Diagnostic imaging is a commonly used tool in both small animal and equine medicine to aid in diagnosis of veterinary patients. Both radiography and ultrasound are used in cattle practice, but the scope of the use is limited compared to our counterparts in other areas of veterinary medicine. Like any other tool the old adage “garbage in-garbage out” applies in diagnostic imaging. Appropriate patient selection, modality selection, as well as proper image capture and identification are all critical to successful outcomes using both radiography and ultrasound in practice.

Radiography
Training on image capture and evaluation using radiography is widespread in veterinary colleges. However, the nuances of the bovine patient are not always focused upon. Most equipment that can be accessed in the field and non-large animal specialty practices has its best utility on youngstock and extremities from the hock distally.

In young calves the lungs, limbs, and portions of the skull can be adequately imaged and interpreted. However, as they grow the capacity of many machines will not have the ability to image the thorax.

In the adult bovine radiography is best used to evaluate bony structures of the distal limb. The mandible can also be imaged in some finer boned adult cattle. Fractures, luxations, metabolic bone disease, infectious diseases of the bones and joints are readily evaluated in bovine patients. In most cases images can be acquired in animals that are standing and well restrained to limit motion. If necessary animals can be imaged in a tilt chute or in lateral recumbency with sedation. Standing radiographs are preferred because they will allow for evaluation of joint space while images obtained in the recumbent animal will not. Similar to our other species standard antero-palmar and lateral images should be acquired as well as both dorsomedial palmerolateral and dorsolateral palmeromedial obliques when imaging joints to allow for appropriate interpretation.

Hock and carpus – 4 views are required for adequate interpretation. Flexed and skyline views may be helpful in isolated cases.
Metatarsus and metacarpus – 2 view are typically adequate
Digit – 4 views of the digit are required for adequate interpretation. Placing a spacer between the toes (roll of brown gauze, cardboard core of vetwrap) will decrease the overlay and highlight the toes for better image quality.

Ultrasonography
The use of ultrasonography in cattle practice has historically been limited to pregnancy diagnosis. The ultrasound is uniquely capable of giving an image of tissue architecture in the awake animal. It is important to recognize the limitations with ultrasound and size of the mature bovine is a significant one. Despite this good quality images up to 20-25 cm in depth can be acquired. In recent years descriptions of appropriate image capture and normal and abnormal findings have been described for a variety of organs in the bovine. Using ultrasound is an acquired skill and takes practice to incorporate it usefully into clinical practice.

Lung – Best done with a 3.5 – 7.5MHz linear or sector probe in the intercostal spaces. The lung borders of the lung field can be outlines from the top of the 11th rib. Middle of the 9th, and point of the elbow. Ultrasound is best used to diagnose superficial lesions unless significant consolidation is present. Thoracic wall and pleural lesions are easily visualized as are superficial abscesses, masses, and pulmonary consolidation.

Heart – Best done with a 2.5 – 3.5MHz probe in adults or a 3.75 – 5 MHz probe in calves. The position of the heart under the thoracic limb and narrow rib spaces at this location may make imaging difficult especially in adults. The heart can be found in the 3rd – 5th intercostal space (ICS) under the elbow. The standard 4 chambered view can be obtained in the 4th ICS on the right in the parasternal region. On the left the caudal long axis view can be obtained in the 4th or 5th ICS just dorsal to the olecranon with the probe angled slightly caudally. Evaluation of the heart is the most difficult of all ultrasounds to gain proficiency. However, evaluation for pericarditis is relatively easy even for novice ultrasonographers.

Liver – This is best accomplished using a 3.5 – 5.0 MHz linear or convex transducer. The liver is located on the right side from caudal to the last rib cranial to the 5th ICS. Gastrointesinal tract - This is best accomplished using a 3.5 – 5.0 MHz linear or convex transducer.
- Abomasum – 10 cm caudal to the xiphoid on the ventral body more on the right but spans both sides. Some of the folds may be visible within the abomasal content.
- Reticulum – imaged on the ventral thorax lateral to the xiphoid on both sides extend up to the level of the elbow.
- Omasum – ICS 6-11 on the right. No inherent motility and laminae are not visible in the normal animal.
- Small intestine – entire right side from the tuber coxae to the 8 ICS from the transverse processes ventrally to the fold of the flank. The wall should be 2-3 mm thick with a lumen of 2-4 cm.
Spleen – This is best accomplished using a 3.5 – 5.0 MHz linear or convex transducer. The spleen can be found in the ICS 7-12 on the left craniodorsal to the rumen.

Urinary system – The left kidney, urethra, ureter, and urinary bladder can be imaged transrectally using a 5.0 MHz linear transducer. In thin cows or smaller calves the left kidney can be imaged in the right caudodorsal paralumbar fossa. However, gas from the colon often overlies the area and limits image quality. The right kidney can be imaged percutaneously in the right paralumbar fossa in the last ICS using a 5 MHz or lower transducer depending on required depth.

Mammary gland and teats – Ultrasonography of the teat has become commonplace while that of the mammary gland is not quite as commonly described. The use of 3.5 and 5.0 MHz transducers has been described with the linear transducers providing superior image quality. While these have been described image quality will improve dramatically with higher frequency transducers. A 7.5 – 10 MHz transducer would be considered ideal. Imaging of the teat is most often perused when milk flow is diminished or absent. A standoff can be used to improve imaging of the teat canal.

Umbilicus – This is best accomplished with a 3.5 – 5.0 MHz linear or convex transducer. Ultrasound is an excellent technique to image the umbilicus of neonatal calves. It is possible to determine the presence and extent of internal remnant swelling in animals with omphalitis.

Tendons – The distal tendons of the limbs can also be imaged by ultrasound using a minimum 5.0 MHz linear transducer. A 7.5 – 10 MHz transducer would be considered ideal.
Implications of Having a Reportable Disease in Your Hospital
Dusty Nagy, DVM, PhD, DACVIM
University of Missouri
Columbia, MO

There are a variety of reportable diseases in the United States on both the state and the national level. In production animal medicine these diagnoses are often made on farm and may lead to a temporary quarantine of the premises until confirmatory testing can be completed. This quarantine typically results in a cessation of animal movement and a limitation to farm travel for the in contact family and workers. As the veterinarian, we recognize the inconvenience to the client but understand the importance in the protection of animal and public health.

Now envision the farm at which the diagnosis is made is your hospital and the in contact “family” are your associates and staff. This now turns from a minor inconvenience, to a catastrophe of epic proportions. Once you are grounded (7-10 days maybe more) that leaves appointments unseen and clients untended to.

This hour we will focus on people and animal movement throughout the hospital and ways to minimize the potential transfer and exposure of disease.

**Personnel**
Personnel fall into 2 main categories - animal caregivers and non-caregivers. The movement of non-caregivers should be extremely limited (nonexistant) in an animal facility to prevent the unnecessary exposure of a staff member. Animal caregivers should practice appropriate barrier nursing and infection control when dealing with all patients. Animals in isolation should have contact with only people critical to the care of the animal.

**Personnel flow**
Many facilities offer both in house and ambulatory services. Occasionally accessing ambulatory vehicles requires/allows for travel through the hospital as one leaves or returns. This again is a point where pathogens can be exchanged and moved.

**Animal location**
True isolation stalls are not common in many practice settings. Often, hospitals that have them available, fail to use them on a routine basis due to the extra time and labor associated with the protocols of animal handling in that segment of the facility.

**Animal flow**
Animal flow thorough the hospital often puts animals in contact with animals from other farms. This poses a point where pathogens can be exchanged and moved.

**Barrier nursing**
Clean coveralls unique to the patient, disinfection of boots between patients, and the use of latex gloves (changed in between patients) are the minimum requirements for preventing the movement of microorganisms between patients in the facility.

**Infection control**
Disinfectant mats (charged with disinfectant and uncontaminated by organic debris) will help minimize the transmission of microorganisms between patients.

**Damage control in absence of dedicated isolation facility**
In the advent that an animal with a potentially infectious disease enters the facility, recognition of the potential and partitioning the animal to a naturally low traffic area may prevent unnecessary exposures of personnel and contamination of equipment.

**Other random logistics**
In addition to the clear issues of biosecurity many other logistical problems may exist that are often overlooked. Many personnel have animals at home that may pose an at risk population. Animals actively hospitalized in the facility may become part of a quarantine when traffic in and out of the facility is prohibited. This can cause significant disruptions in the business including but not limited to deliveries, shipping of samples out of the practice, and disruption of service to clientele.

Part of Veterinary Accreditation is understanding of and mandatory reporting of potential diseases of concern. A variety of mandatory reporting exists for veterinarians within this program. The following should all be reported:

- All foreign animal diseases must be reported to Federal and State Animal Health Officials (SAHO)
- USDA Program Diseases must immediately be reported to Federal and State Animal Health Officials
- States may have additional diseases of interest that they monitor, and thus are reportable at the state level
Zoonotic diseases may need to be reported to the State Health or Public Health department as well as the Centers for Disease Control and Prevention (CDC). Bioterrorism disease agents may be reportable to Federal and/or State Animal Health Officials.

Each state has an independent list of reportable diseases. There is currently a proposal for the development of a national list. Below is the list of diseases for the state of Missouri:

- Anthrax
- Bluetongue
- Bovine babesiosis (Texas fever, piroplasmosis)
- Bovine spongiform encephalopathy (BSE)
- Brucellosis
- Contagious bovine pleuropneumonia
- Foot-and-mouth disease
- Heartwater
- Pseudorabies
- Rift valley fever
- Rinderpest (cattle plague)
- Screwworm
- Tuberculosis
- Trichomoniasis
- Vesicular stomatitis

In addition to state reporting lists the World Organization for Animal Health maintains a list of reportable diseases from nations across the world. Each year the United States puts together a cumulative report detailing the presence and extent of disease prevalence for each disease on the list.

**Recommended resources**

Missouri Department of Agriculture
Anaplasmosis is an infectious Rickettsial disease of cattle caused by *Anaplasma marginale*. The organisms infects the red blood cells of cattle and produces a round structure that can be seen at the periphery of infected erythrocytes. The organism can be transmitted by ticks or by blood transfer between animals. All ages of animals can be infected, but the severity of clinical signs increase with age with animals over 3 years of age showing more severe clinical signs.

**Phases of disease**

Anaplasmosis goes through 4 distinct phases in the cow including incubation, developmental, convalescent, and carrier. Once infected, animals will incubate the organism without showing clinical signs for approximately 4–8 weeks. Once approximately 1% of the animal’s erythrocytes are infected the animal enters the developmental stage and will begin to show early clinical signs of infection. Early signs are often indistinct. Fever, weakness, and anorexia, along with a drop in production often predominate at this stage.

Approximately 15% of the erythrocytes must be parasitized to show clinical signs associated with anemia. Anemia occurs in cases of anaplasmosis due to the removal of infected erythrocytes by the immune system. The majority of the clinical signs in the cow can be attributed to anemia caused by the extravascular hemolysis. These signs include pale mucus membranes, tachypnea, and tachycardia. As an extravascular hemolysis hemoglobinuria and hemoglobinemia are absent in cases of bovine anaplasmosis. As the disease progresses and animals begin to process heme pigments pale membranes may become jaundiced. Mania, likely induced by cerebral hypoxia is also commonly associated with anaplasmosis in cattle. If left untreated, death may result.

The animal enters the convalescent stage once regenerative changes appear in the blood. And continues until the blood smear appears normal. It is still possible to have animals showing severe clinical signs early in the convalescent stage. In addition some animals may have a phase of chronic unthriftyness as they recover from a clinical anaplasmosis episode.

The carrier stage begins once organisms can no longer be found in the peripheral blood. This phase likely extends for the life of the animal. Carrier animals may be clinically normal with low levels of parasitemia which precludes diagnosis via blood smear. These animals remain infectious to their herdmates and are a lifelong source of the organism.

**Diagnosis**

Diagnosis of anaplasmosis can be made using several different testing methodologies. It is important to recognize that no one test will detect all of the potential stages of disease.

Blood Smears have utility in animals during the developmental phase of the infection. Animals with clinical signs consistent with anaplasmosis that have evidence of organisms on a blood smear are considered to be clinically affected. Early in disease (incubation) smears may be negative because a critical load of erythrocytes may not have been reached allowing them to be detected on blood smear. Similarly animals in the carrier state will typically not have enough infected erythrocytes to be detectable by this method. During the convalescent phase organisms may be detectable early. Signs consistent with regenerative anemia (anisocytosis and basophilic stippling) will be present during this phase and may be suggestive of anaplasmosis, but are not considered diagnostic.

Serologic tests (cELISA) will be positive in animals during the developmental and convalescent stages of infection. It will also be positive in many animals in the carrier state of disease. As such these tests will determine exposure of the animal to the organism, but alone it can not adequately separate active infections from carrier animals. A positive serologic test in the presence of clinical signs is suggestive of active infection. The major limitations to the cELISA are detection of early infection prior to the animal mounting an adequate immune response, prolonged recognition of the immune response in animals that have been chemosterilized, and cross reactivity with other Anaplasma species.

Polymerase chain reaction based diagnostics have the ability to pick up very small amounts of Rickettsial DNA and have proven helpful in identifying carrier animals. Some assays have been reported to detect as few as 30 infected cells per milliliter of blood. These assays lack formal validation and results may vary depending on laboratory protocol.

**Treatment**

Treatment is centered on antibiotic therapy and supportive care. Many treatment protocols have been published, but most center on oxytetracycline therapy. Most animals are suffering from significant anemia by the time they are presented for treatment. Minimizing stress and exertion are important to prevent decompensation from the anemia. Oxytetracycline 200 mg/ml can be administered at 9 mg/lb SQ every 72 hours. Blood transfusion may be indicated in some patients with severe life threatening anemia.
When an animal is diagnosed or in the case of a herd outbreak do not forget that other animals are at risk. At risk animals can also be treated with injectable oxytetracycline, oral chlortetracycline at a rate of 0.5mg/lb BW, or combinations of both injectable and oral oxytetracycline.

Prevention and control
Vector control – Tick and fly control is imperative in preventing movement of anaplasmosis through a herd. Insecticide impregnated ear tags, fly blocks, sprays, back scratchers, etc. can be used to decrease the potential for vector transmission. It is important that these methods be reapplied, replaced, or recharged intermittently throughout the vector season for them to remain effective.

Medicated feed and mineral supplements, pulse dosing antibiotics – these methods can be used to prevent clinical disease in endemic herds. It is important to recognize that animals must eat the feed or use the mineral for them to be effective.

Vaccine – In some states a killed vaccine is available for use. It is currently sold as an experimental vaccine and is not licensed by the USDA. However, the USDA has approved the sale and use of the vaccine in multiple states including Missouri, Kansas, and Iowa.

Eliminate carriers – many treatment regimens to eliminate carriers have been suggested. Most of these have failed to hold up in recent evaluations using more stringent test methodology. Several new protocols have shown promise, but have yet to stand up to rigorous reevaluation. Chlortetracycline fed at 4.4; 11; and 22mg/kg/day for 80 days were all effective at eliminating the carrier state in tested animals. An additional study reported success treating with a single SQ injection of oxytetracycline followed by 30 days of chlortetracycline fed at 4.4 mg/kg/day. An additional study showed failure of the 4.4 mg/kg/day chlortetracycline to chemosterilize animals when fed for only 45 days.

Instruments – Blood contaminated instruments including needles, dehorners, tattooing equipment, ear taggers, and surgical equipment are effective at moving anaplasmosis from infected to naïve animals.

Animal movement – It is important to recognize that in some areas of the country and within some herds anaplasmosis is endemic. Care should be taken when moving animals from endemic areas to non-endemic herds. Introduction of a carrier animal to a naïve herd may result in significant numbers of clinically ill cattle since the herd has no background immunity. Conversely, moving a naïve animal to an endemic herd may result in clinical disease in the new introduction.

Recommended reading and resources
anaplasmosisvaccine.com


Reinbold, J. B., J. Coetzee, and R. Ganta, 2009a: Comparison of three tetracycline antibiotic treatment regimens for carrier clearance of persistent Anaplasma marginale infection derived under field conditions. Proceedings of the 42nd Annual Conference of the American Association of Bovine Practitioners (AABP), Omaha, NE


I fear that the physical examination is becoming a lost art. Perhaps every generation of veterinarians has had the same feeling as they see more and more technology enhancing our ability to reach a diagnosis, but at the same time replacing some of the time-tested techniques of the physical examination. I am certainly not against technological advances-most of us at academic institutions are drawn there because of the advanced diagnostic equipment available to us. I am, however, chagrined by the growing dependence upon imaging, laboratory evaluation, and other sophisticated techniques to make a diagnosis when often a physical examination and a very simple confirmatory test would reach the same conclusion in less time and for less cost. My goal in this presentation is to review the techniques of physical examination both for the part-time bovine veterinarian as well as the experienced bovine veterinarian. There is no question that the combination of excellent physical examination and rational use of sophisticated diagnostic equipment will achieve the optimal results.

We often hear the term “complete physical examination,” but how often do we perform one? The truth of the matter is that we do not need to perform a complete physical examination on every patient, nor do we have the time. We routinely perform what might be called a “standard physical examination” which includes a brief review of all important body systems. Based on the history and the results of the standard physical examination, we then perform one or more focused physical examinations. If we performed every one of the focused physical examinations that we knew, we would then perform a “complete physical examination.” But let’s not argue over semantics. Let’s try to learn how to efficiently evaluate an animal by use of the standard physical examination and how to focus on particular areas to gain the most information possible from a physical examination.

There are many ways to approach a physical examination; many correct ways. The approach that I will use in this paper is to begin with observation at a distance and then examination of the restrained animal. I’ll then discuss the acquisition of vital signs and basic auscultation, concluding with regional focused examinations beginning at the head. Because neurological examination is frequently difficult and confusing, I’ll spend a bit more time on that aspect.

The exam at a distance

I believe that physical examination of cattle should begin with observation of the animal from a distance. This is particularly important when one suspects neurological or musculoskeletal disease. The animal should be observed at rest for several minutes and then in motion. Note the general condition of the animal and the breed, as some neurological diseases are heritable. When the animal is at rest, pay particular attention to the animal’s awareness of its surroundings which reflects cerebral function. Note if the animal is depressed, hyper-excited, or otherwise responsive to external stimuli, if it is head pressing, wandering aimlessly, vocalizing abnormally, behaving abnormally or aggressively. Diseases such as polioencephalomalacia, lead poisoning, nervous ketosis, bovine spongiform encephalopathy, rabies, brain or pituitary abscess, nervous coccidiosis, and salt poisoning/water deprivation cause these signs. Before the animal is disturbed, observe the character and rate of respiration, look for a jugular pulse (indicative of right heart failure), and for signs of abdominal pain like bruxism, restlessness, kicking at the belly, or straining. Also look carefully for muscle fasciculation, twitching of the ears or eyelids, tail position and switching and abnormal attempts at swallowing which may indicate nervous system or metabolic disease such as hypomagnesemia, lead toxicity, tetanus, or rabies. Lameness is often detectable in cattle at rest by observing how the animal bears or shifts weight on the limbs. An easy way to assess weight bearing is to observe how far the dewclaws are from the ground. If the dewclaws are higher on one side, the animal is not bearing full weight on that side. Abdominal contour should also be assessed at a distance and from behind the animal. While the animal is in the open and not confined in a chute, careful attention should be paid to the muscle mass, particularly over the rump and hindquarters. In unilateral neurological disease, as well as chronic upper limb lameness, atrophy of the muscles will occur, and asymmetry of the muscles will be obvious.

If the animal is recumbent, observe if and how it rises. It is best to observe an animal in motion as it moves away from and towards the examiner, as well as from each side. To optimally evaluate gait, it should move at its own pace with only slight prompting from an assistant. It should be driven and not led (unless it is very well halter broken) so that the head and neck are free to move. The carriage of the head and neck sometimes give important clues about neurological disease. Observation should be carried out from directly behind the animal and then from each side, with particular attention being paid to the carriage and placement of the legs, to ability of the animal to walk in a straight line, to knuckling, and to other signs of weakness. If hind limb ataxia is suspected, the animal should be pulled from side to side by the tail so that the examiner can assess if the animal is able to place its back feet under itself correctly. Another important observation to make when the animal is moving is to assess its vision. The menace response can be misleading in cattle, particularly young cattle. Therefore, cattle suspected of blindness should be moved through a maze or an obstacle course where they will have to turn to avoid running into objects. In this way their visual capacity can be properly assessed.
The exam up close

The next part of the physical examination is conducted with the animal restrained in a head chute. The order in which most of the examination is conducted is not important except that the rectal exam should be conducted at or near the end of the examination. The following description is the sequence that I usually follow. In dairy cattle particularly, it is often important to collect urine to check for ketonuria. This can most easily be accomplished without catheterization if it is done before the cow is “disturbed” by the physical examination. Stroke the vulva or perineum without touching any other part of the cow. Bulls will often urinate if their sheath is grasped at the orifice and “shaken” vigorously for 30 seconds. If the animal is lying in a stall and rises when the examiner approaches, it will frequently urinate and defecate spontaneously. Rectal temperature, pulse and respiration should always be measured. If the examiner stands on the left side of the animal while taking the temperature, rumen motility can be assessed simultaneously. After measuring and recording the temperature and assessing rumen motility, auscult the heart for rate, rhythm and murmurs. Remember that in order to auscult the heart, the head of the stethoscope must be pushed cranially behind the elbow and humerus. This is especially true in heavily muscled beef cattle. Next, listen to the lung fields and record the respiratory rate. Reference ranges for mature cattle are as follows: RR (12-36 bpm); HR (50-80 bpm); rectal temp (100.5-102.5°F, 38-39°C); Rumen contractions (2-3 in 2 minutes). For calves, these values are: RR (20-50 bpm); HR (90-112 bpm); rectal temp (101.4-103.4°F, 38.5-39.5°C) It is important to remember that lung sounds in cattle are usually quieter than they are in horses and small ruminants. Therefore, careful attention must be paid to detect abnormalities. The most frequent change in the lung sounds of cattle (except feedlot cattle perhaps) is simply an increase in the normal breath sounds which is caused by tachypnea. Heart failure, pulmonary disease, excitement, exertion, or elevated body temperature (which may be due to infection, exertion or high environmental temperature) may cause tachypnea. Except for pulmonary disease and pulmonary edema secondary to left heart failure, all of these other conditions will cause a simple elevation in respiratory rate and effort which is accompanied by louder-than-normal sounds, but which is not accompanied by crackles, wheezes, increased bronchial sounds or areas of dullness. In my experience the most frequent abnormal lung sound is increased large airway or bronchial sounds which are indicative of lung consolidation. It is a misconception that consolidated bovine lungs produce areas of dullness on auscultation. Often severe pneumonia in cattle is accompanied simply by increased large airway sounds but not crackles and wheezes. If areas of diminished or absent lung sounds are noted, one should suspect pleural effusion or lung abscess. It is critical to differentiate between true lung sounds and upper airway (nasal, laryngeal, pharyngeal and tracheal) sounds. Referred upper airway sounds can be heard loudly in the thorax, but if one listens over the trachea and pharyngeal area, the sounds are louder. Also, most sounds associated with breathing that are audible without a stethoscope are associated with the upper airway. Inspiratory sounds are almost always associated with a narrowing of the lumen of the upper airway. Audible grunts are occasionally heard, and these are consciously made sounds that usually reflect pain or severe disease that may not involve the respiratory tract. In young cattle, percussion of the thorax may help detect lung consolidation or pleural fluid, but this technique has been of limited value to me in older cattle, particularly beef cattle. After ausculting the thoracic cavity, move to the abdominal cavity and perform simultaneous auscultation and percussion (pinging) on both sides of the abdomen. Tests for abdominal pain can be conducted at this point. These include the withers pinch test and the xyphoid pressure test. The withers pinch test is performed by abruptly and firmly squeezing the animal rights dorsal midline over the withers. The interpretation of the test is as follows: the animal ventro-flexes and grunts-positive for cranial abdominal pain; animal neither ventro-flexes or grunts or shows signs of discomfort- inconclusive results.

Table 1. Assessing hydration in calves (from Walker and Constable, JAVMA, 1998)

<table>
<thead>
<tr>
<th>% dehydration</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td>eyeball recession (mm)</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>6</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>skin tent duration (secs )</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
</tr>
</tbody>
</table>

After completion of examination of the thoracic and abdominal cavities, one moves to the head of the animal. Hydration is best assessed by measuring eyeball recession and tenting of the skin of the neck. The values for assessing dehydration (Table 1) have been validated for calves by Constable, et al, but not for mature cattle. Anecdotally, I feel that the values for skin tent are probably similar in calves and cattle.

