark yellow in color and has a sticky, viscous consistency. The fluid is technically an exudate since it is high in protein (characteristically from 5 to 12 g/dL) and has a high Specific Gravity ranging from 1.017 to 1.047. Cytological assessment of the fluid is not particularly impressive. Despite the high viscosity, expect the fluid to be relatively hypocellular consisting principally of WBCs, predominantly neutrophils and macrophages, with occasional mesothelial cells.

An **Albumin:Globulin** ratio (determined on abdominal fluid) that is greater than 0.81 is highly predictive for ruling out a diagnosis of FIP. Likewise, an albumin concentration (in the abdominal effusion) greater than 48% of the total protein or a gammaglobulin less than 32% of total protein are very good predictors that the effusion is **not** due to FIP. On the other hand, an effusion in which the globulin fraction is greater than 32% of the total protein (in the fluid) is highly predictive of FIP.

Plasma Proteins: Of particular importance in the diagnosis of the noneffusive form of FIP is the fact that approximately 75% of the cats affected have plasma proteins that are greater than 7.8 g/dl. Characteristically, the albumin is lower than normal and the globulin fraction is abnormally high.

[*IMPORTANT*] Electrophoresis of the serum proteins, routinely available through most commercial clinical pathology labs, will demonstrate an increase in the gammaglobulin fraction of serum in about 75% of cats affected with the **NONEFFUSIVE** form of FIP. The elevated serum globulin level, combined with evidence of ocular/CNS disease is highly suggestive of the non-effusive form of FIP. This is a particularly important diagnostic tool in cats suspected of having FIP but in which a significant accumulation of fluid is lacking.

FeLV Status: While many reports suggest that 40-50% of cats with FIP will also have a positive FeLV test, this assertion has not been established as a consistent finding. Only one report has shown such a high correlation between FIP-positive and FeLV-positive cats. Clinical experience indicates that the percentage of FIP cats that are FeLV positive is considerably lower. In no way should FIP be considered one of the FeLV-related diseases.

Histopathology: Biopsy is the only "test" that CAN confirm an antemortem diagnosis of FIP. Any FIP diagnosis made **without** histologic confirmation must be considered presumptive.

ANTIBODY vs ANTIGEN TESTING

REMEMBER: THERE IS NO “FIP TEST”. Commercial laboratories offering "FIP-antibody titers" are typically reporting "coronavirus antibody titers." While it has been proposed that the disease can be diagnosed by virtue of a high antibody titer, none of the coronavirus antibody tests are diagnostic for FIP. **Also…a positive coronavirus titer is NOT predictive of impending FIP.**

A negative titer, on the other hand, has been suggested to identify cats that have NOT BEEN EXPOSED to a coronavirus…and therefore could be interpreted as NOT FIP. That does not appear to be a valid assessment. The high incidence of FECV exposure among cats & kittens makes a NEGATIVE coronavirus titer a fairly rare finding, but even if infected, coronavirus antibody titers will decline as viral shedding ceases [which is common among infected adult cats].

Recently available through commercial laboratories is the **reverse transcriptase-polymerase chain reaction (rt-PCR) assay** for coronavirus **antigen.** The assay offers the ability to detect viral antigen in effusions, serum,

plasma, and in feces. This is NOT an FIP Test! The value of this test is that can detect viral antigen (compared to antibody) that is present in, especially, an abdominal effusion. Although rt-PCR test results do not distinguish between FECV and FIPV, we have used "positive" test results from abdominal effusions in support of a clinical diagnosis.

Another ('new-and-improved') rt-PCR test that is now commercially available. A number of investigators have discovered that rt-PCR technology identifies m-RNA (messenger RNA) of ***replicating*** feline coronaviruses inside circulating monocytes of infected cats. The biological point of significance here is that even cats with benign FECV can have *circulating* coronavirus in their plasma...but that's NOT necessarily an indication of FIP. However, if m-RNA can be identified in macrophages, the coronavirus is replicating...and that's unique to the FIPV. As with many PCR assays, false positive test results do occur. This test may actually be better used as a tool to rule FIP OUT, rather than IN.