In suspected neurological cases, it is very important to do a thorough examination of the head, mouth and neck region. Begin by observing the animal from directly in front. One can observe the positions of the ears, eyelids, lips and eyeballs. After observing the animal’s head, the examination of the head in neck begins by noting the temperature of the ears. Cold ears indicate hypocalcemia or shock. Look in the ears for otitis externa. The oral examination follows. One should always be mindful of rabies before examining the mouth of any animal with central nervous system disease. Look at the lips, gums, dental pad, hard palate and tongue for color, vesicles and ulcerations. Gingival mucous membrane color and capillary refill time are much more difficult to
assess and interpret in cattle than in horses. Vulvar mucous membrane pallor is usually easier to detect (except in bulls & steers!). While examining the gums, check the incisors for eruption, color, wear and soundness. Grasp the tongue (a towel helps) and pull it to one side assessing consistency and muscle tone as you do. Look for ulceration, foreign body or ranulae on the underside of the tongue. Examine the cheek teeth for wear, points, attrition or overgrowth and the buccal mucosa for lacerations, ulceration or blunting of the papillae. "Impacted cud" may be in the cheek or under the tongue. Pull the tongue to the other side and repeat. Smell the breath and oral cavity for a necrotic odor, ammonia or ketones. Visual examination of the oropharynx can sometimes be accomplished with the use of a speculum (like a Drinkwater gag) and a flashlight. The torus lingua makes visualization of the pharynx difficult in some cases. Be ready to catch brief glimpses, especially when the animal bellows. Retropharyngeal masses, perforations, ulceration, and laryngeal lesions may be observed in this manner. Optional visualization of the pharynx, larynx and esophagus is obtained by endoscopy. Traumatic pharyngitis (usually iatrogenic), necrotic laryngitis, chondritis, etc. can be visualized by nasal endoscopy. (Note: bovine nasal passages are smaller relative to body weight, than equine.) The esophagus can be examined for ulceration, laceration, choke, etc. Unlike the equine stomach, the ruminant forestomachs and abomasum cannot be examined by easily endoscopy. To examine the throat manually, insert the hand into the mouth while pushing the tongue between the cheek teeth nearest you. Do not keep your arm in the mouth for too long as the animal cannot breathe and may struggle and bite.

**Cranial nerve exam**

Proceed with a systematic evaluation of the cranial nerves, beginning with the second cranial nerve. A menace response can be elicited in cattle, as with other species, by moving a hand or other object toward the eye. A positive response is blinking of the eye with or without an attempt to move. One must be very careful when examining cattle to not create wind with the hand or other object, as this may give a false menace response. Animals that cannot see can still perceive the movement of the hand and may react to the air movement on the eyelashes. Also, in young calves, many normally visual calves will not have a menace response. The menace response is a “learned” response and they don’t perceive the need to flinch yet. The menace response assesses the optic nerve (II), the cerebral cortex and the facial (VII) nerve. The optic and oculomotor (III) nerves are involved in the pupillary light reflex (PLR). To evaluate the PLR, with the animal in a dark place, shine a bright light into each pupil and observe that pupil, as well as the pupil in the other eye. If the pupil into which the light is shined constricts, then the direct PLR is intact. This means that cranial nerves II and III, as well as the retina, on that side are intact. If the pupil in the other eye also constricts, then the consensual PLR is intact. This means that in addition to cranial nerves II and III on the first side, cranial nerve III on the opposite side is also intact. The same procedure is repeated for the other eye. If the PLR is intact, but there is no menace response, the lesion is in the cerebral cortex. This occurs in polioencephalomalacia and lead poisoning. The position and movement of the eyeball is under the control of the oculomotor, trochlear (IV), and abducens (VI) nerves. Dysfunction of these nerves results in strabismus. The most common and important clinical strabismus in cattle is probably the dorso-medial strabismus associated with some cases of polioencephalomalacia.

The trigeminal nerve (V) provides sensation to the face and motor function to the muscles of the jaw. Pulling the jaws apart and assessing the strength of the muscles assesses the function of the masseter muscle. In order to assess sensation of the head and face, place a piece of straw into the nasal cavity or gently touch the eyelashes. When the lashes are touched, the animal should blink her eye; this is the palpebral reflex. The following table is a guide to interpreting the menace response, PLR and palpebral reflex.

### Table 2. Reflexes involving the eye

<table>
<thead>
<tr>
<th></th>
<th>Menace</th>
<th>PLR</th>
<th>Palpebral reflex</th>
<th>INTERPRETATION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent</td>
<td>Absent</td>
<td>Present</td>
<td>II or retinal deficit</td>
</tr>
<tr>
<td>Present</td>
<td>Absent</td>
<td>Present</td>
<td>Absent</td>
<td>Cerebral cortical deficit</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>Present</td>
<td>Absent</td>
<td>VII or orbicularis oculi muscle deficit</td>
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Cattle with facial nerve paralysis will have a drooped ear, ptosis, and atonic lips. Occasionally saliva will drip out of the affected side of the mouth. Facial paralysis is seen most often with listeriosis and ear infections. The vestibular system is composed of the auditory nerves and ganglia, and the vestibular apparatuses in the middle ear. Clinical signs associated with dysfunction of the vestibular system include head tilt, circling and loss of balance. Cattle with unilateral lesions tilt their heads and lean toward the lesion; recumbent cattle lie with the lesion side down. If the lesion is peripheral (such as an otitis interna), horizontal nystagmus will be present, and the slow phase is toward the lesion. Central lesions are associated with a vertical or rotary nystagmus. A combination of dysfunction of cranial nerves VII and VIII can be seen in either brainstem disease (listeriosis) or peripheral disease (ear infection) because the facial nerve passes through the petrous bone via the internal acoustic meatus with the auditory nerve. Cattle with deficits
of the glossopharyngeal, (IX) vagus (X) and spinal accessory nerves (XI) usually present with abnormal vocalization, dysphagia (trouble swallowing or regurgitating out of the nose) or abnormal breathing sounds. Pharyngeal paralysis can usually be assessed best by allowing the cow or animal to eat or drink. Sometimes this is difficult because sick cattle will not eat, especially in a strange environment. Alternatively, water can be administered via a dose syringe and the cow’s ability to swallow can be assessed. Endoscopic examination is helpful in determining if nerve dysfunction exists. The hypoglossal nerve supplies motor innervation to the tongue. The tongue’s function is assessed by grasping it and pulling it out and to each side. Unilateral lesions may result in the tongue sticking out one side of the mouth.

Other tips
After the completion of the examination of the head, one should palpate the neck concentrating on the submandibular lymph nodes, the skin and musculature of the neck and trunk, and finally the superficial cervical or prescapular lymph nodes. These lymph nodes should be approximately as big as one’s index finger. When examining the rear legs, the prefemoral lymph nodes should be palpated. Dependent edema, indicating circulatory failure or hypoproteinemia, will be noted when the ventral part of the jaw, thorax and abdomen are examined. When moving from the head to the rear of the animal, move your hand over the back to detect subcutaneous emphysema, parasites or neoplasm, and skin lesions. Particular attention should be paid to the joints of the rear legs. Palpation of the stifle joint and hock joint may reveal accumulation of synovial fluid. Palpation of the stifle joint is best accomplished by first locating the middle patellar ligament, then sliding the fingers medially until the next hard structure is encountered. This is the medial patellar ligament. There should be a depression in the space between the ligaments. Similarly, a soft depression should exist between the middle patellar ligament and the lateral patellar ligament. If the ligaments are difficult to palpate because the space between these ligaments is filled and very firm to the touch, then there is substantial distention of the stifle joint. This can be seen in both septic and non-septic conditions such as rupture of the cranial cruciate ligament. One easy way to differentiate between foot lameness and upper leg lameness or neurologic disease of the rear limbs is by lifting the rear legs. Animals with a foot lesion will often kick violently when the back leg is lifted, while those with upper leg lameness and neurological disease will not. Occasionally, lameness and neurological disease can be confused, especially by owners.

While standing behind the animal just prior to rectal exam, the last part of the neurological exam can be conducted. Tail tone can be assessed by picking the tail up and noticing the ability of the animal to clamp down, and by assessing the tone of the anus and sensation around the perineal area. The final part of the physical examination is the rectal exam. A rectal examination is part of a good physical examination of any cow or bull. The rectal exam, in my opinion, is best conducted last, but must always be conducted after rectal temperature has been taken and pinging has been done. Otherwise pneumorectum can cause a falsely low rectal temperature and can produce right-sided pings that may confuse the examiner. The following is a description of the rectal exam excluding the reproductive organs. The key to obtaining the most information from a rectal exam is in knowing which structures are usually palpable and which are not. There is no standard accepted sequence in which the abdomen is examined per rectum, so I will simply discuss each quadrant beginning with the left dorsal and proceeding clockwise.

1. Pelvic exam. The bovine pelvis has many prominent ridges and bumps with a large prominent symphysis pubis and a step-like sacroiliac junction. Walking or rocking the animal from side to side while palpating can best identify fractures or luxations. Pay particular attention to crepitus and asymmetry. There are several lymph nodes in the pelvis that may go unnoticed in a healthy cow, but become much enlarged in lymphosarcoma. 2. Left Dorsal Quadrant. The dorsal sac of the rumen is palpable several centimeters cranial to the pelvic brim. Sometimes the rumen extends to the pelvic canal. Size, consistency, gas caps and relative position of the rumen can be assessed. Left displaced abomasum is not palpable per rectum, but the rumen may feel displaced medi ally. The left kidney is usually on the midline but may be to either side depending on the fullness of the rumen. 3. Right Dorsal Quadrant. The right kidney lies cranial to and to the right of the left kidney and the caudal pole can be felt in some cattle. The aorta and vena cava run along the dorsal midline and can be palpated. Occasionally the cecum in a healthy cow will be in or near the pelvic brim, but usually it cannot be identified. Spiral colon and small intestines are not palpable in a normal cow. In cattle with obstructions, the intestines may be subtly or obviously distended, but any palpable intestine (other than cecum) is abnormal. Right displaced abomasum is seldom palpable, but abomasal volvulus is often palpable at the furthest extent of the reach in the right mid-to-dorsal quadrant. 4. Right Ventral Quadrant. Distended intestines may be palpated here also. A displaced, displaced or twisted cecum is usually palpated easily in the right ventral or dorsal quadrant or in the pelvic canal. It is situated much more caudally than an abomasum with a volvulus. In vagal indigestion, the right ventral sac of the rumen is prominent. It is occasionally palpable in normal cattle. 5. Left Ventral Quadrant. Usually, only the ventral sac of the rumen is present. The urinary bladder may lie on either side of midline beneath the uterus, but it is usually flaccid and not always easily located.

Other abnormalities that can be detected by rectal examination include pneumorectum which results in the rectum being tightly adhered to the arm like a sleeve, while the examiners arm and hand seem more freely movable than usual. Acites may cause the rumen to float. Adhesions due to peritonitis may give a feeling of roughness to the serosal surfaces, or may create a tearing sensation as
mature fibrinous adhesions are broken down, or may severely restrict movement in the abdomen if extensive firm adhesions are present.

Of course, a complete physical examination is not warranted in every case but it is important to know how to perform one for those cases in which the diagnosis is not obvious.
None of us who have been veterinarians for more than 1 or 2 days has escaped making a mistake from which we can learn. I have nearly 40 years of experience in the mistake-making business; therefore, I consider myself somewhat of an authority. Only my failing memory diminishes the value that I could be to veterinary medicine. Yet, even though I have probably forgotten more than I member, I still think I remember enough screw-ups that I either made myself, or had an opportunity to help remediate after someone else made them, or had an opportunity to discuss them by telephone with colleagues who shared their learning experience with me. To all those people who have made a mistake that I got to share in without doing it myself, I thank you. I hope maybe that this discussion will spare some of you from making the same mistake.

One can organize a series of boo-boos into an innumerable collection of sequences, but I've decided to limit my comments here to the category of Drugs and Treatments. Sometimes we make mistakes using drugs and administering treatments because we do not know. Sometimes we make mistakes because we know a little, but we use a logical or illogical extension that turns out not to be true. The following are some examples.

**Phenylbutazone**

Granted, we do not use this drug much anymore in cattle. The FDA has it on a heightened awareness list. Many suspect (lame) cattle are being tested for this drug, residues are present for an extended time, and there are alternatives. But it still makes a good example of the principle. We use it in horses all the time at 2 g/day. A horse is big; a cow is big. Why not try 2 grams/day for cattle? If you do, you probably will not think that phenylbutazone is very effective in cattle. Let us look at the difference.

The plasma half-life of phenylbutazone in horses is approximately 6 hours. The plasma half-life of phenylbutazone in cattle is greater than 48 hours. So based on pharmacokinetics, an appropriate dosing regimen for phenylbutazone in cattle is 10-20 mg /kg on day one, followed by 2-5 mg/kg every 24 hours or 5-10 mg/kg every 48 hours. I used to administer 8 g/1000 pounds on day 1 followed by 2 g/1000 pounds daily. According to pharmacokinetic principles, if one administered the maintenance dose of 2 g/1000 pounds daily without a loading dose, it would take approximately 1 week to reach therapeutic concentrations. That is why some people never thought phenylbutazone was very effective in cattle. They gave up before therapeutic concentrations were ever achieved.

**Aspirin**

This is an interesting drug from a regulatory perspective. Aspirin is not approved for use in food producing animals. Yet it is labeled for cattle. How can that happen? Because it has been around so long, and no company would ever spend the money to get it approved, is "generally recognized as safe" by FDA. And it has no withdrawal time. But is it effective; and at what dose? The maximum recommended dose for people is 4 g/day. If we agree that the average cow weighs about 1200 pounds, and the dose is the same people as it is for cattle, that 1200 pound cow would receive 32 g. The dose on the label for cattle is 100 mg/kg twice daily. For that 1200 pound cow, that would equal 109 g in a day. That is more than 3 times as much as a 1200 pound person would take. It turns out that the half-life of aspirin in cattle is approximately 30 min. Many contemporary pharmacologists think that even this large dose is not effective in cattle.

**Meloxicam**

This is one of the most popular NSAIDs in cattle right now. It is approved for dogs at a dose of 0.2 mg/kg the first day followed by 0.1 mg/kg each day after that. However, the recommended dose in cattle is 1 mg/kg orally with an expected therapeutic concentration for up to 3 days; or 1 mg/kg orally on day 1 followed by 0.5 mg/kg orally every other day. Therefore, it is obvious that the dose in cattle compared to that of dogs is quite different.

**Long-acting antibiotics are good. Long-acting antibiotics are bad. Long-acting antibiotics are long-acting aren't they?**

"Long-acting" antibiotics have been around for a long time, but in the past 10 years, their availability and use has expanded making them the rule instead of the exception for antimicrobial treatment of cattle. Probably the first thing we should examine is whether they are really "long-acting antibiotics." Let's look at ceftiofur. Naxcel®, Excenel® and Excede® are all products containing the antimicrobial ceftiofur. Once the drug enters the bloodstream, it behaves in exactly the same way irrespective of whether it came from a Naxcel® bottle, an Excenel® bottle, or an Excede® bottle. The ceftiofur molecule doesn't know the difference. The reason the pharmacokinetics and dosing interval is different for these drugs is because the rate at which the salt releases free Cefitiofur into the interstitial fluid and plasma is different. Cefitiofur sodium dissociates rapidly and is absorbed immediately. Cefitiofur hydrochloride dissociates more slowly, and therefore is released into the plasma at a slower rate. Cefitiofur crystalline free acid dissociates much more slowly. Therefore, the cefitiofur is not “long-acting”, but rather slow release.
One of the oldest "long-acting" antibiotics is benzathine penicillin/procaine penicillin combination. It claimed to have therapeutic action for 48 hours. In a pharmacokinetic chart, the total drug available is represented by the area under the concentration curve. If the curve is expanded to the right-the concentration stays above zero for a longer time-the peak concentration has to be lower. It's geometry or something. Take a look at the chart on the left. (Schipper, IA , et al. JAVMA, 1971) Notice several things. First look at the Y axis. Notice the distance between 0 and .1, and how the scale changes between .1 and .2. If we drew this chart in a consistent scale, it would be the height of the page and the peak of the procaine penicillin would be over 10 times higher than that of the benzathine penicillin (0.04 compared to 0.5.) The total dose was the same for the procaine penicillin as it was for the benzathine penicillin in this study. That means that the tail of the benzathine penicillin concentration curve has to go out a long ways to the right before it gets back zero. But notice how low the concentration is. The concentration of penicillin following administration of procaine penicillin does not dip below that of benzathine penicillin until one gets to 36 hours. So the benzathine penicillin is contributing very little to the concentration until after 36 hours. And then it's only holding the concentration steady. Most of us consider concentration of penicillin after administration of procaine penicillin to be below the therapeutic level by 24 hours. So what exactly is the benzathine doing? It's maintaining penicillin at sub-therapeutic concentrations for an extended period. That's worthless unless we are treating an organism that is exquisitely sensitive to penicillin or we are treating cystitis. But because of the dept effect of the benzathine, we will get tissue residues for a long time. Therefore, as Mike Apley likes to say, benzathine/procaine penicillin combination is not long-acting, but is instead, long residue producing. I think this product in unnecessary in modern veterinary medicine.

Therefore, I must be saying that long-acting antibiotics are bad. Not at all. So, long-acting antibiotics are good. They certainly can be. The new macrolides provide therapeutic concentrations against target organisms for many days. My biggest regret is that the target organisms are a rather specific group of respiratory pathogens, and there is scant data on the efficacy of these new drugs against other pathogens. It's is not the fault of the pharmaceutical companies that these data are lacking because they are discouraged or prohibited by regulatory agencies from providing information about organisms which are not on the label.

How you ever heard the question “Can you give drug X to a cow orally?” when the questioner really meant to say "Is drug X effective when administered to a cow by the oral route?" We can also put any route in that question. Sometimes when students ask this question, I answer "Yep. But it won't do any good." Let's look at some mistakes which are made concerning the route of administration of certain drugs.

Trimethoprim-sulfonamide combinations

TMPS it is absorbed readily after administration to monogastrics. What about ruminants? Several studies in neonatal calves have shown that TMPS (all of the studies used Tribissen® which contains sulfadiazine) is efficiently absorbed in baby calves, but not in older cattle. This graph shows the serum concentration curves of calves at 1 day, 1 week and 6 weeks of age following administration of 15 mg/kg of the combination(SE Shoaf, et al., J Vet Pharm Ther, 1987) . As you can see, very little trimethoprim is absorbed after one week of age. While the sulfadiazine was absorbed very readily, it must be remembered that the dose of sulfadiazine when given in combination with trimethoprim is only a fraction of that which would be administered using a sulfonamide alone. That's the whole idea of using the drugs in combination. Because they are synergistic, a lower dose of each drug present at the same time will be effective against bacteria that would be resistant to either drug alone at that same concentration. Interestingly, in other studies, it was suggested that trimethoprim is not only destroyed in the rumen, but it's also efficiently metabolized in the liver of older cattle so that even by parenteral administration, the plasma concentrations are relatively low. The bottom line conclusion of Shoaf was that for calves < 1 week of age, oral administration of 15 mg/kg TMPS once a day should provide therapeutic concentrations while in calves > 1 week of age, oral administration of 30 mg/kg TMPS twice a
day should be administered. Of course, taken literally, this recommendation is ridiculous because calves do not change overnight. I have always recommended 30 mg/kg TMPs twice a day, and only used it in calves less than two weeks of age. In round figures, that is usually about one 960 mg tablet twice a day. With the advent of newer antibiotics on the market, I have used this drug less and less.

**Percutaneous injection of poloxalene into the rumen**

I've never done this, but thanks to some other people who have, I won't have to in order to find out what happens. I've had two cases where someone injected poloxalene into the left paralumbar fossa thinking it was going into a bloated rumen. In both cases it created a massive abscess. Poloxalene must be an irritant because I know that a lot of needles and trocars get stuck into rumens and have very little adverse effect. I've never seen anything written about this, but because I believe this occurred due to more than bad luck, I'm going to avoid it.

**Pulling out the big guns**

Expensive animals with serious diseases deserve high-powered, expensive antibiotics with full-page ads and certainly justify using something-well, not "ordinary". Maybe not. We've all been faced with an owner who goes on about how wonderful a particular animal is as were thinking that the prognosis for the beast in front of us is not so good. And we might get the statement "I don't care what it costs Doc; save her." That's when it's time to pull out the stops and use the newest, greatest, most expensive, least "legal" antibiotic we can find. I have to admit, sometimes it's great to have the economic constraints lifted, but the biology of the organism and the animal doesn't really change. Let's look at a few quick examples. Let's take the case of a show heifer that was administered mineral oil retropharyngeally by a well-meaning Ag teacher who was trying to help a kid whose show heifer had bloat. First of all, it was probably a free gas bloat that didn't need mineral oil or poloxalene, but might've benefited from something as innocuous as some baking soda in the feed. Now it's got a raging retropharyngeal and peri-pharyngeal phlegmon. And who knows, maybe it aspirated a little bit and has "a touch of pneumonia" as some people often say. So that opens the door to enrofloxacin. Why not? It's a broad-spectrum antibiotic that must be good because extra label use is illegal. Well what are we trying to treat? The main problem is inflammation, not infection. Mineral oil is the major component of Freund's adjuvant. That is such an inflammatory substance that it takes special permission to be able to use it in a research environment to produce antibody in rabbits and others laboratory animals. Along with the inflammation, it's probably going to cause some necrosis. The ischemic environment caused by the oil and the necrosis is going to be a perfect place for anaerobic organisms to live and grow. Enrofloxacin, while a great drug, has poor activity against anaerobic organisms. What has good activity against anaerobes? Penicillin. For the infectious process associated with the phlegmon, penicillin would probably be much more effective than enrofloxacin. It’s not new or terribly expensive, but it might do the job. While we’re on the subject of this animal, the number one priority is for the animal to be able to breathe. A tracheostomy may be necessary. Cattle do quite well with tracheostomies, but I'd like to avoid that if possible. If the strider is severe, to me it's time to pull out the dexamethasone. But that might cause immunosuppression and possible secondary infection! I say to my critics, if this heifer's infection is worse in three days, I'll be happy because that means she is still alive. She may not want to (or be able to) eat or drink, and passing a stomach tube repeatedly is not a good idea. So more than expensive antibiotics, a small rumenostomy, which is very simple to perform, might benefit this heifer more.

Let's take a quick look at another case. Last week a practitioner called and told me about a rancher who had a couple of calves die acutely, and the one he performed a necropsy on had blackleg. The owner had actually found it alive and treated with enrofloxacin. First of all that's against federal law. Secondly it's against all the principles of pharmacology. The calf looked very sick so he decided to use a very "strong" antibiotic when the antibiotic of choice would've been penicillin. The value of the animal and the severity of the condition do not dictate which antibiotic is most likely to be effective. That's a fact.

**Have you ever said any of the following?**

- We seem to have really good luck with that. Luck, chance, spontaneous cure-thank goodness we have all of these that help us. It just seems to me that the statement should be reserved for therapeutic regimens that involve horseshoes or shamrocks or something similar. Now I'll accept luck any day, but I like a drug or vaccine to offer more.
- I have been doing it this way for 30 years and I have never had a problem. I can't think of anything I have been doing for 30 years that has not resulted in a problem or at least given the impression of causing a problem at least once. That includes not only veterinary treatments and procedures but other things like breathing and getting up in the morning. Maybe I'm a cynic, but when someone tells me they never had a problem, I think there's a problem.
- Well, it seems to work in my hands.