Auburn University, College of Veterinary Medicine-Molecular Diagnostics Laboratory

WEBSITE: www.vetmed.auburn.edu

SEARCH: Diagnostic Services; then, Molecular Diagnostics

NOTE: FALSE-positive test results have been reported.

AND NOW…a TREATMENT?… it's called GS-441524

The "hottest" FIP topic-du-jour centers around the administration of a novel nucleoside analogue that inhibits FIPV and has been effectively used to treat the four major forms of FIP: effusive, non-effusive, ocular, and neurological. It's called **GS-441524**…it's an RNA-chain terminator of viral RNA dependent RNA polymerase (*but you probably knew that)* .

You've likely heard of **Remdesivir**, the FDA-approved treatment for humans who become seriously ill with COVID 19. Interestingly, remdesivir is the pro-drug (aka, "protide") that is transformed, intracellularly, into GS-441524 following intravenous administration.

The initial studies of GS-441524 in cats with FIP involved IV and SQ administration (U of California-Davis, N. Pedersen). Subsequently, a Chinese company (Nantong Mutian Biotechnology Co. Ltd) developed an oral form of GS-441524 that has been shown to effectively treat cats infected with the FIP virus (FIPV). Over the past few years, additional effective formulations have been developed for cats: IV, SQ, liquid-containing capsules, and tablets (most popular) are currently available.

NOTE: all oral forms of GS-441524 are being sold as a dietary supplement (take note: NONE are FDA-approved). A number of Chinese companies now have made this drug available to cat owners through direct, online sales. (see FIP Warriors CZ/SK at www.facebook.com/groups/fipczsk). The price has continued to decline significantly over the past 2 years, making it very affordable for cat owners…(a few hundred dollars to treat a cat vs. ~$30,000 for a course of IV remdesivir in humans.)

CAUTION: at this time, none of the formulations being sold are licensed or approved by any regulatory agency for administration to cats. All of these products are being sold on the so-called "black market". It is currently, and strongly, recommended that veterinarians NOT purchase this drug directly for re-sale to cat owners seeking treatment of FIP). Cat owners interested in pursuing treatment can purchase a GS-441524 formulation directly; a veterinarian may administer the drug (SQ or IV) and/or supervise administration of an oral preparation. SQ injections are commonly administered initially followed by oral preparations, especially among cats that can't tolerate oral medication.

Not only are these preparations NOT officially licensed in the US for use in cats, it appears that only the manufacturer actually knows the exact concentration of the active ingredient in a given product, which isn't likely to even be listed on the label…oral preparations are typically dosed as 'x' number of pills per cat…and, clinical responses may vary depending on the manufacturer of the product being used.

SOURCES: Mutian and Mutian X are the proprietary names of the first, and possibly the most widely used oral product (sold by Mutian Ltd. thru outlets in Canada). (Tablet forms of Mutian are currently not available for some reason). Also, a recent report from N. Pedersen and UC-Davis (2021) indicates that the therapeutic responses to the oral forms of Mutian have been found to vary. More consistent therapeutic responses from oral formulations (tablets) made by other manufacturers of GS-441524 are currently available online.

For example, Aura tablets have been found to be highly effective against all 4 forms of FIP (N Pedersen and N Jacque, updated Sept 2021). (search: Aura brand gs-441524)

And, while I would never purchase a seat from an airline that has "Lucky" in its name, the Lucky Brand of GS-441524 tablets (1 tablet/24 hr) have been found to be as effective as the Aura Brand tablets. (search: lucky brand gs-441524)

Other brands include: Spark, Capella, Kitty Care, Hero 16, Rainman (popular in China), Mary, Panda, Pany, Sweeper…

The latest update on the oral formulations, dosing recommendations, and manufacturer have been summarized in an online white paper by N Pedersen and N Jacque (Sept 24, 2021). (see REF #6 below)

Typically, the dosage (mg/kg) increases incrementally from 6 mg/kg for cats with the wet (effusive) form of FIP; 8 mg/kg for the dry (non-effusive) form of FIP; 10 mg/kg for ocular FIP and 12 mg/kg for neurological forms of FIP.