So we need to discuss how we define when something "works." Most of us define it as having a favorable outcome following an intervention. It varies with the practice type and the clientele, but I think for most of us, we are called to intervene on patients that have a high probability of a spontaneous recovery. Yet, many times we cannot determine at first examination if a particular patient is one that's going to recover spontaneously or one that is going to require treatment-therefore we treat all of them. If the disease has a 20% probability of resulting in death and an 80% probability of self-resolution, and we can save 50% of them that would die
otherwise with an intervention, will we be able to distinguish if our intervention was really the cause of the animal living? At first blush you say "My goodness. I should be able to tell if I can save 50% of them." But think about it. 80% live anyway. If you treat them, 90% live. And these are averages over time. How long would it take to figure out if 80% or 90% were living? The owner will probably give you credit for (and you're not going to argue) with saving 80% to 90% either way. If you ever have an opportunity to go back through medical records and actually test your "feelings" about the performance of the treatment, it can be quite revealing and surprising. We only remember the really good stuff and the really bad stuff. And let me be clear. It only makes sense to continue doing what seems to be successful. It doesn't make any sense to do something that seems to be unsuccessful. I just think we're more likely to be better veterinarians if we understand that sometimes we make a difference (to the negative or to the positive), and sometimes we don't, and sometimes we have trouble telling the difference. When we start always believing ourselves, that's when we run into trouble. And it's easy to believe yourself if you never get the opinion of someone else.
Serum protein

Serum contains many different proteins, but the two components of diagnostic significance relative to the chemistry profile are albumin and globulin. Albumin is synthesized in the liver and is the protein primarily responsible for the oncotic pressure of plasma. A large portion of the globulin fraction is made up of immunoglobulins which are synthesized by lymphoid tissue. The ratio of albumin to globulin (A:G ratio) is fairly constant in healthy cattle (reference range 0.84 -0.94). Most chemistry profiles include measured albumin and total serum protein, while the value for globulin is typically derived by subtracting the former from the later.

One must remember that if plasma is used instead of serum, fibrinogen will be included in the value for total protein, and hence, the derived globulin value; this may obfuscate the interpretation of the total protein and globulin. The discrepancy cannot be totally rectified by simply subtracting the value for fibrinogen, which is often determined by refractometry, from the value for plasma protein on the profile because of the difference in methods of analysis. Because most reference ranges are established for serum proteins, it is our opinion that serum is the sample of choice when evaluating the blood proteins. More specific and detailed evaluation of the globulin fraction can be achieved using electrophoresis, radial immunoaassay and other methods which will not be discussed here.

Hyperproteinemia can result from an increase in albumin, globulin or both. The only cause of hyperalbuminemia is dehydration. In dehydration, both albumin and globulin rise, but whether they exceed the reference range is determined by the degree of dehydration and the original protein concentration in the serum. Hyperproteinemia without dehydration is almost always the result of hyperglobulinemia. Globulin increases substantially with age in dairy cows. The difference between two year-olds and five year-olds was about 1.5 g/dl, potentially a clinically relevant difference. Causes of hyperglobulinemia include chronic inflammatory diseases (traumatic reticuloperitonitis, liver abscess, chronic pneumonia) and hepatic disease. In chronic inflammatory disease, the A:G ratio usually decreases because of an increase in globulin which is often accompanied by a small decrease in albumin. In chronic hepatic disease, the decrease in albumin may be more substantial. Serum globulin may be one of the most overlooked values on the routine chemistry profile. Changes in the hemogram are often rather subtle and transient in inflammatory disease of cattle, compared to other species. Therefore, the evaluation of serum globulin is of great value in chronic inflammatory disease.

In mature cattle, hypoproteinemia is usually the result of hypoalbinemia or panhypoproteinemia. Hypoalbinemia occurs when 1) hepatic production is insufficient to meet demand, either as a result of insufficient production or increased consumption or 2) there is excessive loss of albumin. Insufficient production can occur in animals with chronic severe hepatic disease or as a result of inadequate protein intake, digestion, or absorption. Because bovine albumin has a half-life of 16.5 days and the reserve capacity of hepatic tissue is so great, liver disease must be chronic and severe to result in severe hypoalbuminemia. In the authors' experience, cattle with chronic debilitating disease of many causes may be hypoalbuminemic with low or normal total protein. If the A:G ratio is low, chronic inflammatory disease should be suspected. In acute and subacute disease, hypoalbuminemia frequently results from loss of albumin. Avenues of albumin loss include the kidney (particularly the glomerulus), the gastrointestinal tract, hemorrhage and exudation. In many instances, loss of albumin may be accompanied by loss of globulin, resulting in panhypoproteinemia.

Renal amyloidosis can result in severe albumin loss in the urine due to glomerular damage. In one report, 5 of 6 cattle with amyloidosis had hypoglobulinemia along with hypoalbuminemia. Panhypoproteinemia is the rule in protein-losing gastrointestinal enteropathies such as nematode parasitism, paratuberculosis and salmonellosis. Because digestion and absorption may be impaired in these diseases, decreased production due to amino acid deficiency may contribute to the hypoproteinemia in chronic cases. Acute hemorrhage results in panhypoproteinemia accompanied by anemia.

Hypoglobulinemia is infrequent in cattle except neonates, either as a result of failure of passive transfer of maternal antibody, or severe infection when transferred antibodies are consumed rapidly prior to the efficient production of endogenous antibody by the young calf.

Hepatic tests

The leakage enzymes aspartate transaminase (AST, formerly SGOT), L-iditol (formerly sorbitol) dehydrogenase(IDH), ornithine carbamoyltransferase (OCT), glutamate dehydrogenase (GDH) and lactate dehydrogenase (LDH) have been used to evaluate the liver. Of these, AST, LDH and IDH are the most popular in the United States. Both AST and LDH are found in a wide variety of tissues, the most important of which are liver and muscle. Muscle damage, especially due to recumbency in cattle, may result in marked increases of both; hence, AST and LDH should be interpreted in conjunction with a liver-specific enzyme (such as GGT), or a muscle-specific enzyme such as creatine kinase (CK) to determine the source of the tissue insult. Usually, high AST or LDH and normal CK indicates liver disease. If serum is allowed to remain on the clot too long or the sample is hemolyzed, the AST and LDH
may be falsely elevated because both enzymes are found in red blood cells. Because concentrations of these enzymes are high in serum when damaged cell membranes allow their escape from hepatic cytosol, they indicate cell damage, not abnormal hepatocellular function. In fact, in chronic or slowly progressive hepatic disease, these enzymes may be within or below reference ranges because few hepatocytes are being damaged at one time, or because hepatocellular mass is substantially reduced. Consequently, these enzymes may be more sensitive indicators of acute disease such as some toxicities and infectious hepatitis. They may also be high in cattle with hepatic lipidosis, passive venous congestion and diseases that cause distension of the forestomachs and abomasum. IDH is a sensitive and specific indicator of hepatocellular damage. Unfortunately, its usefulness is limited by its relatively instability in vitro.

The "cholestatic", enzymes gamma glutamyltransferase (GGT) and serum alkaline phosphatase (SAP), are more sensitive to biliary obstruction caused by conditions such as fascioliasis or choleslithiasis. The cholestatic enzymes are more likely to be high in chronic hepatic disease than are the leakage enzymes because fibrosis constricts and blocks some bile ducts.

Although GGT is found in many tissues, the source of essentially all of the GGT in the serum is the biliary and hepatocellular membranes. Therefore, it is one of the most liver-specific tests available to veterinarians. Serum GGT rises principally in cholestatic disease, although hepatocellular diseases in which cholestasis is a secondary feature, also causes an increase in GGT. Because it tends to decrease less rapidly than the other leakage enzymes, it may be of more value in identifying cattle with chronic hepatic disease. Serum GGT of pre-colostral calves is similar to that of mature cattle, but serum concentrations rise sharply following consumption of colostrum, which is rich in GGT. By 24 hours after colostral intake, serum GGT concentration is 50 to 100 times that of colostrum-deprived calves. In fact, serum GGT can be used to estimate the success of passive transfer, but not to detect hepatic disease in neonates.

Serum alkaline phosphatase, a useful indicator of hepatic or cholestatic disease of dogs, is often included in chemistry profiles of cattle. Several isoenzymes from different tissues have been identified, and almost all of the SAP in healthy cattle is of osseous origin. In cattle with hepatic disease, SAP of hepatic origin increases, but the increase is not large in magnitude. Therefore, SAP is of limited diagnostic value for hepatic disease of cattle. Interestingly, though not clearly explainable, SAP was found to be useful as a prognostic indicator in cattle with abomasal volvulus.

Bilirubin is a breakdown product of hemoglobin that is conjugated and excreted by the liver. Unconjugated (or direct) bilirubin is the result of rapid breakdown of hemoglobin which occurs in acute hemolysis. Conjugated (or indirect bilirubin) accumulates in plasma when there is intra- or extrahepatic biliary obstruction. The plasma concentration of bilirubin in healthy cattle is very low compared to that of the other species; and the magnitude of increase is relatively small, even in severe liver disease. Severe bilirubinemia and icterus in cattle is almost always a result of hemolysis, and hence, is primarily due to unconjugated bilirubin.

Though usually considered an index of renal function, blood or serum urea nitrogen (BUN or SUN) is also an indicator of hepatic function. In the liver, ammonia is converted to urea. In severe hepatic failure or partial vascular anomaly, SUN is low while ammonia is high. However, low SUN is not associated only with hepatic disease. Because rumen microbes use urea to synthesize protein, the rumen acts as a "sponge" for urea in cattle that are anorectic or protein-deprived.

Laboratory reference ranges for mature cattle are invalid for neonatal calves, especially those under a week of age. Neonatal calves have somewhat higher concentrations of bilirubin, AST, SAP, and SBA and markedly higher concentrations of GGT than do mature ruminants.

**Electrolytes**

The serum electrolyte profile typically includes sodium (Na), potassium (K), chloride (Cl), and total carbon dioxide (TCO₂) or bicarbonate (HCO₃⁻). From these values, the anion gap (AG) can be calculated. Although there is a nominal difference between the TCO₂ and HCO₃⁻, the HCO₃⁻ usually being slightly smaller, we will consider them equivalent in this paper. Serum electrolytes are useful in the evaluation of several body systems, as well as for the formulation and monitoring of fluid and electrolyte therapy. Due to the abundance of K and scarcity of Na in erythrocytic fluid relative to serum, hemolysis can falsely increase serum K and decrease serum Na in cattle.

Because their concentrations change in concert in a number of conditions, the electrolytes will be discussed together. Sodium is the major extracellular cation, while Cl and HCO₃⁻ are the major extracellular anions. Chloride and HCO₃⁻ often maintain a reciprocal relationship in extracellular fluid. Because the majority of the exchangeable Na and Cl are found in the extracellular fluid, measuring serum Na and Cl provides an accurate assessment of the total body status of these electrolytes. Serum potassium, on the other hand, provides a less reliable and sometimes paradoxical reflection of total body K status because only a small portion (approximately 5%) of the animal's K is in the extracellular fluid. Changes in blood pH greatly affect serum K by causing the movement of K across cell membranes; K moves into cells during alkalosis and out of cells during acidosis. Therefore, serum K should be interpreted along with serum HCO₃⁻. Serum HCO₃⁻ is a measure of metabolic acid-base balance; concentrations above the reference range indicating metabolic alkalosis and those below indicating metabolic acidosis.

Hyponatremia and hyperchloremia occur in salt toxicity/water deprivation, but are not commonly present in cases of dehydration because typically fluid loss in cattle occurs with concurrent loss of electrolytes. Cattle with clinical "salt toxicity" may have normal
serum Na because clinical signs often do not occur until after the cattle drink, and serum Na concentration and osmolality return to normal. Hyperkalemia is almost always secondary to acidosis as K moves out of the intracellular fluid into the extracellular fluid. Therefore, serum K is an unreliable index of total body K. For example, diarrheic calves often are acidic and hyperkalemic, but they have total-body K depletion because of fecal K loss. In these cases, as in most cases where serum K is increased secondarily to acidosis, K supplementation may be indicated during or immediately following correction of acidosis. Hypochloremia, hypokalemia, metabolic alkalosis and, to a lesser degree, hyponatremia, are typical findings in obstructive gastrointestinal diseases including abomasal volvulus, displaced abomasum, vagal indigestion, intussusception and cecal torsion. In these diseases, HCl is sequestered in the abomasum, causing hypochloremia, metabolic alkalosis, and secondary hypokalemia. In general, the more orad the lesion (abomasal impaction vs jejunal intussusception), and the more complete the obstruction (abomasal volvulus vs LDA), the more severe the alkalosis and hypochloremia. Hypochloremia and metabolic alkalosis are fairly non-specific abnormalities in sick cattle however. In a study of over 500 mature cattle in the authors' hospital, over 40% of the dehydrated cattle were hypochloremic and/or alkalotic.

Serum Na and Cl are consistently low in uroperitoneum, and often are low in diarrhea and renal failure, while serum HCO₃ is variable in these conditions. Urinary obstruction and uroperitoneum are associated with hyperkalemia in non-ruminant species, but not in cattle.

Renal tests
Elimination of nitrogenous wastes, such as urea and creatinine (Cr), and concentration of urine to conserve body water are two of the many vital functions performed by the kidney. Evaluation of these functions is exploited in the diagnosis of renal disease. Serum or blood urea nitrogen (SUN or BUN) and serum creatinine (Cr) are rough indices of glomerular filtration rate. The generous reserve capacity of the kidney makes SUN and Cr insensitive indicators of renal function; 75% loss of functional renal mass is required for azotemia to occur. Slightly more sensitive than SUN and Cr, the urinary specific gravity (USG) can detect about a 67% loss of functional renal tissue. The USG is most easily estimated by refractometry. By convention, USG of ≥ 1.025 is considered indicative of appropriate concentrating ability in the face of dehydration or azotemia. It is quite common, however, for normally hydrated cattle, especially dairy cattle, to have USG <1.025.

Azotemia, the accumulation of nitrogenous wastes in the blood, is reflected in the serum chemistry profile as high SUN and Cr. Remember - AZOTEMIA DOES NOT EQUAL RENAL DISEASE! Azotemia can be classified as renal (due to renal disease), prerenal (due to sluggish renal blood flow, as in shock or dehydration), or postrenal (due to obstruction of urine outflow, as in urolithiasis). Though not without exception, the simplest way to distinguish among the three is by measuring the USG. In azotemic cattle, if the USG is ≥ 1.025, the azotemia is prerenal; if the USG is <1.025, the azotemia is renal. In postrenal azotemia, urine is often difficult or impossible to obtain, and the diagnosis is based on physical examination. In our experience, cattle with prerenal azotemia eliminate urea and Cr rapidly when rehydrated, often returning to or near the reference range in 24-48 hours if appropriate fluid therapy and correction of the primary problem is accomplished.

Urea is formed in the liver by the detoxification of ammonia, a by product of protein metabolism. Therefore SUN is influenced by diet and hepatic function. Urea is recycled in a functional rumen, a process which may tend to moderate the rise in SUN in renal disease and result in a low SUN/Cr ratio. Although Cr, a product of energy metabolism in muscle, can be very low in emaciated cattle with little muscle mass, it tends to be less influenced by extraneous factors than SUN. For this reason, Cr is the test of choice over SUN.

While SUN, Cr and USG can identify renal disease, the final diagnosis cannot be obtained from this information. For example, acorn toxicity, pyelonephritis, and amyloidosis are diseases which cause renal failure in cattle. These diseases cannot be distinguished from one another simply based on the results of the chemistry profile. However, the characteristics of the urine in each of these diseases is very different. Whenever renal disease is suspected, a complete urinalysis should be performed, as well as, rectal palpation of the kidneys. Ultrasonography and renal biopsy may also be informative.

Glucose
Glucose metabolism is unique in ruminants because they absorb essentially no pre-formed glucose from the gut. The reference range for serum glucose in adult cattle is lower than for calves and non-ruminant species. Erythrocytes metabolize glucose in vitro in a blood tube at a rate of about 10% per hour at room temperature. Serum should be separated from the clot within 30 minutes, or sodium fluoride-containing tubes should be used if timely separation is not possible. Hyperglycemia occurs in stress, milk fever, and following administration of dextrose solution, xylazine, or corticosteroids. It is interesting that most milk fever remedies contain dextrose, even though hypocalceemia prevents the release of insulin from the islet cells of the pancreas resulting in hyperglycemia. Endogenous and exogenous steroids increase gluconeogenesis and increase serum glucose. Xylazine causes a dose dependant hyperglycemia that persists for over 6 hours. Diabetes mellitus although uncommon in cattle, causes permanent hyperglycemia if untreated.
Muscle enzymes
As previously mentioned, LDH and AST are released into plasma as a result of muscle damage, but they are not muscle-specific enzymes. Serum CK, on the other hand, is a very sensitive and specific indicator of muscle damage. Subtle increases can occur due to intramuscular injection, exercise or struggling. Recumbent mature cattle may have >100-fold increases due to the secondary pressure damage that is a part of the downer cow syndrome. Very high concentrations of CK in the absence of recumbency, or in young recumbent cattle suggest primary myopathy, such as white muscle disease or *Senna* toxicity. The half-life of CK in serum is short, and CK concentrations fall rapidly in recumbent animals even if they remain recumbent. Because AST concentration rises and falls more slowly, it can be used in combination with CK to stage muscle damage. In recumbent cattle, if the AST is very high and the CK is not, the damage is likely several days old. In an attempt to use laboratory tests for prognosis, New Zealand investigators found that fewer than 5% of cows with an AST value > 7.4 times the upper limit of the reference range survived. For CK, the "critical" value above the reference range was related to the duration of recumbency (Table 2).
Case 1
Signalment and history
4-yr-old Charolais bull. History of a hoof crack repaired 3 weeks ago. Appetite and activity decreased. Laying around a lot but not lame.

Physical examination
T- 102.6 F. RR - 64 bpm - slightly labored. HR - 90 bpm
Lung sounds slightly increased, but no crackles wheezes or areas of consolidation. No lameness. Feces scant and firm. Rumen contractions 1 in 3 min and weak. Rumen small.

Plan
• CBC ( at least PCV and TPP )
• Chemistry profile
• Urine dipstick and specific gravity

Hematology

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Ref Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCV</td>
<td>30%</td>
<td>24 – 42 %</td>
</tr>
<tr>
<td>Total Protein</td>
<td>9.8</td>
<td>6.5 – 8.8 g/dl</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>900</td>
<td>400 – 700 mg/dl</td>
</tr>
<tr>
<td>WBC</td>
<td>6,300</td>
<td>4,000 – 12,000/µl</td>
</tr>
<tr>
<td>Segs</td>
<td>4536(72%)</td>
<td>600 – 4,000/µl</td>
</tr>
<tr>
<td>Lymphs</td>
<td>1197(19%)</td>
<td>2,500 – 7,500/µl</td>
</tr>
<tr>
<td>Monos</td>
<td>504 (8%)</td>
<td>25 – 840/µl</td>
</tr>
<tr>
<td>Eos</td>
<td>63 (1%)</td>
<td>0 – 2,400/µl</td>
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Chemistry panel

<table>
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<tr>
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<th>Ref Interval</th>
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<tbody>
<tr>
<td>Total protein</td>
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<td>Albumin</td>
<td>2.7</td>
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<tr>
<td>Globulin</td>
<td>6.6</td>
<td>3.2 – 4.4 g/dl</td>
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<tr>
<td>Calcium</td>
<td>9.5</td>
<td>8.3 – 10.9 mg/dl</td>
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<td>A:G ratio</td>
<td>0.41</td>
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<td>4.3 – 8.6 mg/dl</td>
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<tr>
<td>Glucose</td>
<td>71</td>
<td>40 – 74 mg/dl</td>
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<tr>
<td>BUN</td>
<td>13</td>
<td>5 – 29 mg/dl</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.8</td>
<td>0.8 – 1.9 mg/dl</td>
</tr>
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</table>

Urine
Specific gravity 1.028; 1+ protein, pH 7.5

Differentials
Chronic Pneumonia; TRP; Abomasal Ulcer; Other Chronic Inflammatory Process

Case 2
Signalment and history
7-month old Boer wether; “Constipated” for 3 days; “Responded” to antibiotics and defecated; Now he is swollen under his belly

Physical examination
T- 101.6 F. RR – 60 bpm. HR – 120 bpm. No rumen contractions. Slightly distended abdomen bilaterally ventrally. Edema on the ventral midline from the umbilicus to the scrotum. Hypersensitive to touch along the shaft of the penis.
Case 3

Signalment and history
- 4 yr old rodeo bull
- Was thin when the owner bought him, but he thought he had flukes; Appetite is fair, attitude is normal
- Diarrhea and weight loss continued after anthelmintic

Physical examination
Unremarkable except for poor body condition

Differential diagnosis
- Johne’s Disease
- Ostertagiasis
- Chronic Peritonitis or Obstruction
- Inflammatory Bowel Disease
- Salmonellosis
- Amyloidosis
- BVD

Plan
- PCV, TPP, Chem profile; Urine analysis - R/O amyloidosis; Fecal exam and serum pepsinogen - R/O ostertagiasis; Johne’s ELISA, AGID, PCR/Culture - R/O Johne’s; Culture or PCR - R/O Salmonellosis

Hematology

Ref Interval

PCV 27 24 – 42 %
Total Protein 6.2 6.5 – 8.8 g/dl
Fibrinogen 600 400 – 700 mg/dl
WBC 16,350 4,000 – 12,000/µl
Seg neutrophil 13,532 (83 %) 600 – 4,000/µl
Lymphs 2,008 (12 %) 2,500 – 7,500/µl
Monos 810 (5 %) 25 – 840/µl
Eos 0 0 – 2,400/µl

Chemistry panel

Ref Interval

Total protein 5.6 6.2 – 8.6 g/dl
Albumin 2.2 3.0 – 4.2 g/dl
Globulin 3.4 3.2 – 4.4 g/dl
A:G ratio .65 0.75–0.85
Calcium 7.2 8.3 – 10.9 mg/dl
Phosphorus 6.4 4.3 – 8.6 mg/dl
Glucose 115 40 – 74 mg/dl
BUN 12 5 – 29 mg/dl
Creatinine 0.8 0.8 – 1.9 mg/dl

Ref Interval

Total bilirubin 0.2 0.0 – 0.2 mg/dl
ALP 89 0.0 – 78 U/L
CK 311 0.0 – 509 U/L
AST 208 0.0 – 107 U/L
GGT 107 0.0 – 100 U/L
Na 144 143 – 141 mEq/l
K 4.2 3.4 – 4.3 mEq/l
Cl 106 90 – 103 mEq/l
HCO₂ 24 24.5 – 35.1 mEq/l

Results
- Urine analysis - No Proteinuria; Fecal exam and serum pepsinogen - No ostertagiasis; Johne’s ELISA, AGID – Negative; Rectal biopsy – Negative (Today I would submit PCR); Culture - Negative

Plan B
- Laparotomy - R/O Johne’s, IBD

Case 5

Signalment and history
- 4 yr-old Charolais Cow; Found her by herself under a tree 2 days ago with a snotty nose. Gave LA-200 injection. No improvement; Has been on rye grass pasture since February. Now it is April.

Physical exam
- Eyes sunken. Skin hard to tent; Slobbering, self-mutilation; Crusted nose; Subcutaneous edema, cracking of skin, and lacerations
### Hematology

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<tr>
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<td>6.6</td>
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<tr>
<td>Fibrinogen</td>
<td>900</td>
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<td>WBC</td>
<td>22,700</td>
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<tr>
<td>Seg neutrophil</td>
<td>18,610</td>
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<td>3,860</td>
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<td>270</td>
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<tr>
<td>PCV</td>
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<td>TPP</td>
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<tr>
<td>Fibrinogen</td>
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####Chemistry profile

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<th>Value</th>
<th>Ref Interval</th>
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<td>Total protein</td>
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<td>6.2 - 8.6 g/dl</td>
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<td>0.0 - 0.2 mg/dl</td>
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<tr>
<td>Albumin</td>
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<td>Globulin</td>
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<td>0.75-0.85</td>
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<td>8.3 - 10.9 mg/dl</td>
<td>GGT</td>
<td>553</td>
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<td>Phosphorus</td>
<td>3.6</td>
<td>4.3 - 8.6 mg/dl</td>
<td>Na</td>
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<td>119</td>
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<td>BUN</td>
<td>11</td>
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<td>Cl</td>
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<td>Creatinine</td>
<td>0.8</td>
<td>0.8 - 1.9 mg/dl</td>
<td>HCO₂</td>
<td>32</td>
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####Diagnosis
Photosensitization - Secondary

####Signalment and history
- 2 yr-old Fleckvieh Bull; Recurrent bloat for 1 week 5 weeks prior to presentation.
- Suspected poloxalene injection into rumen. Bloat resolved, but bull became anorexic and lost weight.

####Physical exam
Good body condition; Slightly dehydrated; Moderate distension; Rectal exam - gas-filled viscus right mid-dorsal abdomen, rumen hard

####Differentials
RDA; Cecal displacement

####Plan
CBC; Chem profile; Abdominocentesis; Exploratory laparotomy

### Hematology

<table>
<thead>
<tr>
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<tr>
<td>PCV</td>
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<td>24-42 %</td>
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<tr>
<td>Total Protein</td>
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<td>Seg neutrophil</td>
<td>9782</td>
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<td>Lymphs</td>
<td>2948</td>
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<tr>
<td>Monos</td>
<td>268</td>
<td>25-840/µl</td>
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<tr>
<td>Eos</td>
<td>402</td>
<td>0-2,400/µl</td>
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####Chemistry panel

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<td>Albumin</td>
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<td>CK</td>
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<td>AST</td>
<td>72</td>
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<td>Calcium</td>
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<td>Glucose</td>
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<td>BUN</td>
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<td>5 - 29 mg/dl</td>
<td>Cl</td>
<td>104</td>
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<tr>
<td>Creatinine</td>
<td>1.4</td>
<td>0.8 - 1.9 mg/dl</td>
<td>HCO₂</td>
<td>30</td>
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128
Revised diagnosis
Not GI obstruction; Chronic inflammatory disease

Rectal exam - Day 2
- Gas-filled viscus smaller and more ventral; Rumen very hard, adhered to left body wall
- Left kidney not palpable

Ultrasonography day 2
Per rectum and transabdominal: Rumen not on left side; Fluid filled mass with fibrin; Aspiration - foul smelling fluid

Revised diagnosis and plan
Periruminal abscess; Left paramedical approach to open abscess; Periruminal abscess; Perioperative antibiotics; Lavage of the abscess
Masses of the neck or head
Swellings of the cranial neck region are fairly common in sheep and goats. There are three important structures that may cause swellings: lymph nodes, thyroid and thymus. The parotid lymph nodes, which are under the ear, and the mandibular lymph nodes, which are just rostral to the larynx, may be sites of abscess. Caseous lymphadenitis is the most likely cause of an abscess in the head and neck region of meat goats. HOWEVER, there are a few other conditions that may be misdiagnosed as abscesses and should always be considered before one begins to poke or lance.

Two conditions which cause swellings of young goats that look similar to each other, and also like abscesses, are enlarged thyroids (goiter) and hypertrophied thymic tissue. Goiter occurs in iodine deficient areas or when goitrogenic plants (Brassica sp) are consumed. Adults can have enlarged thyroids and be relatively healthy. Kids will be weak, poor-doing, have thin or no hair, etc. This is a pathologic condition, but it is relatively RARE and regional. This diagnosis should be made only after conclusive diagnostic investigations and tests are performed.

Swellings in the thyroid area of fast-growing slick-coated, active kids are likely to be thymic tissue. This is normal, and it regresses when the kids mature. We have seen cases where these masses have been aspirated and our lanced resulting in secondary abscesses and cellulites. A problem was created where no problem existed in the beginning. Veterinarians should be aware of this nonpathogenic condition and not intervene.

Caseous lymphadenitis (CL) caused by Corynebacterium pseudotuberculosis is a scourge of the goat and sheep world. Most, but not all abscessed lymph nodes are CL. My approach is to first discuss the condition with the owner to assess their level of awareness as well as their level of concern. Based on the owner’s decision, we choose a course of action. If the owner is aware of CL and is willing to live with it, we treat the abscess like any other abscess. We should remember that slaughterhouse surveys have shown that nearly 50% of cull ewes have lesions, therefore this is a very ubiquitous condition. We document in writing that we have discussed the contagious nature of the disease and have advised against such a practice. In most cases when the owner is not certain of the status of their herd, we culture the abscess before treating it. If we isolate T. pyogenes or something else, we lance the abscess in a routine manner. I STRONGLY RECOMMEND THAT YOU DO NOT LANCE AN ABSCESS ON A GOAT OR SHEEP WITHOUT OFFERING TO CULTURE or discuss the ramifications of not doing so in a herd or flock of unknown CL status. The pus from the draining abscess will contaminate the environment. That is the worse thing that could happen on a previously clean (or relatively clean) farm and I think you could be held liable for your actions.

If we isolate C. pseudotuberculosis we counsel the client, although many sheep and goat owners already know the story. Some owners choose to lance the abscess like any other abscess and live with the disease. Some owners (most of our clients) lance the abscess and keep the goats isolated until the abscess heals and tried to manage their way out of a herd of our problem. Some owners have a zero tolerance and request that the lymph nodes be removed intact with primary surgical closure OR they immediately cull the animal.

A few years ago, one of my colleagues, Dr. Kevin Washburn, developed a new treatment protocol for CL. Some of you may be aware of the procedure whereby formalin is injected into abscessed lymph node. Some have reported excellent success with this method, but extra capsular injection can result in substantial swelling. Kevin proposed lavaging the abscess with saline solution through a 14gauge needle followed by injection with a parenteral dose (1.1 mg/kg) of tulathromycin. In a study he published, the resolution rate was 83% at follow with follow-up examination, no different than with lancing and flushing in the traditional way. However with this method, most of the risk of contaminating the president premise was removed. Also, none of the injected abscesses ruptured spontaneously posttreatment. We have used this technique successfully on many sheep and goats.

There is a serologic test for CL. It is called the synergistic hemolysis inhibition test (SHIT). I am not making this up. There is little data on its sensitivity and specificity. It is not very accurate.

Copper toxicity/deficiency
Sheep are much more likely to develop copper toxicity than are goats, which are more likely than cattle. Animals store Cu in the liver and when stressed, they release it all at once. A hemolytic crisis ensues causing anemia, hemoglobinuria and icterus, followed by pigment (hemoglobin) nephrosis, renal failure and death. We have seen some sheep, particularly flock mates of sheep with classical clinical copper toxicity, which were depressed and not eating well. Some of the sheep have had substantially elevated liver enzymes, and when tested, have had high serum copper. We think this is a form of subacute or chronic clinical copper toxicity. Treatment must be initiated early in acute or peracute disease. Diuresis should be induced to minimize renal damage, and ammonium molybdate (100 mg per head per day orally) or d-penicillamine (52 mg per kilogram body weight per day orally) can be given to chelate Cu. The chelating agents may be better used as preventatives on other exposed animals that have not developed clinical signs rather than as a
treatment. Once icterus and renal failure are present, the prognosis is grave. However we have successfully treated a number of small ruminants in the early stages of copper toxicity. A clinical guide to prognosis is the color of the urine (red is better than dark brown) and the degree of icterus. The creatinine concentration is probably a better indicator of the stage and severity of the disease.

Sheep should never be fed anything with trace minerals formulated for a species other than sheep. What about mineral mixes and feeds labeled “Sheep and Goats.” A good rule of thumb concerning the copper content is that if the copper content is safe for sheep, it will be inadequate for goats; if the copper content is adequate for goats, it will be toxic for sheep. In my experience, most products labeled for “Sheep and Goats” have an appropriate amount of copper for sheep.

We documented copper deficiency in a group of goats using blood, and then liver, copper concentrations. The situation was corrected with oral supplementation of copper.

Urolithiasis

Urolithiasis is a common problem in male small ruminants particularly castrated males in the feedlot and in show wethers. These wethers are fed a high grain diet and maybe on a restricted salt and water intake. The most common type of calculus is struvite, however modern feeding practices and the commonplace practice of providing urinary acidifiers in the feed may have resulted in an increasing proportion of calcium-based crystals. Clinical signs of obstructive urolithiasis include straining, frequent defecation, posturing to urinate, dribbling urine which is sometimes blood tinged, nervousness, depression, anorexia, and shivering. After urethral rupture has occurred, swelling in the perineal or prepubic area may develop as may abdominal distention when the urinary bladder is ruptured. NOTE: if a show whether becomes anorexic, stands by himself, or appears to be “constipated”, he should be immediately assessed for urinary obstruction. Owners who are not familiar with this disease often miss the early clinical signs, administer all sorts of drugs for all sorts of other problems, and allow the condition to develop to an irreversible stage.

The diagnosis of urolithiasis can usually be made based on physical examination. Many times palpation of the penis will elicit pain. Drops of blood tinged urine may be noticed at the prepuce orifice. Pulsing of the urethra immediately ventral to the anus is a frequent sign. In cases of ruptured or leaky bladder, ballotment of the abdomen may reveal a fluid wave. Abdominocentesis may also yield fluid. WARNING: not all goats with uroperitoneum have a ruptured bladder. A severely distended compromised bladder will leak through tiny holes, but the bladder is essentially still intact. Also, it is not difficult to inadvertently puncture the bladder and obtain urine during attempted abdominocentesis. Palpation of the bladder can be difficult if there is abdominal splinting. Therefore, ultrasonography is extremely valuable for determining the size and integrity of the bladder and confirming the diagnosis of urinary obstruction. The penis should be examined for both diagnostic and therapeutic reasons. Exteriorizing the penis is not an easy task, particularly in a young goat. For ease of visualization of the penis, patient welfare and for client satisfaction, sedation should be administered before exteriorizing the penis. If not, the goat will yell as if it is being tortured. I use xylazine at a 0.1 to 0.2 mg per kilogram body weight. Xylazine induces mild diuresis. I counter the argument against using xylazine by saying that I will, one way or another, remove urine from the bladder within 15 minutes of administering the drug. Diazepam is also an effective sedative, but it cannot be reversed with tolazoline.

In order to visualize the penis, the goat should be placed in a sitting position as an assistant supports the goat against his or her body while standing. The assistant should be careful not to allow the goat’s head to hit his or her face and not to allow the goats front legs to hit the operators face. With the goat sitting on its butt, the sigmoid flexure just cranial to the pubis is pressed and straightened while the penis is pushed out of the prepuce with repeated advances down the prepuce. Once exteriorized, the glans is grasped. Young virgin goats pose an additional problem. Their prepuce has never separated from the penis. Therefore, one cannot visualize the end of the urethral process, strip the prepuce proximally freeing it from the penis. This may induce slight hemorrhage. As soon as the glans of the penis is visualized, grasp it with a gauze pad, and continue to pull the prepuce down the shaft. An assistant should grab the penis where the prepuce attaches and hold it using a gauze pad.

After the penis is examined by palpation, the urethral process should be examined and amputated. If there are crystals or "sand" in the prepuce or urethral process, urine may begin to drip after the amputation. It is uncommon to have a strong stream of urine flowing after the obstruction is relieved. Rather, there is typically a dribbling of urine for several hours. If one wishes to attempt to dislodge calculi in the penis, a 3.5 mm to 5 mm polypropylene urinary catheter may be used. Lidocaine 1% in saline may be used as a flush. Currently, we do not vigorously flush the urethra in small ruminants. We only go a few centimeters and remove the calculi at the very distal end. RARELY can a small ruminant’s bladder be catheterized because of the urethral diverticulum.

Our current treatment of choice is installation of glacial acetic acid (Walpole’s solution) and to the urinary bladder by cystocentesis. Briefly, under ultrasound guidance, approximately 150mls or more of urine is removed and about the same amount of Walpole’s solution is placed into the bladder. We add enough Walpole’s to reduce the pH to 5. The goat is then allowed to recover (we usually administer tolazoline) and is monitored for 24 hours or until urination begins. If the goat is not urinating after 12 to 24 hours, the treatment is repeated.
A short-term alternative is perineal urethrotomy. I’ve become very hesitant to perform these because of their tendency to stricture after several months. We only recommend this procedure in goats that will be slaughtered in six months or less. Other adjunctive therapy includes the administration of anti-inflammatory drugs and antibiotics and fluids if indicated. We consider our success rate with Walpole’s solution to be very satisfactory and the cost is very reasonable.

From small ruminants of high-value, particularly rams and bucks, abdominal exploration and the creation of a tube cystostomy is a good alternative. A Foley catheter is placed in the bladder and exteriorized through the ventral abdominal wall. The catheter is left in place for 10 days or more to provide outflow for urine while the calculi in the urethra slough out, and the urethra regains its patency. The catheter can then be removed and the cystostomy will heal spontaneously.

Urinary acidification is recommended to prevent or reduce the formation of crystals. Ammonia chloride is the most frequently used substance to acidify the urine. It has been observed that after a period of weeks, the ammonium chloride is no longer effective, and the urine pH returns to above 7. We have some preliminary data that suggests dosing of ammonium chloride for 3 days per week with a 4-day rest period may prolong the period of efficacy. If the pH can be reduced to less than 6.5, small crystals that have formed may be dissolved, assuming that the crystals are struvite. Some calcium containing crystals do not dissolve in acidic urine and therefore are not amenable to treatment with Walpole's solution or prevention with the ammonium chloride.
The purpose of this lecture is to provide the veterinarian with some basic imaging principals that may be used for percutaneous procedures such as fracture repair and bone biopsy. Multiple imaging modalities may be used in such instances but particular attention will be paid to using the digital x-ray and fluoroscopy units.

**Radiation safety**

The radiation exposure rate for fluoroscopy is lower than conventional radiography 45 mGy/min vs 900 mGy/min respectively, however fluoroscopy exposure times are much longer, a 10 minute fluoroscopic procedure would yield a total dose of 450mGy while a single radiograph with a 200msec exposure, a total dose of 2mGy. A regular C-arm outputs 1,200 to 4,000 mrem/min and recommended yearly dose limits are 5000mrem to the torso and 50,000 to the hands (Singer). To limit radiation exposure proper radiation safety attire should always be worn. In addition to typical lead shielding, radiation attenuating surgical gloves and an extra dosimetry badge worn on the finger should be considered. The fluoroscopy unit itself should be calibrated and measured for scatter and be kept in spec. Previous studies have shown no exposure to dosimeter badges at the anesthesiologist position, 152cm from the fluoroscopy unit. However, all personnel within the room should remain gowned. Significant radiation exposure is present at <70cm from the unit thus operating personnel are at greatest risk for exposure (Mehlman).

**Practices to lower radiation exposures:**

1. Keep radiation-attenuating objects from the field (suture drapes to the patient instead of using towel clamps). The fluoroscope will auto adjust mAs and KVP therefore increased radiation attenuation within the field will yield higher exposures.
2. Keep the field collimated and keep the patient or part nearest the image intensifier.
3. Keep maximal distance from the fluoroscope or radiography unit and always avoid exposure to the primary beam.
4. Use lowest amount of exposure time needed to complete the procedure.

**Equipment**

- Multiple k-wires
- Hypodermic needle with ID large enough to accommodate K-wire
- +/- cannulated drill bits
- Long pair Carmalt or Kelly forceps for manipulating pins while keeping hands out of the primary beam
- Parallel pin guide
- +/- cannulated screws, cannulated depth gauge
- Drill sleeves
- Cannulated pin collet for drill

**Targeting with fluoroscopy and radiography**

Most surgeons will have access to a single fluoroscopic or radiographic unit capable of creating a 2 dimensional image. To accurately place an implant or biopsy device in a desired location using single imaging plane the surgeon must take 2D orthogonal images to gain a 3 dimensional perspective. First and foremost the orthogonal projections must be straight relative to the anatomical part receiving the fixation. For example, in an SI luxation the sacrum is the “target” thus the lateral view should be aligned with the anatomic site of implant placement (ie the sacral body not the ilial wing). In the spine, lateral positioning is easily achieved by superimposing the base of the vertebral transverse processes to gain rotational and cranial caudal alignment (a true lateral projection). Another example in a femur would be to use superimposition of the condyles to gain a true lateral projection of the bone.

Next, the target site of desired implantation should be centered in the image to limit projection artifact. A K-wire or needle can then be superimposed over the target. This K-wire is first placed perpendicular to the beam and moved along the skin using a long grasping forceps until it the tip is centered over the desired area of placement (indicated by the A labeled arrow in Fig 1A). A stab incision is then made at the tip of the pin and the pin is advanced through the incision and moved parallel to the radiographic beam. This creates a “aesnaoweed” view of the implant such that only the outer diameter of the pin is seen (arrow B...
in Fig 1A). For a clinical example, a sacroiliac luxation is used. When the sacrum is in straight lateral as indicated by the transverse process alignment, and the pin is deshadowed over the target, the site of expected course of the implant is clearly outlined. This is shown in Fig 1B for a trans-ilial bolt placement and Fig 1C (pin on the left) for a k-wire placement prior to lag screw fixation of a sacro-iliac luxation. Once centered the pin is held in position and then driven a short distance at this angle and rechecked again for alignment. The orthogonal VD view can then be used to evaluate depth. If placement is not ideal this initial pin can be used as a guide for a second K-wire placement.

When predrilling for placement of a screw or threaded pin, a drill sleeve may be placed first to protect the soft tissues and allow the surgeon to more easily relocate the drill hole if the bit is removed. A hypodermic needle of appropriate gauge may also be used as a drill sleeve for a k-wire. When these guides are “deshadowed” in the image the central hole will be radiolucent and can help aid in drill bit placement as discussed with placement of a K-wire. A cannulated drill bit can help ease complex implant placements as they glide over a preplaced K-wire which nearly guarantees that a bit will follow this path (Fig 3A). Additionally a cannulated screw can be placed over a k-wire ensuring is that it can be placed directly over the K-wire following drilling improving efficiency. Many cannulated screws are self drilling and self tapping thus predrilling of the cancellous bone may not be required (Fig 3B, C).

![Figure 3A](image1) ![Figure 3B](image2) ![Figure 3C](image3)

**Bone biopsy**

Percutaneous techniques may be used to help guide sampling of bone lesions such as osteosarcoma. In this particular tumor the central portion of the osteolytic lesion should be targeted for biopsy and one may easily use digital radiography to help position biopsy devices. The author prefers to first aspirate these lesions with an 18g needle to limit tumor seeding of large biopsy tracts. Once the needle is applied to the bone it is aggressively forced at a slight angle to skim the periosteum then aspirated with a 6 cc syringe. In some cases the needle may be driven through the cortex and the medullary canal aspirated. It is important to provide history to the pathologist and request ALP staining. Aspirates with positive ALP staining had a sensitivity of 100%, and the specificity of 89% for differentiating osteosarcoma from other vimenten positive tumors (Barger).

**Percutaneous fracture repair**

Minimally invasive fracture repair has been shown to significantly decrease time to radiographic union (Pozzi). Intraoperative imaging can be used to facilitate reduction and guide implant placement while minimizing damage to soft tissues and blood supply.

To aid fracture reduction a hanging limb prep may be kept throughout the procedure to place traction on the limb during the operation. This type of positioning works well for fluoroscopic placement but can be difficult to achieve under digital radiography, as the imaging platform may not be manipulated (some mobile units do allow for this option). When using standard digital radiography the limb is draped into the field and patient repositioning is planned to obtain orthogonal views. The lateral view is most often used to help target implants in extremities.

For this procedure, preoperative radiographs should be of good quality and fully reviewed for fissures and fracture configurations as a plan should be made following AO principles. Furthermore anatomic knowledge of critical structures such as vascular bundles, tendons, etc. should be reviewed. Percutaneous placement of implants can be then targeted using imaging guidance, which may be quite advantageous when a fissure, critical structure or joint surface require adjacent implant placement. The proximal pin in Figure 4 is being targeted between a growth plate proximally and fissure cranial distally.

**Physeal fracture**

Repairing physeal fractures using fluoroscopy is previously mentioned (Guiot, Simpson). The main advantage for using a minimally invasive technique in this fracture is to limit further damage to the blood supply and proliferating cells of the growth plate, which may occur to a greater degree with an open approach. In cases such as capital physeal fractures (figure 5) resorption and secondary remodeling occur following devascularization and result in a radiographic “apple core” lesion or narrowing the femoral
neck in up to 70% of cases which may progress to fracture and collapse. Most physeal fractures are repaired in a minimally invasive fashion using percutaneous pins in parallel or cross pin fashion and intraoperative image guidance can be quite helpful to achieve pin guidance.

References
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Canine tendinopathies may be acute or chronic in nature and are seen in both athletic and companion type dogs. Pathology may result from either partial or complete rupture in an acute setting or repetitive micro-trauma that outweighs the reparative process in chronic cases. This chronic inflammatory process along with hypoxia and other factors leads to collagen disorganization and condroid metaplasia resulting in thickening, loss of tensile strength, and pain.

Tendon pathology can be difficult to isolate on physical exam particularly in the shoulder where exam findings do not correlate well with specific musculotendinous groups (Devitt). Diagnostic imaging options include radiographs, ultrasound and MRI. Radiographs help to rule out other causes of lameness but are often low yield. Specialized views may be selected to differentiate the involved tendon such as a skyline view in the shoulder to delineate biceps vs supraspinatus calcification. Ultrasound is an inexpensive modality in musculoskeletal imaging but requires a steep learning curve. US findings include increased joint fluid, changes in fibril pattern, tendon thickening and tendon loss in cases of complete or partial ruptures. MRI can show loss of normal tendon architecture, tendon edema and periarticular swelling and has the advantage of imaging the entire musculotendinous unit. Positive contrast arthrogams may be performed with MRI to further delineate intra-articular structures.

**Biceps tenosynovitis**
Underlying causes for acute bicipital tenosynovitis include strain, partial rupture, entrapment of osteochondral fragments, direct trauma, and impingement by supraspinatus tendon enlargement. Dogs are often painful on a biceps test and this maneuver will accentuate the lameness. Diagnostic options include radiographs, ultrasound and MRI.

Treatment options for bicipital tendonitis include both medical and surgical approaches (Wall). Medical therapy is reserved for inflammation only with no major tear and consists of intrarticular injections of methylprednisolone acetate or triamcinalone using sterile technique with at least 6 weeks of activity restriction (Stobie). Surgical therapy involves either tenodesis or tenotomy. Reports on both surgical techniques subjectively demonstrated a good to excellent results (Wall). Tenotomy is considered preferable by some as no implants are required and it is readily performed via a minimally invasive arthroscopic procedure (Wall). When considering a tendon release, care should be taken not to over interpret secondary biceps changes for primary pathology. The biceps origin may become severely inflamed secondary to global joint inflammation and tenotomy in these cases would be contraindicated as the biceps does contribute to shoulder stability.

Torn biceps tendon origin on the L with normal biceps tendon for comparison on the R image.

**Supraspinatus tendinopathy**
The supraspinatus tendon originates on the scapula and crosses the shoulder joint to broadly insert on the greater tubercle. Labradors and Rottweilers have shown some predisposition to this disease. Microtrauma and hypoxia due to the low vascularity of this tendon are two proposed etiologies. Our clinic has an increase in case numbers at the start of upland bird season when the unconditioned dog is taken out for their first few times. A recent retrospective review of 327 dogs with ST, found failed NSAID therapy and rehabilitation in 75% and 41% of cases respectively. On physical exam these authors found pain on the following maneuvers: shoulder flexion in in 64%, biceps stretch 48%, pain on direct pressure in 59%. Mineralization was present in 37 of 283 cases with radiographs. US examination showed enlargement, irregular fiber pattern and mixed echogenicity. On shoulder arthroscopy biceps impingement was seen in 38.7% of cases. Other intra-articular lesions in the biceps, subscapularis and glenohumeral ligaments were common. Additionally, 257 elbows in 191 dogs were evaluated concurrently with elbow arthroscopy and 54.5% had concomitant pathology.
Initial treatment of SST may consist of simple rest and NSAID therapy, which should be combined with a rehabilitation plan. Other nonsurgical therapies consist of extracorporeal shockwave therapy, and regenerative medicine (PRP and stem cell injection). Extracorporeal shockwave therapy has been used to reduce mineral opacity radiographically in a case series (Danova). Most recently the Canap’s group reported on injections of adipose derived stem cells and PRP delivered via US guided injection in 116 cases with resolution of lameness in 88%. They are currently performing a prospective trial. In cases of concurrent biceps tenosynovitis additional injection of intra-articular steroids may be considered.

Surgical removal of mineral bodies within the tendon has been performed in addition to tendon splitting in non-calcified cases. This resulted in 11/19 dogs gaining excellent postop function, 5 good and 3 poor. Mineralized vs nonmineralized tendinopathy groups had no difference in prognosis (LaFuente). Another study reported on surgical removal of calcified tendon but all dogs in this series reformed mineral deposition with a mean follow-up time of 5 years (Latinen).