Treatment of cats with any formation (oral or parenteral) of GS-441524 is reasonably considered a work in progress. Before advising or treating any client's cat one or more formulations of GS-441524, do your homework:

1) review the science, what there is of it;
2) increase your awareness of the various Brands being offered,
3) do not purchase drug formulations on behalf of a client (let the client do the purchasing).

The FIP VACCINE (topical)

Zoetis (formerly Pfizer Animal Health) provides the only vaccine licensed as an aid in the prevention of FIP (Felocell FIP, also called PRIMUCELL in some markets). It is a temperature sensitive (therefore, modified live) coronavirus "designed" to grow only at the cooler temperatures of the upper respiratory tract. The vaccine virus will not replicate at core body temperatures. Therefore, it is purportedly effective only if exposure is VIA the oro-nasal mucous membranes (which is the MOST common route of infection); the vaccine is administered intranasally (applied directly onto the oral-nasal mucosa). Protection is apparently mediated by Secretory IgA produced at the level of the upper respiratory tract and oral mucous membranes combined with an enhanced cell-mediated immune response. The vaccine has been specifically developed so that it does NOT stimulate detectable levels of serum (circulating) neutralizing antibody.

Due to purported low (or lack of) efficacy, published vaccination guidelines today generally do not recommend administering this vaccine to cats.

ADDITIONAL READING (FIP)

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7. Pedersen NC, et al: Efficacy and safety of the nucleoside analog GS-441524 for treatment of cats with naturally occurring feline infectious peritonitis. *J Fel Med & Surg.* 21(4):271-281, 2019.

FIP Facts

- Enteric Coronavirus infection in cats is common (virtually 100% of all cats)...fecal shedding among infected cats is common...while clinical illness associated with FECV infection does not manifest.
  .
- The benign Feline Enteric Coronavirus (FECV) is the parent of the virulent FIP virus (FIPV). The FECV mutation that results in the emergence of FIPV is unique to each cat.
- FIP is not regarded to be a contagious disease of cats (rare and unique exceptions occur).
- There is *conflicting* evidence that certain cat breeds, and lines within breeds, are genetically predisposed to develop FIP once viral mutation does occur...ie, mutation alone may not cause the disease...genetics are believed to play role (example: in **Persian** and **Burmese** cats predominate, Balinese, Birman, and Himalayan are mentioned frequently as well)…but this point has not been conclusively proven.
- The risk of FIP is greatest among cats living in cluster (multiple-cat) households, ie, there's more virus transmission and, therefore, more virus replication, and therefore, more chance for mutation.
- Infection is most likely to occur in kittens as opposed to adult cats; clinical signs may require days to months (or even years) to develop…if they develop at all.
- The confirmatory diagnostic test for FIP is histopathology (Lesions: vasculitis)

Updated: January 2023

FELINE VIRAL UPPER RESPIRATORY DISEASE

Why it Persists!

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There is little argument among veterinarians that feline viral upper respiratory disease is perhaps the most common respiratory disorder for which cats are presented. In multiple-cat households and animal shelters world-wide, transmissible feline upper respiratory disease (URD) represents *the* most prevalent clinical disease in the population of cats at risk. The question that must be asked is: despite widespread use of vaccines against viral (herpesvirus and calicivirus) and bacterial (*Chlamydophila felis* and *Bordetella bronchiseptica*) respiratory disease, why do these infections persist? …and, what can be done to effectively manage these infections within households?

This question is important, but today there are answers that will help veterinarians manage the infected cat and minimize spread of infections among cats living within a closed population. This presentation addresses the most common cause of both acute and chronic upper respiratory infection in cats: feline herpesvirus-1 (cause of feline rhinotracheitis) and feline calicivirus. From diagnosis, to clinical management of infected cats, to vaccination…the critical issues surrounding this respiratory complex will be discussed.