Infraspinatus

Infraspinatus tendopathy is typically reported in high activity dogs as an acute injury. The tendinopathy that follows is similar to the supraspinatus but likely more inflammatory given the typical acute pathologic event. Pain may be present on direct palpation over the tendon and internal rotation. A circumducting gait may be noted 3-5 weeks following injury as the tendon undergoes fibrosis and contracture producing external rotation of the paw and adduction of the elbow. Tendon release is performed in these cases. Other pathologies in this tendon such as calcification and osteochondromas of the bursa are treated with surgical and non surgical means (McKee).

Subscapularis

The subscapularis arises from the medial aspect of the scapula to then insert medially at the proximal humerus. Due to the location deep in the axilla, ultrasound examination is somewhat limited while MRI allows imaging of the entire structure. A portion of the distal tendon is seen on arthroscopic exam as it is intra-articular and fans out just medial to the cranial aspect of the medial glenohumeral ligament (MGHL). Large case numbers of subscapularis pathology are not reported however, we found nearly 50% of dogs had a lesion in the subscapularis during MRI and arthroscopic exam of the shoulder (Murphy). Subscapularis pathology may often occur in conjunction with medial glenohumeral ligament pathology resulting in medial shoulder instability. However isolated tears are also seen with normal abduction angles. Treatment is similar to medial shoulder instability with conservative management consisting of prevention of abduction, exercise restriction and rehabilitation. Regenerative therapies such platelet rich plasma and stem cells may also be injected within the tear at arthroscopy. Surgical reconstruction of the medial joint or thermocapsuloraphy is also described (Franklin).

Torn intrarticular portion of the subscapularis tendon (left image). A normal subscapularis tendon with a normal medial glenohumeral ligament (right image). foreground.

Abstract

Objective

To report the long-term clinical outcomes and radiographic results in dogs diagnosed with partial bicipital rupture and treated by arthroscopic tenotomy.

Materials and methods

The medical records of dogs that had undergone arthroscopic tenotomy were retrospectively reviewed. Inclusion criteria for this study were: performance of an arthroscopic tenotomy between August 1999 and July 2007, availability of arthroscopic records data for review, and ability to obtain follow-up data for more than one year after arthroscopic tenotomy. In all cases, owners were interviewed during follow-up appointments or via telephone to determine perceived outcome after surgery.

Results

Forty-seven arthroscopic tenotomies were performed on 40 dogs without any major surgical complications. Long-term follow-up examinations, ranging from 12 months to 48 months (mean 26 months) after the tenotomy, were obtained for 24 dogs (25 shoulders). Clinical outcome was assessed as excellent in 22 shoulders, with each dog showing a full return of limb function. A total of 10 dogs (11 joints) were evaluated radiographically; six joints revealed no progression of pathology, and five joints showed a limited progression of pathology.

Conclusion

Arthroscopic tenotomy in the treatment of bicipital partial rupture yields favourable long-term clinical results and a high degree of owner satisfaction. The feasibility of this technique and the long-term clinical and radiographic outcome from our study indicate that this technique can be considered a reliable and safe treatment for partial bicipital rupture.
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Long-term follow-up after arthroscopic tenotomy for partial rupture of the biceps brachii tendon.
Bergenhuyzen AL1, Vermote KA, van Bree H, Van Ryssen B.
The canine shoulder has the largest range of motion of any joint. Passive stabilizers such as glenohumeral ligaments, joint capsule and joint fluid provide static stability while musculotendinous units consisting of the supraspinatus, infraspinatus, biceps, subscapularis, and teres minor provide active stability. Damage to any of the anatomic structures may result in lameness. However, sorting out pathology in this complex set of ligaments and tendons can be challenging. In addition, concurrent elbow pathology often may coincide further complicating these cases.

A detailed physical exam is crucial and first consists with a gait exam. Most commonly forelimb lameness is associated with decreased contact time during the stride phase of the gait resulting in reduced stride length. This may cause cervical motion to occur creating the always useful “down on sound” acronym to characterize the head bob. In many cases the lameness may be mild and difficult to characterize. Flexion and extension tests much like that used in equine medicine may help to induce lameness or isolate pain and should start distally with the foot and progress to the shoulder as it is more difficult to isolate range of motion in the proximal joints. A gait exam follows each joint manipulation to see if the lameness is increased with these motions. In occult lameness it may also be beneficial to have the owner exercise the animal prior to exam and withhold pain medications.

Next the standing orthopedic exam is performed, palpation and comparison of the spinatus musculature and prominence of the spine of the scapula and acromion will help to define atrophy in the affected limb. The animal must be in a square stance with equal weight bearing. Each joint is then palpated for swelling, joint effusion and periarticular fibrosis when moving up the limb. This palpation is again performed in the recumbent exam and each joint is tested for instability and ROM recalling that one starts distally.

Specialized tests in the forelimb exam involve internal rotation of the antebrachium with combined elbow flexion, which may increase pressure over the medial coronoid process to help further define pain in elbow dysplasia. The flexors on the medial aspect of the elbow are also palpated carefully for pain as an insertional tendinopathy is often present in conjunction with elbow dysplasia. In the shoulder, abduction angles may be measured using a goniometer with the animal in lateral recumbencey to evaluate medial shoulder stabilizers (Cook). Additionally internal and external rotation of the shoulder will evaluate lateral and medial stabilizers respectively. A biceps test places the shoulder in flexion and the elbow in extension to elongate the biceps yielding pain in animals with tendonitis or a partial tear.

In occult cases of lameness intra-articular anesthesia may be considered to block the lameness as well. An intra-articular injection of mepivicaine has improved lameness in 87% of dogs with elbow pathology and 28/30 dogs with shoulder lameness (Van Vynckt). Finally, gait analysis with pressure sensitive walkways or force plates may be considered in occult cases and to monitor treatment progress and provide objective gait information.

While many of these tests seem specific they were limited in their ability to predict arthroscopic assessed pathology (Devitt).

References
Cranial cruciate ligament (CrCL) rupture is usually a chronic event with varying degrees of stifle inflammation, osteoarthritis and ligament pathology. Bennet coined the term “cruciate disease” to describe the syndrome of lameness, effusion, progressive arthritis and ligament weakening. Thus there is often progressive disease with clinical signs acutely worsening in cases with complete rupture or meniscal tearing. Most cases have some inflammatory process started long before the animal is evaluated for the lameness (Bleedhorn). The chronic lameness leads to disuse muscle atrophy, which can be easily measured using a girthometer. Our group found on average a 7% loss of thigh circumference preoperatively when measured at 70% of femoral length and compared to the contralateral non-ruptured side. The amount of atrophy may certainly vary depending on lameness. Dogs presenting with meniscal tears and complete CrCL ruptures were found to be significantly more lame than dogs with these structures intact in our recent study.

Diagnosis of partial tears and occult ligament pathology can be simplified with comprehensive anatomic knowledge. The cranial cruciate originates on the lateral femoral condyle and inserts on the medial aspect of the cranial tibia adjacent to the cranial horn of the meniscus. This anatomic configuration results in three major functions as it limits: internal rotation, hyperextension and cranial translation of the tibia relative to the femur. In early partial tears, lameness may be minimal and the injury more difficult to diagnose as cranial drawer is negative. Often times loading the ligament in hyperextension will produce pain and lameness increasing the suspicion of a partial CrCL tear. Similarly, flexion and internal rotation can be used to induce a painful response. These maneuvers are compared to the contralateral leg keeping in mind that the disease is often bilateral.

Effusion and periarticular fibrosis resulting from the inflammatory cascade may also be used as an examination tool. Bilateral palpation of the medial aspect of the tibia is done to evaluate buttress formation in the standing position. Additionally, palpation of the patellar tendon between the thumb and index finger is performed paying attention to the prominence of the tendon and associated adjacent swelling. In slender dogs the tendon outline is very evident and may be partially grasped like a pencil while dogs with short confirmation, high body condition or giant breed status may be more challenging. When palpation of effusion is still questionable, effusion is readily imaged with radiography. Stifle effusion will produce cranial displacement of the infra-patellar fat pad and caudal budging of the joint capsule which obliterates the facial plane cranial to the gastrocnemius (center image below compared to normal stifle image on left). One should take care to produce a true lateral projection with superimposition of the femoral condyles and fabella. A poorly taken lateral projection is often non-diagnostic. Additionally, a film at 90 degrees of flexion will increase the amount of effusion in the cranial compartment adjacent to the infrapatellar fat pad improving sensitivity in cases with mild effusion (image on R). Large amounts of effusion in the suprapatellar region may indicate a more severe inflammatory process such as septic arthritis. Cranial displacement of the tibia relative to the femur in cases with CrCL rupture may also be measured from this view and compared to the intact side (right vs center image below).

Preoperative considerations for repair
Patient size, activity level, client expectations, body condition score and concomitant orthopedic disease are important preoperative considerations. Based on these factors conservative vs operative treatment is first addressed. In previous reports smaller dogs may have a better outcome with non-operative management. Vasseur reported on 28 dogs <15kg that underwent conservative management. He found that 75% were clinically normal after an average follow-up of 36.6 months while 11% were improved. Only 14% required surgery for progressive or continued lameness. He also studied 57 dogs >15kg but found only 19% (11/57) could be medically managed with only 4 of these 11 classified as normal and 7 of 11 improved at an average follow-up of 49.1 months. The remaining 46 dogs had progressive or continued lameness necessitating surgical repair at an average of 10.2 months. The author stated the purpose, size and body condition of the dog must be evaluated, as physical examination did not predict successful non-surgical outcomes. One must also keep in mind this study was retrospective and lacked objective gait analysis. Other experimental studies with large breed dogs undergoing cruciate transection have shown significant lameness at all time points over a 4-year course of study when force plate...
gait analysis is used (Budsberg). Contrast this data with a study by Ballagas where experimental CrCL transection was followed by a TPLO, at 18 weeks there was no significant difference in weight bearing from baseline preoperative values.

A recent prospective clinical trial randomized overweight large breed dogs with unilateral CrCL rupture to undergo conservative therapy with weight loss, physical therapy and pain control versus TPLO surgery with these same treatments (Wucherer). Overall the surgical dogs had lower pain scores and significantly higher weight bearing on some outcome measures but not all. Dogs that had at least 85% of normal weight bearing were defined as having a successful outcome in the study. At 6 months and one year 33% and 64% of dogs treated non-surgically, and 93% and 75% of surgically treated dogs were defined as a successful outcome. Bilateral rupture was the most common reason dogs were taken out of the study and this may complicate conservative management. Future contralateral CrCL rupture is reported in 37% of cases at an average of 17 months and 59% if there are radiographic changes at initial evaluation (Vasseur).

Finally limb alignment, coexisting patellar luxation and patient size are important factors in choosing a surgical type. Osteotomy procedures may be considered in cases with malalignment or patellar luxation. Such surgeries become more complex often involving advanced imaging and planning. In giant breed dogs it is best to avoid lateral suture stabilization due to poorer outcomes in this group. Additionally, while there are many opinions on the “best technique” and the “best technique in my hands”, discussion with a non-bias surgeon can point owners in a direction that is best for both the patient and owner. One should always use an evidence-based approach when possible.

A previous systematic review of the literature showed no one procedure as being superior. However, a more recent systematic review of additional studies favored TPLO over lateral suture for restoring dogs to normal function (Bergh). Regarding TTA outcomes, a recent Cornell study showed TTA restored dogs to normal function at a walk. However, when trotting over a force plate dogs receiving a TTA were significantly more lame than control dogs. Cases receiving a TPLO had no difference in weight bearing when compared to control dogs at 150–299 days, and >300 days. Dogs receiving a lateral suture repair had significantly lower weight bearing at a walk and trot at all time points throughout the study. Thus TPLO outperformed both procedures, and while TTA improved dogs, there was residual lameness at a trot.

TTA and TPLO were compared in a prospective randomized study with our group. Dogs receiving a TTA did well with short-term recovery, but weight bearing at 24wks was significantly higher in TPLO dogs. At 48 weeks TPLO had higher weight bearing that approached significance. Latent meniscal tears were a major complication in dogs receiving TTAs. No meniscal release was performed in either study group however 50% of dogs that had a complete CrCL rupture and an intact meniscus at the time of surgery went on to have a latent tear in the TTA group which was significantly higher than TPLO cases. Interesting a torn vs intact meniscus or a torn vs partially torn CrCL had no effect on weight bearing as measured by force plate gait analysis. We concluded that a meniscal release should be considered in dogs receiving a TTA and owners with higher performance expectations may consider a TPLO.

References
Arthroscopy in veterinary medicine continues to develop and recent evidence shows increasing acceptance in clinical cases. The major benefits of arthroscopy are that it is minimally invasive and improves visualization.

1) Minimally invasive
The standard stifle arthroscope diameter is 2.7mm, requiring only a small parapatellar portal for placement. Arthroscopic instruments (shaver, grasper, punch and knives) are of similar size and a contralateral portal is required for their use. This small form factor allows for significantly smaller incisions to be made over a typical arthrotomy. The proposed benefit is less tissue disruption resulting in early return to function and possibly less progression of OA.

The evidence: Millis found dogs returned to function sooner when a arthroscopic assisted approach was used to place a lateral suture over a typical open approach. Regarding OA development, a full parapatellar arthrotomy alone produced long standing degenerative change nearly equal to that of an arthrotomy with cruciate transection in experimental models (Järvinen M, Clin Orthopedics 1995). In clinical cases of CrCL rupture a full medial parapatellar arthrotomy was compared to a limited caudal medial arthrotomy in dogs undergoing TPLO. The limited arthrotomy group had significantly less OA progression on follow-up radiographs (Lineberger).

2) Improved visualization
While the limited arthrotomy may limit OA development, the trade off is less visualization. A caudal medial arthrotomy was shown to be the least accurate technique in assessing meniscal tears in a cadaver model of a CrCL deficient stifle. A cranial medial approach had improved accuracy while arthroscopic examination had the highest (Pozzi). This is very important clinically and economically as missing a meniscal tear at the time of the initial surgery may result in progression of the tear and lameness with the need for additional surgery. Thieman showed cases explored with an arthrotomy were 3.8 times more likely to develop a meniscal tear after the initial surgery vs those undergoing arthroscopy without a meniscal release.

Improved visualization is also dependent on equipment and operator use. Newer and scope optics allow for a high definition image to be displayed to the user and current technology takes resolution to 4K. Image quality of in addition to magnification allow the trained clinician to gain a detailed analysis of the joint. Veterinary specific instruments and techniques are also improving allowing joint pathology to not only be defined but also treated. Currently, isolated meniscal tears, OCD lesions, traumatic (non congenital) patellar luxation are treated with arthroscopy alone.

References
Lineberger JA1, Allen DA, Wilson ER, Tobias TA, Shaiken LG, Shiroma JT, Biller DS, Lehenbauer TW.
Cranial cruciate ligament (CrCL) rupture is usually a chronic event with varying degrees of stifle inflammation, osteoarthritis and ligament pathology. Bennet coined the term “cruciate disease” to describe the syndrome of lameness, effusion, progressive arthritis and ligament weakening. Thus there is often progressive disease with clinical signs acutely worsening in cases with complete rupture or meniscal tearing. Most cases have some inflammatory process started long before the animal is evaluated for the lameness (Bleedhorn). The chronic lameness leads to disuse muscle atrophy, which can be easily measured using a girthometer. Our group found on average a 7% loss of thigh circumference preoperatively when measured at 70% of femoral length and compared to the contralateral non-ruptured side. The amount of atrophy may certainly vary depending on lameness. Dogs presenting with meniscal tears and complete CrCL ruptures were found to be significantly more lame than dogs with these structures intact in our recent study.

Diagnosis of partial tears and occult ligament pathology can be simplified with comprehensive anatomic knowledge. The cranial cruciate originates on the lateral femoral condyle and inserts on the medial aspect of the cranial tibia adjacent to the cranial horn of the meniscus. This anatomic configuration results in three major functions as it limits: internal rotation, hyperextension and cranial translation of the tibia relative to the femur. In early partial tears, lameness may be minimal and the injury more difficult to diagnose as cranial drawer is negative. Often times loading the ligament in hyperextension will produce pain and lameness increasing the suspicion of a partial CrCL tear. Similarly, flexion and internal rotation can be used to induce a painful response. These maneuvers are compared to the contralateral leg keeping in mind that the disease is often bilateral.

Effusion and periarticular fibrosis resulting from the inflammatory cascade may also be used as an examination tool. Bilateral palpation of the medial aspect of the tibia is done to evaluate buttress formation in the standing position. Additionally, palpation of the patellar tendon between the thumb and index finger is performed paying attention to the prominence of the tendon and associated adjacent swelling. In slender dogs the tendon outline is very evident and may be partially grasped like a pencil while dogs with short confirmation, high body condition or giant breed status may be more challenging. When palpation of effusion is still questionable, effusion is readily imaged with radiography.

Stifle effusion will produce cranial displacement of the infra-patellar fat pad and caudal budging of the joint capsule which obliterates the facial plane cranial to the gastrocnemius (center image below compared to normal stifle image on left). One should take care to produce a true lateral projection with superimposition of the femoral condyles and fabella. A poorly taken lateral projection is often non-diagnostic. Additionally, a film at 90 degrees of flexion will increase the amount of effusion in the cranial compartment adjacent to the infrapatellar fat pad improving sensitivity in cases with mild effusion (image on R). Large amounts of effusion in the suprapatellar region may indicate a more severe inflammatory process such as septic arthritis. Cranial displacement of the tibia relative to the femur in cases with CrCL rupture may also be measured from this view and compared to the intact side (right vs center image below).

Preoperative considerations for repair
Patient size, activity level, client expectations, body condition score and concomitant orthopedic disease are important preoperative considerations. Based on these factors conservative vs operative treatment is first addressed. In previous reports smaller dogs may have a better outcome with non-operative management. Vasseur reported on 28 dogs <15kg that underwent conservative management. He found that 75% were clinically normal after an average follow-up of 36.6 months while 11% were improved. Only 14% required surgery for progressive or continued lameness. He also studied 57 dogs >15kg but found only 19% (11/57) could be medically managed with only 4 of these 11 classified as normal and 7 of 11 improved at an average follow-up of 49.1 months. The remaining 46 dogs had progressive or continued lameness necessitating surgical repair at an average of 10.2 months. The author stated the purpose, size and body condition of the dog must be evaluated, as physical examination did not predict successful non-surgical outcomes. One must also keep in mind this study was retrospective and lacked objective gait analysis. Other experimental studies with large breed...
dogs undergoing cruciate transection have shown significant lameness at all time points over a 4-year course of study when force plate gait analysis is used (Budsberg). Contrast this data with a study by Ballagas where experimental CrCL transection was followed by a TPLO, at 18 weeks there was no significant difference in weight bearing from baseline preoperative values.

A recent prospective clinical trial randomized overweight large breed dogs with unilateral CrCL rupture to undergo conservative therapy with weight loss, physical therapy and pain control versus TPLO surgery with these same treatments (Wucherer). Overall the surgical dogs had lower pain scores and significantly higher weight bearing on some outcome measures but not all. Dogs that had at least 85% of normal weight bearing were defined as having a successful outcome in the study. At 6 months and one year 33% and 64% of dogs treated non-surgically, and 93% and 75% of surgically treated dogs were defined as a successful outcome. Bilateral rupture was the most common reason dogs were taken out of the study and this may complicate conservative management. Future contralateral CrCL rupture is reported in 37% of cases at an average of 17 months and 59% if there are radiographic changes at initial evaluation (Vasseur).

Finally limb alignment, coexisting patellar luxation and patient size are important factors in choosing a surgical type. Osteotomy procedures may be considered in cases with malalignment or patellar luxation. Such surgeries become more complex often involving advanced imaging and planning. In giant breed dogs it is best to avoid lateral suture stabilization due to poorer outcomes in this group. Additionally, while there are many opinions on the “best technique” and the "best technique in my hands”, discussion with a non-bias surgeon can point owners in a direction that is best for both the patient and owner. One should always use an evidence-based approach when possible.

A previous systematic review of the literature showed no one procedure as being superior. However, a more recent systematic review of additional studies favored TPLO over lateral suture for restoring dogs to normal function (Bergh). Regarding TTA outcomes, a recent Cornell study showed TTA restored dogs to normal function at a walk. However, when trotting over a force plate dogs receiving a TTA were significantly lame than control dogs. Cases receiving a TPLO had no difference in weight bearing when compared to control dogs at 150–299 days, and >300 days. Dogs receiving a lateral suture repair had significantly lower weight bearing at a walk and trot at all time points throughout the study. Thus TPLO outperformed both procedures, and while TTA improved dogs, there was residual lameness at a trot.

TTA and TPLO were compared in a prospective randomized study with our group. Dogs receiving a TTA did well with short-term recovery, but weight bearing at 24wks was significantly higher in TPLO dogs. At 48 weeks TPLO had higher weight bearing that approached significance. Latent meniscal tears were a major complication in dogs receiving TTAs. No meniscal release was performed in either study group however 50% of dogs that had a complete CrCL rupture and an intact meniscus at the time of surgery went on to have a latent tear in the TTA group which was significantly higher than TPLO cases. Interesting a torn vs intact meniscus or a torn vs partially torn CrCL had no effect on weight bearing as measured by force plate gait analysis. We concluded that a meniscal release should be considered in dogs receiving a TTA and owners with higher performance expectations may consider a TPLO.

References
Dogmas of Clinical Pathology: Adjusted Calcium, Modified Transudates, Acidemias of Acidoses, and More

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Ken Jenning’s wrote Because I Said So! The Truth Behind the Myths, Tales, and Warnings Every Generation Passes Down to its Kids. In his book, he considered the evidence that supports or refutes common dogmas within the United States. For example, “Was the nail you stepped on rusty? You’ll get tetanus!” Is the statement true, sometimes true, sometimes false, or false? Or, “Your first answer is usually the right one.” Is the statement true, sometimes true, sometimes false, or false?

A dogma is “a settled or established opinion, belief, or principle.” “Blind belief in authority is the greatest enemy of truth.” (Albert Einstein) “Education has failed in a very serious way to convey the most important lesson science can teach: skepticism.” (David Suzuki) “Most institutions demand unqualified faith; but the institution of science makes skepticism a virtue.” (Robert King Merton)

Are dogmas of clinical pathology valid? The following sections explore a few dogmas that have been or are being passed down from one generation to the next generation of veterinarians.

Adjusted calcium formula can be used to determine if the hypocalcemia is due to hypoalbuminemia.

This dogma initially arose from a retrospective study that was published in 1982 (JAVMA 180: 63-67, 1982) in which two formulas were derived from measured concentrations of serum tCa\(^{2+}\), albumin, and total protein (values expressed in non-SI units).

- Canine-adjusted \([t\text{Ca}^{2+}]\) = measured \([t\text{Ca}^{2+}]\) – \([\text{Alb}]\) + 3.5
- Canine-adjusted \([t\text{Ca}^{2+}]\) = measured \([t\text{Ca}^{2+}]\) – 0.4 \(\times\) \([\text{TP}]\) + 3.3

The proposed concept for the calculated adjusted \([t\text{Ca}^{2+}]\) values was that if the value was within the reference interval for \([t\text{Ca}^{2+}]\), the hypocalcemia was due to hypoalbuminemia (or hypoproteinemia) and there is not a decrease in the \([f\text{Ca}^{2+}]\). If the calculated adjusted \([t\text{Ca}^{2+}]\) was decreased, then there was a decreased \([f\text{Ca}^{2+}]\). [Note: \(f\text{Ca}^{2+}\) (free calcium ion) is frequently called ionized calcium even though all calcium in the body is ionized; some \(Ca^{2+}\) ions exist as free ions; other \(Ca^{2+}\) ions are bound to a variety of anions.]

There are three major aspects of the 1982 article that are frequently ignored. The derived formulas represented the regression lines for the raw data that contained considerable individual animal variation. Considering the 95%–confidence intervals for the regression line, the formulas should be as follows. Accordingly, there is considerable variability in the calculated adjusted \([t\text{Ca}^{2+}]\) values.

- Canine-adjusted \([t\text{Ca}^{2+}]\) = measured \([t\text{Ca}^{2+}]\) – \([\text{Alb}]\) + 3.5 \(\pm\) 1.3
- Canine-adjusted \([t\text{Ca}^{2+}]\) = measured \([t\text{Ca}^{2+}]\) – 0.4 \(\times\) \([\text{TP}]\) + 3.3 \(\pm\) 1.6

Second, the authors stated that about one-third of the variability in the \([t\text{Ca}^{2+}]\) was due to changes in albumin concentrations. Lastly, the formulas were derived from data obtained in one clinical laboratory many years ago and people use the formulas for data obtained from different analytical methods without establishing analytical agreement.

Some of the same authors of the 1982 article wrote another article that was published in 2005 (Am J Vet Res 66: 1330 – 1336, 2005). They concluded that adjusted total \(Ca^{2+}\) concentrations are unacceptable for predicting free \(Ca^{2+}\) (ionized calcium) status in dogs.

The adjusted calcium statement is mostly false. However, adjusted calcium formulas do emphasize that the total protein and albumin concentrations do influence a patient’s \([t\text{Ca}^{2+}]\) and thus should be considered when interpreting laboratory data.

Pseudohypocalcemia is present when the hypocalcemia is due to hypoalbuminemia (or hypoproteinemia).

This more recent statement should not be used. When the \([t\text{Ca}^{2+}]\) is decreased, there is a hypocalcemia if there is or is not a hypoalbuminemia or hypoproteinemia present. Those who wish to use the term “pseudohypocalcemia” in this context should consider what they should call the neutrophilia that occurs due to shifting of cells from marginated to circulating pools, or the hyperproteinemia that occurs due to decreased plasma water, or the erythrocytosis that occurs due to splenic contraction. Just because there is not a convenient term for a decreased \([f\text{Ca}^{2+}]\), let’s not use terms that are incorrect.

In acute inflammation, the release of endogenous cortisol causes the lymphopenia or Stress of the acute inflammatory disease causes a lymphopenia.

These statements have been in the veterinary literature for decades – but where is the evidence that they are true? The statements reflect the concept that the inflammatory state stresses the animal sufficiently to cause a release of cortisol which induces the movement of lymphocytes from the circulating blood and thus a lymphopenia develops.

Increased cortisol activity (or activity of other glucocorticoids) are known to create a lymphopenia. If the lymphopenia in an acute inflammatory state is due to excess cortisol, should we also see other evidence of excess cortisol such as mature neutrophilia,
A transudate occurs because of hypoalbuminemia; usually when plasma [albumin] is < 1.5 g/dL (or < 1.2 g/dL, or < 1.8 g/dL). Or A pure transudate is hypocellular (< 1000/µL) and has a TS concentration < 2.5 g/dL.

First, let’s consider the statement that “a transudate occurs because of hypoalbuminemia.” An inherited disorder is recognized in people in which there is no synthesis of albumin by hepatocytes; i.e., analbuminemia. Their albumin concentrations are < 0.1 g/dL and they typically do not develop pleural or peritoneal transudates. How can we attribute the formation of transudates to hypoalbuminemia when people with analbuminemia do not have transudative effusions? Also, how can we state that certain albumin concentrations lead to transudation when analbuminemia does not lead cavitary transudates?

A transudate is an effusion produced by changes in mechanic factors such as oncotic pressure or hydraulic pressure in capillary beds. Basically, the determining factor for the accumulation of cavitary transudates is the difference between the hydraulic pressure gradient (hydraulic pressure within vessels – hydraulic pressure in interstitial fluid) and the oncotic pressure gradient (oncotic pressure within vessels – oncotic pressure in interstitial fluid). When this difference leads to more fluid leaving the vascular bed than what can be removed by lymphatic vessels, a transudate forms. If transudation occurs in blood vessels that have minimal protein permeability, then a protein-poor transudate accumulates.

It is important to recognize that the plasma oncotic pressure is due to both albumin and globulins; albumin molecules are the major contributors to oncotic pressure but combined contributions of the globulin molecules are also important.

Two common canine disorders that cause the formation of protein-poor transudates are protein-losing nephropathies and hepatic cirrhosis. In these disorders, hypoproteinemia does reduce the plasma oncotic pressure but there also is an increased hydraulic pressure gradient in the portal blood vessels created by the retention of Na⁺ and H₂O. The combination results in transudation and the formation of protein-poor transudates; the transudation is not solely caused by hypoalbuminemia.

A less common reason for the formation of a protein-poor transudate is presinusoidal portal hypertension. In this state, there is an increased hydraulic pressure gradient in the portal blood vessels but not a hypoproteinemia. Accordingly, the transudation is not caused by hypoalbuminemia.

For the second statement, (A pure transudate is hypocellular (< 1000/µL) is typically true as there is no reason for the migration of leukocytes from blood to the cavitary fluid. However, the second portion of the statement (TS concentration < 2.5 g/dL) may or may not be true.

It is important to recognize that a serum or plasma “total solids concentration” is not equal to a “total protein concentration.” The total protein concentration is due to the concentrations of albumin and globulins. The total solids concentration includes the total protein concentration plus the concentrations of all other solids in the serum or plasma; i.e., glucose, urea, electrolytes, and other solutes. This data in the following table was extracted from a complete table in Wolf AV:

**Aqueous solutions and body fluids. Their concentrative properties and conversion tables, 1966.**

<table>
<thead>
<tr>
<th>Human plasma [TP] (g/dL)</th>
<th>0.8</th>
<th>1.0</th>
<th>2.0</th>
<th>3.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human plasma [TS] (g/dL)</td>
<td>2.5</td>
<td>2.7</td>
<td>3.6</td>
<td>4.7</td>
</tr>
</tbody>
</table>

There are clinical refractometers that have a calibrated total solids scale (e.g., TS Meter Refractometer Model 10400B, Leica Microsystems). Most clinical refractometers have a calibrated total protein scale (even those that are called “TS Meters”) and the lowest unit commonly on the scale is 2.5 g/dL. The [TS] for a protein-poor transudate may be < 2.5 g/dL, but that should not be confused with a [TP] of < 2.5 g/dL.

A modified transudate is a transudate that has been modified by the addition of cells or protein. A modified transudate has a higher TS concentration than a pure transudate and moderate cellularity. A modified transudate has 1,000–7,000 cells/µL and a variable protein concentration (2.5–5.0 g/dL). Using one or more of these definitions or criteria, a variety of cavitary effusions have been classified as modified transudates including the effusions of heart failure, feline infectious peritonitis, noninfectious exudates, hemorrhagic effusions, chylous effusions, uroperitoneum, neoplastic effusions, and bilious exudates. If we define a transudate as an effusion produced by changes in mechanic factors such as oncotic pressure or hydraulic pressure in capillary beds,” then only the heart failure effusion qualifies as a transudate. None of the other effusions form via transudation and thus should not be called transudates or modified transudates.

The heart-failure effusions form when there is an increased hydraulic pressure gradient within blood vessels that are permeable to proteins. The classic mechanism occurs when central vein or hepatic vein congestion lead to increased hydraulic pressure with hepatic
sinusoids and the pressure forces out an excess amount of protein-rich fluid. When lymphatic vessels are not able to compensate adequately, then a protein-rich transudate accumulates. Pulmonary vessels are also protein-permeable, but not to the same degree as the hepatic sinusoids.

**The acidemia of a lactic acidosis is due to increased production of lactic acid by cells.**

This statement sounds logical but it does not reflect the true changes in biochemical pathways that occur in lactic acidosis. The cause of the acidemia was addressed in an article by S.C. Dennis, et al (J. Mol. Cell Cardiol. 23: 1077–1086, 1991).

When tissues have an inadequate supply of oxygen (i.e., when hypoxia is present), the cells attempt to generate ATP via anaerobic respiration (fermentation) (also called anaerobic glycolysis). In the final reaction and for each glucose molecule, this reaction occurs and is catalyzed by lactate dehydrogenase: 2 pyruvate + 2 NADH + 2 H+ → 2 L-lactate + 2 NAD+. It should be noted that L-lactate (an anion) is formed and not lactic acid; it should also be noted that H+ is consumed in the reaction and thus makes the medium more alkaline, not more acidic.

Anaerobic respiration is an inefficient method of generating ATP from glucose; only 2 ATP molecules are produce for each glucose molecule. When there is an inadequate formation of ATP, the cells start the rapid hydrolysis of ATP to ADP and finally AMP. For each ATP molecule that is converted to AMP, 2 H+ ions are formed.

One might say – if there is excessive formation of L-lactate and the excessive formation of H+, doesn’t that mean there is excessive formation of lactic acid? Considering the pK_a of lactic acid is 3.86, the ratio of lactate to lactic acid at a physiologic pH is greater than 1000:1.

The acidemia that occurs in animals with a lactic acidosis is due to excessive ATP hydrolysis in hypoxic tissues; not excessive formation of lactic acid.

**The acidemia of a ketoacidosis is due to increased production of ketoacids by hepatocytes.**

This statement sounds logical but it does not reflect the true changes in biochemical pathways that occur in ketoacidosis. The cause of the acidemia was addressed in an article by K.G. Alberti (Ciba Found. Symp. 87: 1–19, 1982).

The process called ketogenesis involves the conversion of 3-hydroxy-3-methylglutaryl-CoA (3HMGCoA) to acetoacetate, β-hydroxybutyrate, and acetone (the traditional ketone bodies). This process actually consumes H+ and the molecules formed are not acids (i.e., not acetoacetic acid or β-hydroxybutyric acid).

As explained by Alberti, the excess generation of H+ in ketoacidosis occurs before ketogenesis and not during ketogenesis. The greatest amount of H+ is formed from triglyceride molecules when there is β-oxidation of fatty acids to AcCoA in hepatocytes. The processes of triglyceride lipolysis in adipose tissue and the conversion of AcCoA to 3HMGCoA also generate H+.

The acidemia in animals with a ketoacidosis is due to the excessive formation of H+ during the mobilization and catabolism of triglycerides when there is a negative energy status; not due to ketogenesis or the formation of ketoacids.

**The increased anion gap seen with renal failure is due the accumulation of uremic acids.**

This statement sounds logical. When there is a true increase in the anion gap concentration, there is an increased concentration of anions other than Cl− or HCO3− in the serum/plasma. Are the acids anions?

When an animal is in renal failure, the decreased glomerular filtration rate leads to an accumulation of phosphates, sulfates, and citrate in plasma. At a pH of 7.4, most of the phosphates exist as HPO4^{2−} and a lesser amount of H2PO4− (both anions and both acids). The sulfates exist mostly as SO4^{2−} and a minute amount of HSO4− (both anions, SO4^{2−} is not an acid). Citrate exists as an anion, there is very little citric acid present at a pH of 7.4; citric acid is not an anion.

As some of the “uremic acids” do exist as anions at a pH of 7.4, the statement is partially true. However to reduce confusion, I attempt to consistently state that increased anion gap concentration is due to anions other than Cl− and HCO3−.

**The increased serum osmolality is due to dehydration (i.e., ↓ plasma H2O).**

It is important to recognize that serum osmolality represents the total concentration of the solutes in the serum and usually dehydration is not the reason for an increase concentration of solutes. The three major reasons for hyperosmolar serum are azotemia (increase urea concentration), hyperglycemia, and presence of exogenous solutes (e.g., ethylene glycol or mannitol). Dehydration does not cause hyperglycemia or an excess of exogenous solutes. Dehydration can lead to azotemia, but only when dehydration creates sufficient hypovolemia to lead to a prerenal azotemia. Decreased plasma H2O by itself does not create a significant increase in urea concentration.

When dehydration results in hypernatremia and hyperchloremia, then dehydration is the cause of the increased serum osmolality. However, most dehydrated animals do not have hypernatremia and hyperchloremia. Hypernatremic dehydration occurs when there is a loss of “pure water” as it occurs in central and renal diabetes insipidus and when there is an insensible loss of water via respiration. Another cause of hypernatremic dehydration occurs when an animal does not have access to water (e.g., frozen water tank).
A measured or a calculated osmolality should not be used to establish the presence or absence of dehydration in an animal. Dehydration is usually not the cause of hyperosmolar serum.

An increase in [Pi] will cause the [tCa2+] to decrease because of the calcification of tissues. Or When Ca X P is > 70, soft tissue calcification is likely; mineralization occurs if when > 90.

The concept of the Ca/P product is based on the mass-law concepts in which higher concentrations of Ca^{2+} or PO_4 will shift this reaction (Ca^{2+} + PO_4^{3-} \rightarrow Ca_3(PO_4)_2) to the right and thus more Ca_3(PO_4)_2 forms. On the surface, this concept is flawed because not all of the measured [tCa^{2+}] is present as free Ca^{2+} and thus is not available to participate in the reaction. Second, very little of the serum inorganic phosphorus concentration exists as PO_4^{3-}. Also, when Ca^{2+} & PO_4^{3-} were added to human plasma, precipitation did not occur until the Ca/P product was > 200 (O’Neill W.C.: Kidney International 72: 2007). If the Ca/P product concept is not valid, is it true that “An increase in [Pi] will cause the [tCa^{2+}] to decrease”?

If there is a prolonged increase in plasma [PO_4] (as it occurs in chronic renal disease), the PO_4 inhibits renal 1-hydroxylase and thus there is less conversion of calcidiol to calcitriol. Lower calcitriol concentrations do lead to lower [fCa^{2+}] (thus lower [tCa^{2+}]) due to less intestinal absorption of Ca^{2+}, less mobilization of Ca^{2+} from bone, and more renal excretion of Ca^{2+}.

If there is a rapid increase in plasma [PO_4], colloidal complexes of Ca^{2+} and PO_4 form in plasma and the complexes are engulfed by macrophages and the plasma [tCa^{2+}] decreases.
Clinical instruments for generating blood gas data and common electrolytes became available in the 1950’s and ion-selective electrodes became available in the 1970’s. For veterinary medicine, these instruments were almost exclusively used within veterinary schools and thus methods to control the quality of the patient samples and sample analysis were achievable. In the early 1990’s, a few point-of-care instruments became available for use in veterinary practices and they have become common within the past 10 years. These instruments can be purchased and used by individuals who have minimal training regarding appropriate sample collection and handling or of a quality assurance program. Easier access to blood gas and electrolyte data does not automatically lead to better patient care.

When reading current veterinary literature, when listening to discussions of clinical cases, or when addressing questions from residents and students, there is frequently a need to revisit major concepts of acid-base data and the renal aspects of acid-base disorders. This presentation will address a few of the preanalytical errors that are too common and major acid-base concepts that are sometimes incompletely explained in veterinary literature.

**Preanalytical errors**

A 6-yr-old Dachshund was presented because of weight loss and recent vomiting and diarrhea. Physical examination findings included 7% dehydration, petechiae, tachycardia, and tachypnea. Blood gas results for a heparinized venous blood sample were the following.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Units</th>
<th>Ref. Int.</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.07</td>
<td>7.38 – 7.47</td>
</tr>
<tr>
<td>PCO2</td>
<td>22 mmHg</td>
<td>25 – 40</td>
</tr>
<tr>
<td>HCO3⁻</td>
<td>6 mmol/L</td>
<td>15 – 24</td>
</tr>
</tbody>
</table>

The data represent the findings of acidemia, metabolic acidosis (↓ [HCO3⁻]), and a compensatory respiratory alkalosis (↓ PCO2) (traditional classifications in which metabolic states are defined by HCO3⁻ concentrations and respiratory states are defined by PCO2 values). It is important to remember the relationship between pH, PCO2, and HCO3⁻ as defined by the Henderson-Hasselbalch equation. When the ratio of [HCO3⁻] to the product of PCO2 x 0.03 is 20, the pH must be 7.4. If the [HCO3⁻] changes and the PCO2 does not, the pH must change. If the PCO2 changes and the [HCO3⁻] does not, the pH must change.

W.E. Wingfield and colleagues reported a comparison of blood gas data obtained from the analysis of paired samples – arterial blood and central venous blood (J Vet Emerg Crit Care, 1994).

For arterial and venous pH values (left graph), there was a constant bias with the venous blood being more acidic than arterial blood. This expected finding occurs because H⁺ is being produced by metabolic pathways in tissues and is being transported to lungs and kidneys for removal. For PCO2 values (center graph), there was a marked proportional bias with the venous blood having higher PCO2 values. This expected finding occurs because CO2(g) is being produced by metabolic pathways in tissues and is being transported to lungs for removal. For [HCO3⁻] (right graph), there was a slight proportional bias with the venous blood having higher concentrations. This occurs because of the relationship between H⁺, HCO3⁻, and PCO2. It should be noted that the differences between venous and arterial HCO3⁻ concentrations are less at lower concentrations – this observation supports the concept that a venous [HCO3⁻] may be adequate for characterizing metabolic acidoses but may not be adequate for metabolic alkaloses.

It is clearly evident that the venous PCO2 does not reflect the ability of the respiratory system to remove CO2(g) from blood. For diagnostic decisions, do we really need to consider respiratory function when the patient clearly has a metabolic disorder and there is no evidence of pulmonary dysfunction?
The patient’s [HCO₃⁻] was decreased compared to the provided reference interval, but is the reference interval valid? Using the lower reference limit of [HCO₃⁻] (i.e., 15 mmol/L) and a common Pco₂ of 40 mmHg, the calculated pH is 7.2 which is too low for a physiologic pH value.

\[
pH = 6.1 + \log \left( \frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]} \right) \quad \text{pH} = 6.1 + \log \left( \frac{15}{40 \times 0.03} \right) \quad \text{pH} = 7.2
\]

A common reason for a falsely low [HCO₃⁻] in a blood sample (a pseudometabolic acidosis) is exposure to air that has a Pco₂ ≤ 1 mmHg. If the samples collected for establishing reference intervals were not handled appropriately, can we confidently conclude that the patient’s [HCO₃⁻] is correct? The blood sample’s Pco₂ value is additional evidence for a pseudometabolic acidosis – the low Pco₂ could be present because the sample was not handled anaerobically. If one concludes that the Pco₂ and HCO₃⁻ values are not valid, then the sample’s pH is not valid.

Pseudometabolic acidoses are too common because blood samples are not being handled anaerobically. This is especially true for serum [HCO₃⁻] (or [tCO₂]) when blood is collected into a Vacutainer tube or serum is exposed to air prior to analysis. Data from one of several published studies illustrate the erroneous results. R.D. Herr & T. Swanson completed a study in which blood samples were collected into clot tubes (red tops) (Ann Emerg Med, 1992). Blood samples (1 mL, 3 mL, and 10 mL) were collected in 10-mL clot tubes. Samples were processed and analyzed within 1 hr; caps were removed during processing of some samples whereas others remained capped. The measured HCO₃⁻ concentrations are shown in the following table.

<table>
<thead>
<tr>
<th>Blood volume collected</th>
<th>10 mL</th>
<th>3 mL</th>
<th>1 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg. [HCO₃⁻] mmol/L (capped)</td>
<td>22</td>
<td>19</td>
<td>16</td>
</tr>
<tr>
<td>Avg. [HCO₃⁻] mmol/L (uncapped)</td>
<td>23</td>
<td>20</td>
<td>17</td>
</tr>
</tbody>
</table>

It is clearly evident that CO₂(g) escapes from incompletely filled clot tubes and causes falsely low HCO₃⁻ concentrations. “Short samples” are submitted to laboratories – it should not be surprising to find falsely low HCO₃⁻ concentrations in those samples.

As the serum HCO₃⁻ concentration is used in the calculation of the anion gap, a falsely low [HCO₃⁻] leads to a falsely increased anion gap. How many animals have a “metabolic acidosis with an increased anion gap” because of preanalytical errors? How often are reference intervals for serum HCO₃⁻ and anion gap concentrations established using samples that are not handled anaerobically?

### Renal compensation in metabolic alkalosis

A 5-yr-old Holstein cow had clinical signs indicative of a displaced abomasum; she was mildly dehydrated. Serum electrolyte concentrations were determined to assess her disorder.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Patient</th>
<th>Units</th>
<th>Ref. Int.</th>
<th>Analyte</th>
<th>Patient</th>
<th>Units</th>
<th>Ref. Int.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>136</td>
<td>mmol/L</td>
<td>135–153</td>
<td>HCO₃⁻</td>
<td>40</td>
<td>mmol/L</td>
<td>21–31</td>
</tr>
<tr>
<td>K⁺</td>
<td>1.8</td>
<td>mmol/L</td>
<td>3.9–6.0</td>
<td>tCO₂</td>
<td>41</td>
<td>mmol/L</td>
<td>22–32</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>80</td>
<td>mmol/L</td>
<td>92–117</td>
<td>Anion gap</td>
<td>18</td>
<td>mmol/L</td>
<td>10–15</td>
</tr>
</tbody>
</table>

The data represent the classic findings of a displaced abomasum: hypochloremic metabolic alkalosis and hypokalemia. The [Na⁺] in a dehydrated cow reflects a Na⁺-depleted state. The reason for the mildly increased anion gap is not recognized at this point; it could represent the error created when four values (each with inherent analytical imprecision) are used to calculate a concentration or there could be a mild ketonemia. It is commonly stated that the hypochloremic metabolic alkalosis is due to the sequestration of H⁺ in the abomasum. Is that statement completely true? A concurrent finding is an alkalemia. What is the pathogenesis of the alkalemia? Is it the sequestration of H⁺ in the abomasum? When gastric secretions are lost (vomiting) or when the abomasal secretions do not enter the intestine, then the physiologic cycling of H⁺, HCO₃⁻, and Cl⁻ is broken (Fig. 1, next page).

1. The Cl⁻ that entered the parietal cell from the plasma is not replaced and thus hypochloremia occurs.
2. The HCO₃⁻ that entered the plasma from the parietal cell is not used to produce CO₂ & H₂O and thus HCO₃⁻ accumulates to contribute to the metabolic alkalosis.
3. But why is the animal typically alkalemic? The described processes do not cause a loss of H⁺ from plasma.

One reason for the alkalemia involves the renal principal epithelial cells when the animal is hypovolemic, hypochloremic, and hypokalemic (Fig 2).

1. Hypovolemia activates the renin-angiotensin systems (RAS) to stimulate the release of aldosterone from the adrenal glands which then enters the principal epithelial cells. The aldosterone-receptor complex stimulates the synthesis of aldosterone-induced proteins, which include components of the Na⁺-K⁺-ATPase pump and membrane channels for Na⁺ and K⁺.
2. The peritubular exchange of 3 Na\(^+\) for 2 K\(^+\) creates an electrical gradient that promotes paracellular resorption of Cl\(^-\).

3. In the presence of hypochloremia, less Cl\(^-\) is available in the tubular fluid and thus the electrical gradient created by Na\(^+\) and K\(^+\) movements promotes less H\(^+\) from being passively resorbed – thus, more H\(^+\) is excreted (a contribution to the paradoxical aciduria).

4. The excreted H\(^+\) came from the peritubular fluid and thus this process contributes to the alkalemia.

5. The current hypokalemia also contributes to the aciduria because more K\(^+\) returns to the peritubular fluid (thus plasma) through an open channel and thus there is less K\(^+\) available to exchange for Na\(^+\) of the tubular fluid.

With less K\(^+\) exchange, more H\(^+\) must be excreted to maintain electrical neutrality.

The Type A intercalated cells in the renal collecting ducts also participate in the renal response to hypovolemia and hypokalemia (Fig 3).

1. Aldosterone-induced proteins include an H\(^+\)-ATPase pump that actively secretes H\(^+\) into the renal tubule.

2. An H\(^+\)-K\(^+\) pump also actively secretes H\(^+\) when hypokalemia is present. Both of these processes contribute to the aciduria, but the source of the H\(^+\) ions is H\(_2\)O, and thus the secretion does not directly contribute to the alkalemia.

3. Carbonic anhydrase in the cells promotes the formation of HCO\(_3\)\(^-\) that is exchanged with Cl\(^-\) from the plasma; the Cl\(^-\) is excreted in urine. This process contributes to the hypochloremia and the metabolic alkalosis (\(\uparrow\) \[HCO\(_3\)\(^-\)\]).

It is important to recognize that the gastric/abomasal parietal cells (as part of the primary pathologic process) and the Type A intercalated cells (as part of the renal response to hypovolemia and hypokalemia) produce HCO\(_3\)\(^-\) ions that enter the plasma. As noted earlier, an increase in [HCO\(_3\)\(^-\)] without a change in the PCO\(_2\) requires the pH to increase (see earlier Henderson-Hasselbalch equation). Thus, the major reason for the alkalemia is the marked increase in HCO\(_3\)\(^-\) concentration in this animal; there also is some renal excretion of H\(^+\) (see principal epithelial cells). In addition to the gastric/abomasal secretion of Cl\(^-\), the renal response also contributes to the hypochloremia (see Type A intercalated cell).