Several infectious organisms are known to produce clinical signs of upper respiratory disease (URD) in cats. The most important, and most common, are:

Feline Herpesvirus-1 (FHV-1)

Feline Calicivirus (FCV)

Chlamydia felis (formerly *Chlamydophila felis;* formerly, *Chlamydia psittaci*)

Bordetella bronchiseptica

Reports on the prevalence of individual pathogens in outbreaks of feline respiratory will vary from country to country. In the United Kingdom, for example, it has been estimated that *Chlamydophila felis* infections constitute up to 30% of the cases of respiratory disease in cats. In North America, it's estimated to cause fewer than 5% of cases of feline respiratory disease. Today, most authors agree that between 80% and 90% of the cases of feline viral URD are caused by one of two viral groups, either (FHV-1), cause of feline viral rhinotracheitis (FVR), or feline calicivirus (FCV). Although a number of other viruses (cat pox, FeLV and FIV) and bacteria (*Haemophilus felis, Mycoplasma spp.*) have been shown to be associated with clinical signs of

respiratory disease in cats, their clinical importance is largely linked to either herpesvirus or calicivirus infection…and occasionally, both!

ACUTE VIRAL UPPER RESPIRATORY INFECTION

The hallmark clinical sign of acute viral URD is sneezing. Initially intermittent, the frequency and severity of sneezing episodes increases over a 3 to 5 day period. Fever and a bilateral or unilateral serous nasal-ocular discharge typically accompany sneezing episodes. As normal respiratory bacterial flora colonize in the upper respiratory tract membranes, the serous discharge becomes mucopurulent; this represents the most common problem for which affected cats are presented to a veterinarian. Left untreated, the nares obstruct, the eyelids become adherent to each other with viscous purulent secretions, and sneezing actually stops. Oral (especially lingual) ulceration is common and may be accompanied by hypersalivation, severe dehydration, anorexia, malnutrition. Secondary bacterial infections can become life threatening (pneumonia and sepsis) therefore; empiric antimicrobial therapy is always indicated. Clinical signs are most intense during the end of the first week and the second week of infection but may persist for as long as three weeks.

In practice, a diagnosis of acute viral URD is justifiably established on the basis of history and physical signs. Seldom is it necessary to isolate the specific virus responsible for causing infection in the individual cat. Laboratory profiles are more important in monitoring patient progress during therapy than establishing a diagnosis. Although morbidity can reach 100% in multiple-cat households, mortality is more common among kittens (<6 months of age) with secondary bacterial infections than in older cats. Therefore survival rates among affected cats are expected to be high presuming antibacterial, hydration, and nutritional support can be provided.

In multiple-cat households the problem of acute viral URD in kittens does not stop despite successful management of individual cat infections, implementation of a comprehensive vaccination program, and a seropositive adult population. It is important to note that approximately 80% or more of cats that survive acute FCV infection will become chronic carrier cats. One-hundred percent of kittens that recover from acute FHV-1 infection are expected to become chronic carrier cats. Healthy appearing carriers maintained in the population serve as reservoirs and can spread virulent virus to susceptible kittens, *as well as adult cats*, through direct cat-to-cat contact or fomite contamination.

THE CHRONIC CARRIER STATE

Unlike the feline panleukopenia virus, FHV-1 and FCV are relatively unstable outside the host cat (<18 hours for FHV-1 and about 2 weeks for FCV assuming ideal conditions of temperature and humidity). Therefore, the persistence of viral URD within a population depends on the ability of these viruses to sustain themselves in adult carrier cats.

NOTE: the FCV carrier cat sheds virulent calicivirus from the oropharynx *continuously!* FCV carrier cats, therefore, pose a substantial threat to susceptible kittens in multiple-cat population. It has been estimated that as many as 25% of clinically healthy breeding cats and approximately 10% of healthy household cats are FCV carriers. On the other hand, the FHV-1 carrier cats have a truly latent infection. Viral shedding is not continuous, but can occur subsequent to physiological stress (e.g., general anesthesia, boarding) or pharmacological stress (e.g., administration of corticosteroids). Although the virus is consistently recovered from tonsils of affected carriers, tonsillectomy does not eliminate virus excretion. Obviously, other sites of persistence in the oropharynx must exist.

The occurrence of repeat outbreaks of feline viral upper respiratory disease within a multiple cat household, particularly when kitten morbidity is high, supports the hypothesis that one or more chronic carrier cats live within the population. Diagnosis of the chronic carrier cat can be quite difficult even when virus isolation is attempted. Clinical signs in affected cats are variable to nonexistent. When present, however, they may provide important clues regarding the presence of a chronic carrier within a given population.

Clinical signs associated with the chronic carriers state, *if present,* typically manifest as paroxysmal sneezing episodes with continuous or intermittent mucopurulent nasal and/or ocular discharge. Characteristically, the sneezing and nasal discharge respond, usually completely, to empiric antibiotic treatment. However, resolution of clinical signs is only effective during the time of treatment. Within 3 days following discontinuation of the antibiotic, clinical signs typically re-occur. In addition to paroxysmal sneezing and nasal discharge, stomatitis, chronic gingivitis, gingival ulceration, and periodontal disease with premature loss of teeth will be evident. In our experience, this is especially true in cats with FCV *and* FIV infections. Radiographs may reveal secondary frontal sinusitis.

Recrudescent FHV-1 infections in adult cats manifest in a variety of ways: herpesvirus keratitis, corneal ulceration, and symblepheron in severe cases. Sneezing and nasal discharge is relatively uncommon. The author has proposed that feline vestibular syndrome is, in fact, yet another manifestation of feline herpesvirus-1 recrudescence.

Both FeLV and FIV infection are reported to be common concomitant (predisposing?) infections in cats determined to be chronic respiratory virus carriers. Routine testing of suspected carriers for both FeLV and FIV is highly recommended.

MANAGEMENT CONSIDERATIONS: THE CHRONIC CARRIER HOUSEHOLD

Unfortunately, even the most comprehensive vaccination program will not guarantee protection against persistent virus infections occurring within a household. Objectively, management of chronic feline viral URD within a household or cattery must be directed at effective control: strategic vaccination programs, strict environmental regulation, minimizing exposure, and, when possible, identification and isolation of carrier cats. Although parenterally vaccinated cats do develop significant, sometimes referred to as "protective," circulating antibody levels, immune carrier cats are commonplace. Use of intranasal vaccination, if available, has been

shown to mitigate the risk of outbreaks within a closed household and for reducing kitten losses associated with enzootic viral URD.

Several drugs have been used in an attempt to manage clinical signs of chronic, intermittent upper respiratory disease attributed to a chronic FCV or FHV-1 carrier state. For example, any broad spectrum antibiotic will control the clinical signs but, as described above, the response is typically limited to the time the cat is receiving the drug. **Amoxicillin-clavulanate**, **metronidazole**, and **doxycycline** have been recommended. In our experience, **azithromycin**, administered at 5 mg/kg, orally, once daily for 10 to 14 days (a liquid preparation is now available) has effectively managed clinical signs for periods longer than other conventional antimicrobials.

Immunomodulation has been attempted using human recombinant interferon (30 I.U. per day, orally, indefinitely). In our experience, little to no discernable response has been detected. A new recombinant feline-origin omega interferon (Virbagen Omega) is being studied at this time (10.000 I.U. per day, administered orally) in chronically affected cats (NOTE: this product currently has limited availability and is not licensed for use in the United States…not to worry, the clinical studies conducted to date are not impressive).

L-lysine: Administration of **L-lysine** (a non-prescription amino acid available in health food stores as tablets or capsules) has been reported (in limited studies) to compete, pharmacologically, with arginine, which is required by herpesviruses to replicate. While the efficacy of L-lysine continues to be challenged (because of the lack of supporting data), some recent studies have actually shown that in stressful housing environments (ie shelters), routine feeding of L-lysine does, in fact, decrease episodic viral re-activation and shedding. Other studies have shown than L-lysine fed cats actually had increased shedding (in group-housed cats). In the individual house-cat with signs of recrudescent upper respiratory signs consistent with FHV-1 carrier-state, it's still worth trying.

L-lysine has been formulated into a commercially available paste and as a treat (very well accepted by cats) for convenient administration. (NOTE: buyer beware…during a recent "price search" on L-lysine…it's apparent that the cost per cat per year varies significantly…from well under $100 to over $500).