Renal compensation in metabolic acidosis

A vomiting 7-yr-old dog had clinical signs indicative of diabetes mellitus; she was mildly dehydrated. Serum electrolyte concentrations were determined to assess her disorder.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Patient</th>
<th>Units</th>
<th>Ref. Int</th>
<th>Analyte</th>
<th>Patient</th>
<th>Units</th>
<th>Ref. Int</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na(^+)</td>
<td>135 mmol/L</td>
<td>141–156</td>
<td>HCO(_3)(^-)</td>
<td>12 mmol/L</td>
<td>20–26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>K(^+)</td>
<td>3.2 mmol/L</td>
<td>3.8–5.5</td>
<td>tCO(_2)</td>
<td>13 mmol/L</td>
<td>21–27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cl(^-)</td>
<td>98 mmol/L</td>
<td>109–124</td>
<td>Anion gap</td>
<td>28 mmol/L</td>
<td>12–20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The data represent classic findings of ketoacidotic diabetes mellitus: hypochloremic metabolic acidosis, hyponatremia, hypokalemia, and increased anion gap concentration. The metabolic acidosis is frequently explained to be the result of increased generation of ketoadicds and the subsequent reduction of [HCO\(_3\)\(^-\)] as it buffers the excess H\(^+\) (note: this topic will be addressed in the “Dogmas revisited” presentation). The hypochloremia is frequently attributed to vomiting – even when there is minimal historical or current evidence of significant vomiting. When functional, the kidneys are major contributors to the development of hypochloremia.

When an animal is acidemic due to nonrenal disorders, the kidneys attempt to compensate by excreting more H\(^+\). When Type A intercalated cells (illustrated above) are stimulated by acidemia, they secrete H\(^+\) and produce HCO\(_3\)\(^-\). However, the major method of removing H\(^+\) from plasma is increased excretion of NH\(_4\)\(^+\) (Fig. 4).

1. The response of the proximal tubular epithelial cells to acidemia includes the uptake of glutamine and its subsequent
1. Deamination to form NH₃. The NH₃ quickly combines with H⁺ that entered the cell from plasma to form NH₄⁺. The NH₄⁺ enters the tubular fluid in a Na⁺ exchange.
2. The presence of NH₄⁺ in the tubular fluid obligates the excretion of an anion – the major anion in the tubular fluid is Cl⁻. This process leads to increased renal excretion of Cl⁻ (without a corresponding Na⁺) and contributes to the hypochloremia.
3. In the collecting duct epithelial cells, there is a diffusion of NH₃ from plasma to tubular fluid.
4. As a response to acidemia, there is increased carbonic anhydrase activity that generates H⁺ ions that are secreted with Cl⁻ via a membrane pump.
5. The H⁺ ions combine with NH₃ to form NH₄⁺ that is excreted with Cl⁻. This process leads to increased renal excretion of Cl⁻ (without a corresponding Na⁺) and contributes to the hypochloremia.
6. In response to the acidemia, the proximal tubular epithelial cells and the collecting duct epithelial cells produce HCO₃⁻; this production represents a compensatory metabolic alkalosis to the nonrenal acidemic state.

Vomiting may contribute to the hypochloremia in an animal that has a metabolic acidosis. However, the expected renal compensation for an acidemia of nonrenal origin is the excretion of NH₄⁺ and Cl⁻; the increased renal Cl⁻ excretion contributes to the hypochloremia.

**Calculated electrolyte data: SID, anion gap, and others**

The measured electrolyte concentrations frequently are used to calculate other data; i.e., Na⁺: K⁺ ratio, anion gap, SID, corrected Cl⁻ concentration. However, there are reasons for interpreting the calculated data cautiously.

True changes in the strong-ion difference (SID) basically represent changes in plasma/serum HCO₃⁻ concentrations. As it not clinically practical to measure the true SID, a variety of formulas have been proposed to estimate the SID. However, the formulas are based on assumptions that may or may not be true and thus the calculated SIDs may or may not be reliable estimates. Another factor that should be considered is that the validity of calculated results is dependent on the accuracy of the measured concentrations used for the calculation. The simplest SID formula is: SID = [Na⁺] + [K⁺] – [Cl⁻]. Considering the analytical precision of the Na⁺ and Cl⁻ methods, the measured concentrations should be considered the reported values ± 1 mmol/L (or perhaps ± 2 mmol/L); the precision of the K⁺ methods are better. For a cautious perspective, the calculated SID is the value ± 4 mmol/L. Thus, any minor difference when compared to appropriate SID reference intervals (or interpretive guidelines) should be interpreted cautiously.

The potential for imprecision to affect the calculated value increases with each added variable. For example, a common formula for anion gap is: anion gap = ([Na⁺] + [K⁺]) – ([Cl⁻] + [HCO₃⁻]). The addition of patient’s HCO₃⁻ concentration (again, at best ± 1 mmol/L) adds to the uncertainty of the calculated anion gap concentration. And as mentioned earlier, the HCO₃⁻ concentration can easily be falsely decreased if the blood/plasma/serum samples are not collected and processed properly.
Results from the analysis of an effusion and other clinical information are used to determine the process or processes that are creating effusions. Interpretation of fluid analysis results is based on the knowledge of the factors that contribute to the composition of the effusion.

The chemical composition of a body cavity fluid is primarily determined by permeability of capillaries to H₂O and solutes and, to a lesser extent, permeability of pleural and peritoneal mesothelium. Capillaries are permeable to H₂O, electrolytes (e.g., Na⁺, K⁺, Cl⁻, Ca²⁺, bicarbonate, and phosphates) and small nonprotein solutes (e.g., glucose, urea, and creatinine) and thus most effusions have electrolyte, urea, glucose, and creatinine concentrations similar to plasma; the major exceptions to the concept are chylous effusions and uroperitoneum.

For some effusions, the major alteration in chemical composition is the protein concentration. Interstitial fluid is the source of most pleural and peritoneal fluid proteins. Variations in capillary permeability to plasma proteins cause variations in interstitial total protein concentration. In people, the interstitial fluid total protein concentration is near 1.5 g/dL in skeletal muscle, near 2.0 g/dL in subcutaneous tissue, near 4 g/dL in intestine, and near 6 g/dL in liver.

If there is one pathologic process causing a pleural or peritoneal effusion, then basically there are five types of cavitary effusions. Knowing the pathologic processes that produce the effusion allows the veterinarian to appropriately interpret results of a cavitary fluid analysis.

1. Transudates form when there are changes in oncotic or hydraulic pressure gradients within capillary beds. In transudates, vascular permeability is not altered and vascular damage is not present.
2. Exudates form when inflammatory mediators increase the vascular permeability to plasma proteins which leads to altered oncotic pressure gradients; there may be concurrent alterations in the hydraulic pressure gradients.
3. Hemorrhagic effusions (hemothorax, hemoperitoneum) form when blood enters a body cavity because of blood vessel damage or a defective hemostasis system.
4. Lymphatic effusions (chylous and nonchylous thorax or abdomen) form when lymph accumulates in a body cavity because of lymphatic vessel damage or impaired lymph drainage.
5. Uroperitoneum occurs when damage to the urinary tract allows urine to enter the peritoneal cavity.

Before the pathogeneses of effusions are described, a basic review of the flow of fluid in an out of capillaries is needed.

**Starling’s law of capillaries**

![Figure 1: Peripheral Capillary](image)

In the healthy peripheral capillary beds, there is a net flow of fluid out of the blood on the arterial side of the capillary bed and a net flow of fluid into the blood on the venous side of the capillary bed. This flow out of and back into the blood is governed by the differences between the hydraulic pressure gradient and the oncotic pressure gradient (Fig. 1).

- On the arterial side, the hydraulic pressure gradient ($\Delta P$) is greater than the oncotic pressure gradient ($\Delta \pi$) and thus fluid moves out of the blood. In Fig. 1, $\Delta P - \Delta \pi = 13 \text{ mmHg}$.
On the venous side, the hydraulic pressure gradient ($\Delta P$) is less than the oncotic pressure gradient ($\Delta \pi$) and thus fluid moves into blood. In Fig. 1, $\Delta P - \Delta \pi = -7$ mmHg.

Because there is essentially no change in the plasma protein concentration in the capillary blood or in the surrounding interstitial fluid, the oncotic pressure gradient is nearly constant across the capillary bed and thus the movement of fluid out of and into the capillary bed is because of higher blood pressure in arterial blood than venous blood.

The capillary beds have more vessels on the venous side of the bed. The overall result is a slight loss of fluid from blood which is removed by lymphatic vessels. This net effect is illustrated in Fig. 2; the key concepts are as follows.

- $H_2O$, electrolytes, and small molecules (e.g., glucose, urea, and creatinine) freely pass out of and into the capillary blood and thereby providing nutrients to tissues and removing metabolic waste from tissues.
- Any major changes in either the $\Delta P$ or $\Delta \pi$ can result in an accumulation of fluid outside of the capillaries and thus can cause edema or a cavitary effusion.
- Proteins create the oncotic pressure and thus hypoproteinemia will lower the oncotic pressure within the capillary. However as long as the $\Delta \pi$ does not change, extravascular fluid will not accumulate. When there is a mild hypoproteinemia, the oncotic pressure in the vessel and outside the vessel both decrease and thus there is no change in the $\Delta \pi$. This is part of the “Safe Zone” in which effusions do not form. When there is a marked hypoproteinemia (especially hypoalbuminemia), this “Safe Zone” is exceeded and the $\Delta \pi$ decreases. Increased lymph drainage may prevent formation of a transudate.

**Transudates**

Transudates form when there are changes in oncotic or hydraulic pressure gradients within capillary beds. Depending on the blood vessels involved, the transudates can be protein-poor or protein-rich.

**Protein-poor transudates** (aka, pure transudates) form primarily in the peritoneal cavity in animals with hepatic cirrhosis, protein-losing nephropathy, and protein-losing enteropathy. They are formed because of two factors:

- Multiple factors lead to renal retention of $Na^+$ and $H_2O$ which results in an expanded plasma volume which creates increased capillary hydraulic pressure and thus an $\uparrow \Delta P$.
- Concurrently, each disorder results in a hypoproteinemia (especially hypoalbuminemia) which decreases the capillary oncotic pressure and thus a $\downarrow \Delta \pi$.

The combination of $\uparrow \Delta P$ and $\downarrow \Delta \pi$ results in the extravasation of protein-poor fluid and eventually a protein-poor transudate (Fig. 3); usually just in the peritoneal cavity.

A less common protein-poor transudate forms when a disorder causes a noncirrhotic portal hypertension. The increased hydraulic pressure within the portal veins results in the extravasation of protein-poor fluid and an accumulation of a protein-poor transudate in the peritoneal cavity.

Hypoalbuminemia is frequently stated as the cause of protein-poor transudates. An inherited defect in people results in the inability of hepatocytes to produce albumin and their albumin concentration is less than 0.1 g/dL – and they do not have cavitary effusions. By itself, hypoalbuminemia will not cause the formation of a transudate.

**Figure 2: Starling’s forces in average peripheral capillary bed**

**Figure 3: Protein-poor transudate**

**Figure 4: Protein-rich transudate**

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Protein-rich transudates form when there is increase hydraulic pressure within blood vessels that are naturally permeable to plasma proteins; i.e., hepatic sinusoids and pulmonary capillaries (Fig. 4). Protein-rich transudates in the peritoneal cavity form when there is postsinusoidal hypertension caused by disorders such as right-sided heart failure, constrictive pericarditis, and hepatic vein thrombi. Protein-rich transudates in the pleural cavity form primarily when there is left-sided heart failure which results in congestion in pulmonary capillaries. These effusions have been called “modified transudates,” but they are formed simply by transudation and thus there is no “modification.”

In heart failure, the increased hydraulic pressures created by defective cardiac function are complicated by increased Na⁺ and H₂O retention. A vicious cycle develops as the kidneys perceived hypovolemia which results in Na⁺ and H₂O retention which causes increased extravasation of plasma water which creates hypovolemia which initiates Na⁺ and H₂O retention, etc.

Exudates
Exudates form when inflammation causes increased vascular permeability to plasma proteins which results in a decreased oncotic pressure gradient within capillary beds and thus less fluid returning to blood from interstitial space. The same events result in the exudation of plasma whether it is an infectious exudate or noninfectious exudate; typically, the infectious process causes greater vascular permeability to proteins and thus a greater movement of fluid from capillaries to body cavities.

The major event in the formation of an exudate is the oozing of plasma proteins from the capillaries to the interstitial space (Fig. 5). This causes the extravascular (interstitial) fluid’s oncotic pressure to increase, when reduces the oncotic pressure gradient – which reduces the “suck” of fluid into the vessel on the venous side of the capillary bed. Concurrently, inflammatory mediators may be causing vasodilation to allow increase blood flow to the inflamed tissue – and thus increased intravascular hydraulic pressure which will increase the flow of fluid out of the capillaries.

For most exudates, there will be chemokines in the cavity effusion which will induce the movement of inflammatory cells into the effusion – thus increasing the total nucleated cells count (TNCC).

Hemorrhagic effusions
The formation of hemorrhagic effusions is simple – damage to blood vessels or a defective coagulation system results in blood escaping from blood vessels and entering the pleural or peritoneal cavities (Fig. 6). However after the initial bleeding, the properties of the fluid change because of multiple factors.

- The extravasation of plasma proteins reduces the oncotic pressure gradient and thus fluid may be added from other blood vessels.
- Lymphatic vessels return RBCs, WBCs, and proteins to blood (autotransfusion)
- Cells are removed from the fluid by macrophages (leukophages, erythrophages)

Lymphatic effusions
The most commonly recognized lymphatic effusion is the chylothorax in which chylomicron-rich lymph leaks from the thoracic duct and accumulates in the pleural cavity. If the leakage occurs in the abdomen, then a chyloabdomen forms.

It is much more difficult to recognize lymphatic effusions when chylomicrons are not present. These effusions may result from damage of other lymphatic vessels or when there is impaired lymph drainage because of lymph node or other lymphatic system disorder.

Effusion of uroperitoneum
Uroperitoneum simply occurs when urine leaks from the urinary tract into the peritoneal cavity and initially the fluid has the chemical properties of urine. With time, electrolytes and small molecules (e.g., urea and creatinine) diffuse down concentrations to alter concentrations in the peritoneal fluid and plasma. Also, a mild secondary inflammatory process results in exudation.
Neoplastic effusions
Effusions caused by the neoplastic process can result from transudation, exudation, hemorrhage, lymphatic damage, or a combination of factors.

Modified transudates
Modified transudates have been a part of the effusion classifications in veterinary literature for nearly 30 years; there is not a similar category in the human effusions. The classification has been based on the results of fluid analysis; that is, the fluid had a total protein concentration or total nucleated cell count “too high” for a pure transudate and it did not have the features of an exudate. Thus, it became a “catch all” or “lumper” classification for effusions that were not “pure transudates” or exudates.

One “modified transudate” is the effusion of heart failure – that effusion is a protein-rich transudate described above. Other “modified transudates” described in textbooks include the FIP exudate, hypocellular exudates, chylous effusions, uroperitoneum, bilious peritonitis, and uroperitoneum – these are not transudates; they are not transudates modified by the addition of protein or cells.

Nucleated cells in effusions
The total nucleated cell concentration in an effusion and the type of nucleated cells also aid in the identification of effusions. Their value will be described in the case analyses in subsequent presentations.
Pleural or peritoneal fluid analysis will be classified by evaluating the results of routine fluid analysis and virtual microscopy of digital slides.

### 1-1 Effusion CVC: Peritoneal fluid; direct smear

**Case 315135**

Cat, DSH, female (spayed), 8 yr

The cat was presented because of a sudden onset of lethargy, anorexia, and more recently, vomiting. Physical examination revealed an increased rectal temperature, mild dehydration, depression, abdominal tenderness, and abdominal distension. Radiographs revealed a peritoneal effusion – fluid was collected for analysis.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Color, precentrifugation</th>
<th>Clarity, precentrifugation</th>
<th>Color, postcentrifugation</th>
<th>Clarity, postcentrifugation</th>
<th>Total protein (ref)</th>
<th>Hct</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNCC</td>
<td>Tan</td>
<td>Cloudy</td>
<td>Colorless</td>
<td>Clear</td>
<td>5.1 g/dL</td>
<td>&lt; 3 %</td>
</tr>
<tr>
<td>Neutrophils</td>
<td></td>
<td>Neutrophils</td>
<td>Monocytes/macrophages</td>
<td>Lymphocytes</td>
<td>Reactive mesothelial cells</td>
<td>Other</td>
</tr>
</tbody>
</table>
The cat was presented because of a progressive lethargy and inappetence during the past week. Physical examination revealed an increased rectal temperature, mild dehydration, and abdominal distension; the abdomen did not appear tender or painful. Radiographs revealed a peritoneal effusion – fluid was collected for analysis.

**The viscosity of the fluid prevents accurate pipetting and thus a total nucleated cell concentration cannot be determined accurately.**

The cat was presented because it was having a hard time breathing. Physical examination revealed muffled heart sounds. Radiographs revealed a pleural effusion – fluid was collected for analysis.

The dog was presented because of difficult breathing. The owner reported intermittent inappetence for the past two weeks; also, the dog did seemed to tire easily. Physical examination revealed a lethargic dog with muffled heart sounds. Radiographs revealed a pleural effusion – fluid was collected for analysis.

The dog was presented because of an acute onset of vomiting. Physical examination revealed icteric mucous membranes and intense abdominal pain. Peritoneal fluid was collected for analysis.

The dog was presented because of an acute onset of vomiting. Physical examination revealed intense abdominal pain. Peritoneal fluid was collected for analysis.
1-7 Effusion CVC: Peritoneal fluid, cytocentrifuge prep  Case 075542
Dog, Cairn terrier, female (spayed), 3 years old
The dog was presented because icterus and difficult breathing. Physical examination revealed a distended abdomen due to a peritoneal effusion. Peritoneal fluid was collected and submitted for analysis.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color, precentrifugation</td>
<td>Dark yellow</td>
</tr>
<tr>
<td>Clarity, precentrifugation</td>
<td>Cloudy</td>
</tr>
<tr>
<td>Color, postcentrifugation</td>
<td>Dark yellow</td>
</tr>
<tr>
<td>Clarity, postcentrifugation</td>
<td>Nearly clear</td>
</tr>
<tr>
<td>Total protein (ref)</td>
<td>4.0 g/dL</td>
</tr>
<tr>
<td>Hct</td>
<td>&lt; 3 %</td>
</tr>
</tbody>
</table>

1-8 Effusion CVC: Peritoneal fluid direct smear  Case ASVCP 10-9
Dog, miniature Australian shepherd, female (spayed), 8 months old
One week after intestinal resection, the dog was presented because of anorexia. Physical examination revealed a distended abdomen due to a peritoneal effusion. A direct smear of peritoneal fluid was prepared and submitted for evaluation (fluid for analysis was not available).

<table>
<thead>
<tr>
<th>Patient</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color, precentrifugation</td>
<td>Blood-tinged</td>
</tr>
<tr>
<td>Clarity, precentrifugation</td>
<td>Hazy</td>
</tr>
<tr>
<td>Color, postcentrifugation</td>
<td>Light yellow</td>
</tr>
<tr>
<td>Clarity, postcentrifugation</td>
<td>Clear</td>
</tr>
<tr>
<td>Total protein (ref)</td>
<td>0.5 g/dL</td>
</tr>
<tr>
<td>Hct</td>
<td>&lt; 3 %</td>
</tr>
</tbody>
</table>

1-9 Effusion CVC: Peritoneal fluid, cytocentrifuge prep Case ASVCP 08-9
Dog, Nova Scotia Duck-tolling retriever, male (neutered), 5 years old
The dog was presented because hematemesis and melena. Physical examination revealed pale mucous membranes. Abdominal ultrasound demonstrated multiple enlarge abdominal lymph nodes and a peritoneal effusion. Peritoneal fluid was collected and submitted for analysis.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color, precentrifugation</td>
<td>Light yellow</td>
</tr>
<tr>
<td>Clarity, precentrifugation</td>
<td>Hazy</td>
</tr>
<tr>
<td>Color, postcentrifugation</td>
<td>Light yellow</td>
</tr>
<tr>
<td>Clarity, postcentrifugation</td>
<td>Clear</td>
</tr>
<tr>
<td>Total protein (ref)</td>
<td>3.2 g/dL</td>
</tr>
<tr>
<td>Hct</td>
<td>&lt; 3 %</td>
</tr>
</tbody>
</table>

Pleural or peritoneal fluid analysis will be classified by evaluating the results of routine fluid analysis and virtual microscopy of digital slides.
Dog, Labrador retriever, male (neutered), 8 years old

The dog was referred because of an acute onset of a distended abdomen and a hypoproteinemia (TP = 4.2 g/dL, Alb = 2.2 g/dL). Physical examination revealed a distended abdomen due to a peritoneal effusion and muffled heart sounds. Pleural and peritoneal fluid samples were collected and submitted for analysis.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Color, precentrifugation</th>
<th>Clarity, precentrifugation</th>
<th>Color, postcentrifugation</th>
<th>Clarity, postcentrifugation</th>
<th>Total protein (ref)</th>
<th>Hct</th>
<th>Color, postcentrifugation</th>
<th>Clarity, postcentrifugation</th>
<th>Total protein (ref)</th>
<th>Hct</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Blood-tinged</td>
<td>Cloudy</td>
<td>Colorless</td>
<td>Clear</td>
<td>2.9 g/dL</td>
<td>&lt; 3 %</td>
<td>Other</td>
<td>Neutrophils</td>
<td>Reactive mesothelial cells</td>
<td>%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Neutrophils/macrophages</td>
<td></td>
<td>%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lymphocytes</td>
<td></td>
<td>%</td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Lymphocytes</td>
<td></td>
<td>%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reactive mesothelial cells</td>
<td></td>
<td>%</td>
</tr>
</tbody>
</table>
2-2 Effusion CVC: Peritoneal fluid, cytocentrifuge prep. Case 079234
Dog, Labrador retriever, male (neutered), 8 years old
See CVC 2-1 information

<table>
<thead>
<tr>
<th>Color, precentrifugation</th>
<th>Blood-tinged</th>
<th>TNCC</th>
<th>&lt; 1,000/µL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarity, precentrifugation</td>
<td>Cloudy</td>
<td>Neutrophils</td>
<td>%</td>
</tr>
<tr>
<td>Color, postcentrifugation</td>
<td>Colorless</td>
<td>Monocytes/macrophages</td>
<td>%</td>
</tr>
<tr>
<td>Clarity, postcentrifugation</td>
<td>Clear</td>
<td>Lymphocytes</td>
<td>%</td>
</tr>
<tr>
<td>Total protein (ref)</td>
<td>3.0 g/dL</td>
<td>Reactive mesothelial cells</td>
<td>%</td>
</tr>
<tr>
<td>Hct</td>
<td>&lt; 3 %</td>
<td>Other</td>
<td>%</td>
</tr>
</tbody>
</table>

2-3 Effusion CVC: Peritoneal fluid, cytocentrifuge prep. Case 079660
Horse, quarter horse, male (neutered), 20 years old
The horse was referred because of an acute colic that now is of 24-hours duration. Physical examination revealed pawing and kicking of abdomen, tachycardia, and very few gut sounds.

<table>
<thead>
<tr>
<th>Color, precentrifugation</th>
<th>Yellow</th>
<th>TNCC</th>
<th>&lt; 1,000/µL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarity, precentrifugation</td>
<td>Hazy</td>
<td>Neutrophils</td>
<td>%</td>
</tr>
<tr>
<td>Color, postcentrifugation</td>
<td>Yellow</td>
<td>Monocytes/macrophages</td>
<td>%</td>
</tr>
<tr>
<td>Clarity, postcentrifugation</td>
<td>Clear</td>
<td>Lymphocytes</td>
<td>%</td>
</tr>
<tr>
<td>Total protein (ref)</td>
<td>1.8 g/dL</td>
<td>Reactive mesothelial cells</td>
<td>%</td>
</tr>
<tr>
<td>Hct</td>
<td>&lt; 3 %</td>
<td>Other</td>
<td>%</td>
</tr>
</tbody>
</table>

2-4 Effusion CVC: Peritoneal fluid, direct smear Case 507605
Horse, Thoroughbred cross, male (castrated), 14 yr
The horse was presented because of colic of 12-hr duration. The referring veterinarian reported that the horse passed a small amount of mucoid feces yesterday, rectal palpation revealed gas-distended loops of intestine, and gut sounds were absent. A small amount of peritoneal fluid was collected and submitted for analysis.