L-lysine DOSING RECOMMENDATIONS: ~250 to 500 mg administered orally, with food, once daily, for an indefinite period, has been recommended to prevent (or lessen) the consequences of viral recrudescence of FHV-1 (this does not TREAT FHV-1 nor is it effective in chronic calicivirus. Administration of L-lysine is generally based on the empirical decision that a cat has viral upper respiratory disease and therefore might benefit from L-lysine administration. The reason is that confirming a diagnosis of FHV-1 (carrier state) requires isolation of the virus…which is intermittent and much more difficult to do. In clinical practice, therefore, the decision to treat with lysine is seldom based on diagnostic confirmation of FHV-1 infection. Perhaps more reasonable criterions to use are: 1) administer to cats with evidence of intermittent clinical signs of upper respiratory disease and, especially, conjunctivitis, or 2) try it and see how the cat responds.

NOTE: antiviral drugs used to treat herpesvirus infections in humans (e.g., acyclovir) are not effective against feline herpesvirus and, in fact, are contraindicated. Likewise, ribavirin is an antiviral drug effective against FCV, however the drug is quite toxic to cats and should not be used.

Famciclovir: Ophthalmologists are prescribing an oral (human-label) anti-herpes product called **famciclovir** in the treatment of feline herpesvirus-1. The drug is used to treat human herpesvirus infections (Famvir: NOVARTIS), but *much less* expensive formulations are available for use in cats. After several years of using famciclovir in cats, guidance on dosing and duration of treatment has not been clarified (or agreed upon among ophthalmologists). Famciclovir for cats ia currently available as 125 mg, 250 mg, and 500 mg tablets. Tablets can be cut or crushed as needed to facilitate administration. Current dosing recommendation range from as low as 15 mg/kg (2-3 times daily) to as much as 90 mg/kg (2-3 times daily). Clinical resolution is reported to occur faster at higher doses (no surprise there). But, side effects, although seemingly low, tend to center on the GI tract. For convenience of administration, and lower risk of side effect, the lower doses can be prescribed over a longer period. Treatment duration is large based on the resolution of clinical signs. Reports on treatment duration range from 10 days(higher dosage) to a few weeks (lower dosage).

Cats with Idiopathic Vestibular Disease: While this has NOT been studied nor validated at this time…I am recommending the use of **famciclovir**, at the empirical dosage outlined above, for the treatment of feline idiopathic vestibular disease (FIVD). Reports have suggested that FIVD represent the most common cause of peripheral neurological disease in cats. There is no sex or breed predilection. The average age is reported to be around 4 years, although cats of any age are susceptible. The primary sign, head tilt, may resolve spontaneously (it make take as long as 3 weeks to do so) or it may persist indefinitely. There is no known treatment. HERE's a suggestion:

I am assuming that FIVD is, in fact, the consequence of recrudescent FHV-1, manifest at the level of the 8th cranial nerve (or within nerve ending attached to the semi-circular canals). If this is correct, treatment with famciclovir may, in fact, shorten the course or effectively treat the affected cat. Given the drug is well tolerated in cats at the levels outlined above, it's worth trying. The duration of treatment is unknown…however, in the event a cat does respond to the drug, continued treatment for an additional week is not unreasonable. (anecdotal reports from veterinarians who have tried this suggest a response to the treatment).

IMMUNIZATION

Serologic response following vaccination with modified-live virus bivalent (FHV-1 and FCV) vaccines, whether administered parenterally or topically, is consistently characterized by the development of high titers. Vaccinated cats, however, do not necessarily enjoy complete protection. The immunity derived from vaccination does protect cats against developing severe disease following exposure. Vaccination, however, *does not* protect cats against infection. This is referred to a "non-sterilizing immunity", and is characteristic of many vaccines used in veterinary medicine today (eg, FCV, FHV, CIV [both strains]). Even if immunized *prior to exposure,* vaccinated against herpesvirus and calicivirus (regardless of route of administration), exposed cats can become infected, may develop mild or no clinical signs, and can still develop a chronic carrier state (which mean chronic virus shedding, as well!). Efforts to prevent development of the chronic carrier state through the use of topical FHV-1/FCV vaccines have not been consistently successful.

Although immunization cannot guarantee complete protection from respiratory infection nor from the development of a chronic carrier state, routine vaccination of kittens using a modified-live bivalent (FHV-1 and FCV) vaccine, is recommended, particularly in multiple-cat households. An extensive review of available data on the immunogenicity of FHV-1 and FCV vaccines by the AAFP Panel on Vaccine Recommendations (2006) has led to significantly revised vaccination protocol. Whether using a parenterally administered (SQ) vaccine or topically administered vaccine:

Initial Series: First dose at 9 weeks of age; a second dose is administered at 12 weeks of age.. **Today**: The 2020 AAFP Vaccine Guidelines for cats recommendation administering a 3rd dose of vaccine to all cats at 15-16 weeks of age. REASON: maternal antibody interference can persist beyond 12-13 weeks of age. A significant percentage of cats that *do not* receive this 3rd booster inoculation will not be immunized against panleukopenia (feline parovirus).

1st Booster Inoculation: 1 year following the last dose in the initial series.

Subsequent Boosters: Administer 1 dose every 3 years thereafter.

The *minimum* duration of immunity in adult, vaccinated cats has been shown to be at least 5 years.

INTRANASAL (IN) VACCINATION: Modified live, bi-valent (FHV-1/FCV) vaccines are licensed for administration to cats (Zoetis 0.5 mL volume and Heska 0.2mL volume). While these vaccines do protect as well as the parenterally administered (SQ) vaccines, they have been shown to protect from challenge within 72 hours v. 6 to 7 days for SQ vaccines. The quality of local immunity conferred by topical IN vaccination, however, may be moot as any local (secretory) antibody induced does *not* appear to prevent local infection nor establishment of a carrier state. There are 2 drawbacks to the IN vaccines when compared to a SQ modified-live vaccine: 1) post-vaccinal sneezing occurs in about a third of cats…in kittens, some can become ill as virus vaccine (probably calicivirus) replicates in the nasal epithelium, and 2) one of the topical products (Heska) also includes topically administered panleukopenia. This may not be the best route of inoculation for preventing this infection. Current recommendations suggest that IF one elects to use the 3-way IN vaccine (FPL+ FHV-1 + FCV), the patient should ALSO receive a parenteral panleukopenia vaccine…in other words…use a parenteral FPL vaccine.

It is important to note that vaccination against FHV-1/FCV induces what is now called “non-sterile” immunity. This means that vaccination (*either IN or SQ)* will prevent clinical signs (for the most part, albeit not completely), but will not prevent infection…nor the establishment of a chronic carrier state…nor will vaccination prevent virus shedding. By contrast, cats vaccinated and immunized against panleukopenia are completely protected in the event of subsequent exposure…they will not become infected. This is called “sterile” immunity.

SOMETHING TO TRY!

Intranasal VACCINATION FOR THE "TREATMENT" OF CHRONIC URD…FOR YOUR CONSIDERATION:
Topical vaccination, although having limited global distribution, has been recognized to lessen, and in some cases eliminate, clinical signs of rhinitis in chronic carrier cats.

Prior to administering vaccine, 2-3 days of pretreatment with an antimicrobial may be necessary to reduce the amount of nasal discharge. A single dose of intranasal vaccine is administered in accordance with manufacturers' recommendations: 1 drop in each eye and the remaining volume onto the nose-web. A response is expected within 10 to 14 days as the volume of discharge and associated sneezing diminishes significantly. If there is no initial response, some cats may respond to a second dose administered 30 days following the first dose. We have routinely re-isolated virus from cats despite the diminution of clinical signs. Topical administration of vaccine to chronic carrier cats is NOT expected to eliminate the chronic carrier state.

TOPICAL UPPER RESPIRATORY CURRENTLY AVAILABLE IN THE US

(FHV-1 and FCV and Panleukopenia)

- Felocell FVR-C (Zoetis Animal Health): modified live, herpesvirus-1 and calicivirus. (0.5 ml)
- **Feline Ultranasal FVRC Vaccine-Bivalent (Heska-Elanco, labeled under Diamond Laboratories): modified-live, feline herpesvirus-1 and calicivirus. (0.2 ml) (This preparation is recommended over the Panleukopenia-containing preparation-below)**
- Feline Ultranasal FVRCP Vaccine-Trivalent (Heska-Elanco): modified live, feline panleukopenia in addition to herpesvirus-1 and calicivirus. (0.2 ml) (topical Panleukopenia vaccine is currently NOT recommended; parenteral vaccination is preferred to assure a protective immune response following vaccination).

ADDITIONAL READING

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