<table>
<thead>
<tr>
<th>Color, precentrifugation</th>
<th>yellow</th>
<th>TNCC</th>
<th>202,000/µL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarity, precentrifugation</td>
<td>cloudy</td>
<td>Neutrophils</td>
<td>%</td>
</tr>
<tr>
<td>Color, postcentrifugation</td>
<td>yellow</td>
<td>Monocytes/macrophages</td>
<td>%</td>
</tr>
<tr>
<td>Clarity, postcentrifugation</td>
<td>clear</td>
<td>Lymphocytes</td>
<td>%</td>
</tr>
<tr>
<td>Total protein (ref)</td>
<td>5.5 g/dL</td>
<td>Reactive mesothelial cells</td>
<td>%</td>
</tr>
<tr>
<td>Hct</td>
<td>&lt; 3 %</td>
<td>Other</td>
<td>%</td>
</tr>
</tbody>
</table>

2-5 Effusion CVC: Peritoneal fluid, direct smear Case 051233
Dog, Labrador retriever, male (neutered), 6 yr
Owner first noticed abdominal distension about one week ago; the dog’s appetite and activity has not changed. Physical examination revealed a fluid-filled, distended abdomen and possibly a peripheral lymphadenopathy.

<table>
<thead>
<tr>
<th>Color, precentrifugation</th>
<th>Red</th>
<th>TNCC</th>
<th>7,500/µL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarity, precentrifugation</td>
<td>Opaque</td>
<td>Neutrophils</td>
<td>%</td>
</tr>
<tr>
<td>Color, postcentrifugation</td>
<td>Pink</td>
<td>Monocytes/macrophages</td>
<td>%</td>
</tr>
<tr>
<td>Clarity, postcentrifugation</td>
<td>Hazy</td>
<td>Lymphocytes</td>
<td>%</td>
</tr>
<tr>
<td>Total protein (ref)</td>
<td>5.0 g/dL</td>
<td>Reactive mesothelial cells</td>
<td>%</td>
</tr>
<tr>
<td>Hct</td>
<td>30 %</td>
<td>Other</td>
<td>%</td>
</tr>
</tbody>
</table>

2-6 Effusion CVC: Peritoneal fluid, cytocentrifuge prep. Case 079781
Dog, Anatolian shepherd, male (neutered), 8 yr
The dog had intermittent episodes of diarrhea for about 2 months. About 2 weeks ago, it was dribbling urine and the referring veterinarian treated for a urinary tract infection. Urine dribbling continued up to yesterday; no urine passed in last 24 hours. Physical examination revealed a depressed dog with a distended and painful abdomen.

Initial laboratory data included a mild inflammatory leukocytosis, mild hyperproteinemia, almost an erythrocytosis, azotemia (UN 105 mg/dL, Crt 3.6 mg/dL), mild hyperphosphatemia, mild hyponatremia, almost hyperkalemia, and metabolic acidosis (HCO₃⁻ 14 mmol/L)
2-7 Effusion CVC: Peritoneal fluid, line prep.  Case 08-69874
Dog, mixed breed, female, 1 yr
A veterinarian in NE Kansas submitted pleural and peritoneal fluid from a dog. Historical or physical examination findings were not provided.

<table>
<thead>
<tr>
<th>Color, precentrifugation</th>
<th>Blood-tinged</th>
<th>TNCC 2,700/µL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarity, precentrifugation</td>
<td>Cloudy</td>
<td>Neutrophils</td>
</tr>
<tr>
<td>Color, postcentrifugation</td>
<td>Pink</td>
<td>Monocytes/macrophages</td>
</tr>
<tr>
<td>Clarity, postcentrifugation</td>
<td>Clear</td>
<td>Lymphocytes</td>
</tr>
<tr>
<td>Total protein (ref)</td>
<td>1.3 g/dL</td>
<td>Reactive mesothelial cells</td>
</tr>
<tr>
<td>Hct</td>
<td>&lt; 3 %</td>
<td>Other</td>
</tr>
</tbody>
</table>

Other microscopic findings:
Note: A line prep. tends to concentrate cells in the line, but also makes that area thick.
Note: The analysis of pleural fluid yielded essentially the same results except the TNCC was 5,000/µL.

2-8 Effusion CVC: Pleural effusion, cytocentrifuge preparation  Case 047859
Cat, Birman, male (neutered), 16 yr
The cat was presented because of dyspnea. The owner reported intermittent inappetence during past week. Physical examination revealed muffled heart sounds. Radiographs revealed a pleural effusion – fluid was collected for analysis.

<table>
<thead>
<tr>
<th>Color, precentrifugation</th>
<th>Pink</th>
<th>TNCC 8,000/µL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarity, precentrifugation</td>
<td>Hazy</td>
<td>Neutrophils</td>
</tr>
<tr>
<td>Color, postcentrifugation</td>
<td>Light yellow</td>
<td>Monocytes/macrophages</td>
</tr>
<tr>
<td>Clarity, postcentrifugation</td>
<td>Clear</td>
<td>Lymphocytes</td>
</tr>
<tr>
<td>Total protein (ref)</td>
<td>2.6 g/dL</td>
<td>Reactive mesothelial cells</td>
</tr>
<tr>
<td>Hct</td>
<td>&lt; 3 %</td>
<td>Other</td>
</tr>
</tbody>
</table>

2-9 Effusion CVC: Peritoneal fluid, cytocentrifuge prep.  Case 080190
Dog, fox terrier, male (neutered), 6 yr
The dog was referred because of abdominal ascites that might be due to heart failure. Physical examination revealed a grade 2-3, left-sided systolic murmur and a fluid-filled abdomen. Preliminary laboratory data found UN of 16 mg/dL, Crt 3.6 mg/dL), hypoproteinemia (TP 2.5 g/dL, albumin 1.2 g/dL), hypocalcemia (tCa²⁺ 5.7 g/dL), mild hyponatremia (144 mmol/L), normochloremia, decreased anion gap, and urine with a specific gravity of 1.009, and negative chemistry results.

<table>
<thead>
<tr>
<th>Color, precentrifugation</th>
<th>colorless</th>
<th>TNCC &lt; 1,000/µL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarity, precentrifugation</td>
<td>clear</td>
<td>Neutrophils</td>
</tr>
<tr>
<td>Color, postcentrifugation</td>
<td>colorless</td>
<td>Monocytes/macrophages</td>
</tr>
<tr>
<td>Clarity, postcentrifugation</td>
<td>clear</td>
<td>Lymphocytes</td>
</tr>
<tr>
<td>Total protein (ref)</td>
<td>0.1 g/dL</td>
<td>Reactive mesothelial cells</td>
</tr>
<tr>
<td>Hct</td>
<td>&lt; 3 %</td>
<td>Other</td>
</tr>
</tbody>
</table>
A cytologic biopsy (aka, fine needle biopsy or fine needle aspiration biopsy or “cytology”) of cutaneous and subcutaneous lesions (lumps and bumps) can result in a specific diagnosis or perhaps can better characterize a lesion. For nearly all lesions, the cytologic biopsy will not be as definitive as an incisional or excisional biopsy with a histopathological examination; but will be less expensive and yield results quicker.

For some lesions (e.g., lipoma), it takes minimal expertise and diagnostic methods to arrive at a correct diagnosis; but other lesions require extensive knowledge gained through experience and excellent equipment. For those who wish to develop their cytologic biopsy skills, the following should be considered essential.

- Develop techniques to obtain cytologic preparations that have monolayers of cells
- Have a quality cytologic stain that can provide reproducible results; quick stains can be acceptable
- Have a quality microscope that has excellent 40x- or 50x-oil and 100-x oil objectives (these objectives might cost $3000 to $5000 each)
- Have excellent textbooks and atlases for the species of interest
- Have knowledge of the types of lesions that can be found and the many variations of each disorder

During the microscopic examination of aspirates, scrapes, imprints, or other cytologic preparations, general goals are to arrive at one of these conclusions or opinions:

- Definitive diagnosis: can be achieved with a few neoplasms and some inflammatory lesions
- Consistent with ________: cells populations are seen in this condition but the findings are not unique to one diagnosis; additional diagnostic efforts are needed to confirm
- Suspicious of ________: findings are suggestive stated diagnoses but definitive evidence is not seen; additional diagnostic efforts are needed
- Not consistent with ________: A preliminary diagnosis had been made; the findings in this sample are not likely to be found in that disorder; or, the findings do not support the preliminary diagnosis

The following flowchart provides a basic guideline for the evaluation of a cytologic preparation. The concepts of the flow chart will be used during the virtual microscopy of several lesions involving the skin and subcutaneous tissues of dogs and cats.
A smear of serosanguineous to purulent fluid was submitted; the fluid was collected from a subcutaneous swelling that had a draining tract.

**Case: 176517**

**Dog, mixed breed, 3-yr-old, female (spayed)**

A 2x4x3 cm mass was located in the lateral skin of the left hind thigh or hip. The owner first noticed the mass a few weeks ago and it has been getting larger. The mass protruded slightly and felt like it extended into the subcutaneous tissue. A fine-needle aspirate of the mass was collected and a smear was prepared for examination.

**Case: 02-1975**

**Dog, Labrador retriever, 4-yr-old**

The dog was presented because of a mass located on the dorsal aspect of the tail head. Physical examination revealed 2-cm, soft mass in the dermis and was covered with haired skin. A fine-needle aspirate of the rear leg mass was collected and a smear was prepared for examination.

**Case: 02885**

**Dog, Golden retriever, male, 12-year-old**

The dog was presented because of perianal masses. Physical examination revealed a small perianal mass and possibly enlarged regional lymph node. A fine-needle aspirate of the mass was collected and a smear was prepared for examination.

**Case: 030056**

**Dog, basset hound, male (neutered), 7-year-old**

The dog had been coughing for 2-3 weeks. During a physical exam, a mass was found in the subcutaneous tissues of the left lateral thoracic; it appeared to be firmly attached to underlying tissues. A fine-needle aspirate of the mass was collected and a smear was prepared for examination.

**Case: 02-2357**

**Dog, breed, age, and gender not provided**

A smear of an aspirate obtained from a mass in the skin of a foot was submitted for evaluation.

**Case: 024854**

**Dog, schipperke, male (neutered), 15-yr-old**

The dog was presented because of skin lesions. Physical examination revealed several, pea-size, cutaneous masses. One mass was excised and imprints of the mass were submitted for evaluation.

**Case: 256285**

**Dog, mixed breed, male (neutered), 4-yr-old**

The preparation is an imprint of the ulcerated area after superficial debris and hair were removed.

**Case: ASVCP 1988-11**

**Cat, domestic short hair**

The cat was presented because of skin lesions. Physical examination revealed several, pea-size, cutaneous masses. One mass was excised and imprints of the mass were submitted for evaluation.

Additional slides will be reviewed if time permits.
A cytologic biopsy (aka, fine needle biopsy or fine needle aspiration biopsy or “cytology”) of cutaneous and subcutaneous lesions (lumps and bumps) can result in a specific diagnosis or perhaps can better characterize a lesion. For nearly all lesions, the cytologic biopsy will not be as definitive as an incisional or excisional biopsy with a histopathological examination; but will be less expensive and yield results quicker.

Please see previous proceeding’s document (Part 1) for an introduction to the goals and approach of a cytologic biopsy.

2-1 L&B CVC: fine-needle aspirate of vulvar mass Case: 026163
Dog, mixed breed, female, 5-yr-old
A 1x1 pink mass was protruding slightly from the vulvar mucosa. The owner first noticed the mass yesterday. The mass protruded into the vaginal vault; it might be extending into the submucosa. A fine-needle aspirate of the mass was collected and a smear was prepared for examination.

2-2 L&B CVC: fine-needle aspirate of cutaneous mass Case: 02-7821
Dog, boxer, 1-yr-old
A 1x1x1 cm, pink mass was located in the lateral skin of the right shoulder. The owner first noticed the mass a few days ago. The mass seemed to involve the dermis and epidermis and did not extend into the subcutaneous tissues. A fine-needle aspirate of the mass was collected and a smear was prepared for examination.

2-3 L&B CVC: fine-needle aspirate of cutaneous mass Case: 028857
Dog, Golden retriever, male (neutered), 5-yr-old
The dog was presented because of a 2x2x1 cm mass located in the lateral thoracic skin. The preparation is a smear of the sample aspirated from the mass.

2-4 L&B CVC: fine-needle aspirate of cutaneous mass Case: 039973
Cat, domestic short hair
The preparation is a smear of a sample aspirated from one of several small (< 1 cm) cutaneous masses.

2-5 L&B CVC: fine-needle aspirate of cutaneous mass Case: 56535-98
Dog, mixed breed
A smear of serosanguineous to purulent fluid was submitted; the fluid was collected from a subcutaneous swelling that had a draining tract.

2-6 L&B CVC: fine-needle aspirate of cutaneous mass Case: 028729
Dog, terrier-mix, female (spayed), 14-year-old
A 5x4x23 cm mass was found in the dorsal thoracic skin. The dog has several other similar masses in its thoracic and abdominal skin. The mass extends above the skin surface, the surface is ulcerated, and appears to involve dermal and possibly subcutaneous tissues. A fine-needle aspirate of the mass was collected and a smear was prepared for examination.

2-7 L&B CVC: fine-needle aspirate of cutaneous mass Case: 029402
Cat, Persian, female (spayed), 19-year-old
The cat was presented because of a large (about 8 cm), broad-based mass located in the area of the 3rd to 4th left mammary gland. Physical examination revealed was covered with haired skin and appeared to involve the dermis and subcutaneous tissues. A fine-needle aspirate of the mass was collected and a smear was prepared for examination.

2-8 L&B CVC: fine-needle aspirate of cutaneous mass Case: 028874
Dog, shar pei, male (neutered), 9-year-old
The dog was presented because of a mass in its skin. Physical examination revealed a dermal or subcutaneous mass of the right thorax. A fine-needle aspirate of the mass was collected and a smear was prepared for examination.

Additional slides will be reviewed if time permits
Virtual Microscopy of Lymph Nodes: Lymphoma or Just Reactive?

Steve Stockham, DVM, MS, DACVP
Kansas State University
Manhattan, KS

The major reason for a cytologic biopsy of lymph node aspirates is looking for the reason for an enlarged lymph node. Lymph nodes become enlarged from many diseases and typically are classified into one of the following groups.

**Hyperplastic lymph node**
Lymph node hyperplasia is characterized by increased numbers of lymphocytes: B-lymphocytes, T-lymphocytes, or both. The proportions of different types of lymphocytes may appear normal, in which case hyperplasia is suggested by normal cell populations in association with lymphadenomegaly. There may be increases in large lymphocytes and/or plasma cells, in which case the terms reactive or reactive hyperplasia are often used in place of hyperplasia, though the nodes are enlarged because of hyperplasia. A variety of infectious and noninfectious diseases, including bacterial, viral, fungal, and neoplastic disorders, can lead to the stimulation and proliferation of lymphocytes. If there is generalized lymph node hyperplasia, a systemic illness should be considered. If only one node is hyperplastic, a disease within the drainage field of that node should be considered.

**Reactive lymph node**
A node classified as reactive typically has increased numbers of plasma cells and/or large lymphocytes. The percentage of large lymphocytes is expected to be less than 50% in a reactive node and is usually less than 10%. An increase in plasma cells indicates B-lymphocyte stimulation.

The causes of a reactive lymph node are essentially the same as those for lymph node hyperplasia.

**Lymphadenitis**
Lymphadenitis is characterized by an increased number of nonlymphoid inflammatory cells in a lymph node. One inflammatory cell type might dominate (e.g., neutrophils), or there can be a mixture of inflammatory cells (e.g., neutrophils, macrophages, and eosinophils) The cause of the inflammatory state may be within the lymph node or, more commonly, in the node’s drainage field. For example, an allergic dermatitis may result in an eosinophilic lymphadenitis, or a lymph node draining a necrotic hemorrhagic lesion may have many macrophages containing cell debris and Fe pigments. Lymphadenitis is often associated with reactive (proplastic) changes, and the term reactive lymphadenitis is sometimes used to reflect both changes.

**Lymphoma**
Cytologically, lymphoma can be diagnosed when there is nearly a single population of atypical lymphocytes rather than the heterogeneous mixture of typical cell types present in normal, reactive, or inflamed lymph nodes. However, depending on the appearance of the cells, lymphoma can be an easy or difficult diagnosis cytologically.

When cytologic preparations consist of single populations of large lymphocytes with prominent nucleoli, the diagnosis of lymphoma is clear.

It is more difficult when the cells are of small to intermediate size or when substantial numbers of non-neoplastic cells are intermixed with neoplastic cells because of a nondiffuse form or a recent onset. In these cases, histologic examination may be necessary for a diagnosis.

**Metastatic neoplasm**
Lymph nodes can be enlarged because of the growth of non-lymphoid neoplastic cells in the node. Metastatic cells can also be found during biopsies of lymph nodes that do not appear enlarged. Many neoplasms have the potential to spread to regional lymph nodes. Those seen more frequently in the peripheral lymph nodes included squamous cell carcinoma, mammary carcinoma or adenocarcinoma, melanoma, mast cell neoplasia, and some hemic neoplasms.

**Cell Populations in lymphadenopathies other than lymphoma**
Typical lymph nodes include popliteal, inguinal, and prescapular lymph nodes. Percentages are provided to illustrate the differences between the pathologic states. They are not firm decision limits; a true differential count is rarely completed.
<table>
<thead>
<tr>
<th>Normal</th>
<th>Hyperplasia #1*</th>
<th>Hyperplasia #2</th>
<th>Hyperplasia (reactive)</th>
<th>Lymphadenitis***</th>
<th>Metastatic neoplasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoid</td>
<td>&gt; 95 %</td>
<td>&gt; 95 %</td>
<td>&gt; 95 %</td>
<td>&gt; 95 %</td>
<td>???</td>
</tr>
<tr>
<td>Small</td>
<td>&gt; 80 %</td>
<td>&gt; 80 %</td>
<td>&gt; 60 %</td>
<td>&gt; 60 %</td>
<td>? &gt; 60 %</td>
</tr>
<tr>
<td>Intermediate</td>
<td>&lt; 10 %</td>
<td>&lt; 10 %</td>
<td>&lt; 30 %</td>
<td>&lt; 30 %</td>
<td>? &lt; 30 %</td>
</tr>
<tr>
<td>Large</td>
<td>&lt; 5 %</td>
<td>&lt; 5 %</td>
<td>&lt; 10 %</td>
<td>&lt; 10 %</td>
<td>? &lt; 10 %</td>
</tr>
<tr>
<td>Plasma cell</td>
<td>&lt; 2 %</td>
<td>&lt; 2 %</td>
<td>&lt; 2 %</td>
<td>&lt; 2 %</td>
<td>? &lt; 2 %</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>&lt; 2 %</td>
<td>&lt; 2 %</td>
<td>&lt; 2 %</td>
<td>&lt; 2 %</td>
<td>? &gt; 2 %</td>
</tr>
<tr>
<td>Macrophages</td>
<td>&lt; 2 %</td>
<td>&lt; 2 %</td>
<td>&lt; 2 %</td>
<td>&lt; 2 %</td>
<td>? &gt; 2 %</td>
</tr>
<tr>
<td>Mast cells</td>
<td>&lt; 1 %</td>
<td>&lt; 1 %</td>
<td>&lt; 1 %</td>
<td>&lt; 1 %</td>
<td>? &gt; 1 %</td>
</tr>
<tr>
<td>Organisms</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>Maybe</td>
</tr>
</tbody>
</table>

* Mandibular lymph nodes and mesenteric lymph nodes frequently have higher percentages of neutrophils, macrophages, or plasma cells

** The cell populations in this hyperplastic lymph node look like normal lymph node cells, but they came from an enlarged lymph node.

*** The distribution of the cell populations vary with the severity of the inflammatory process. The aspirate may look like a normal LN with only a minor increase in neutrophil percentage. Or, the aspirate may contain very few lymphoid cells as nearly all of the cells are inflammatory cells.

** Cell populations in most lymphomas**

<table>
<thead>
<tr>
<th>Lymphoma (intermediate cell)</th>
<th>Lymphoma (large cell)</th>
<th>Lymphoma** (small cell)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoid</td>
<td>&gt; 90 %</td>
<td>&gt; 90 %</td>
</tr>
<tr>
<td>Small</td>
<td>&lt; 50 %</td>
<td>&gt; 10 %</td>
</tr>
<tr>
<td>Intermediate</td>
<td>&gt; 20 %</td>
<td>&gt; 30 %</td>
</tr>
<tr>
<td>Large</td>
<td>&lt; 10 %</td>
<td>&gt; 30 %</td>
</tr>
<tr>
<td>Plasma cell</td>
<td>&lt; 2 %</td>
<td>&lt; 2 %</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>&lt; 5 %</td>
<td>&lt; 2 %</td>
</tr>
<tr>
<td>Macrophages</td>
<td>&lt; 5 %</td>
<td>&lt; 2 %</td>
</tr>
<tr>
<td>Mast cells</td>
<td>&lt; 1 %</td>
<td>&lt; 1 %</td>
</tr>
</tbody>
</table>

* Lymphoma classification based on the diameters of most of the neoplastic lymphoid cells in the sample:  small cell = nuclei < 10 μm; intermediate (medium) cell = nuclei 10–15 μm; large cell = nuclei > 15 μm

** The small-cell lymphoma is difficult to recognize with certainty in an aspirate; the cell populations are similar to those of a normal lymph node or a hyperplastic lymph node. Histopathologic examination of an incised or excised lymph node is typically needed to establish the diagnosis.

** 1 LN CVC: Mandibular LN aspirate  Case: 053394  
Dog, Labrador retriever, 4-yr-old  
Healthy dog

<table>
<thead>
<tr>
<th>Lymphoid</th>
<th>%</th>
<th>Neutrophils</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small lymphocytes</td>
<td>%</td>
<td>Macrophages</td>
<td>%</td>
</tr>
<tr>
<td>Intermediate lymphocytes</td>
<td>%</td>
<td>Mast cells</td>
<td>%</td>
</tr>
<tr>
<td>Large lymphocytes</td>
<td>%</td>
<td>Organisms</td>
<td></td>
</tr>
<tr>
<td>Plasma cell</td>
<td>%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2 LN CVC: Mandibular LN aspirate  Case: 021111  
Dog, German shepherd, 3-yr-old, female (spayed)

The dog was presented because inappetence and lethargy. Physical examination revealed several mildly enlarged peripheral lymph nodes. An aspirate from the right mandibular lymph node was submitted for analysis.

<table>
<thead>
<tr>
<th>Lymphoid</th>
<th>%</th>
<th>Neutrophils</th>
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<tbody>
<tr>
<td>Small lymphocytes</td>
<td>%</td>
<td>Macrophages</td>
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<tr>
<td>Intermediate lymphocytes</td>
<td>%</td>
<td>Mast cells</td>
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<tr>
<td>Large lymphocytes</td>
<td>%</td>
<td>Organisms</td>
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<tr>
<td>Case: 079237</td>
<td>3 LN CVC: Axillary LN aspirate</td>
<td>Dog, German shepherd, 3-yr-old, female (spayed)</td>
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<tr>
<td>The dog was presented because of right, foreleg lameness. Radiographs revealed a small lytic bone lesion in the humerus. An aspirate from an enlarged axillary lymph node was submitted for analysis.</td>
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<td>LN CVC:</td>
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<td>Neutrophils</td>
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<tr>
<td>Lymphoid</td>
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<td>Macrophages</td>
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<td>Intermediate lymphocytes</td>
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<td>Large lymphocytes</td>
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<tr>
<td>Plasma cell</td>
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<thead>
<tr>
<th>Case 053708</th>
<th>4 LN CVC: Prescapular LN aspirate</th>
<th>Dog, Golden retriever, 5-yr-old, female (spayed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The dog was presented because of anorexia and lethargy. Several peripheral lymph nodes were enlarged. An aspirate from an enlarged prescapular lymph node as submitted for analysis.</td>
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<td>LN CVC:</td>
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<tr>
<td>Lymphoid</td>
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<tr>
<td>Plasma cell</td>
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</tbody>
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<thead>
<tr>
<th>Case 032086</th>
<th>5 LN CVC: Popliteal LN aspirate</th>
<th>Dog, Basset hound, 6-yr-old, male (neutered)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The dog was presented because of polyuria and polydipsia. Initial laboratory data revealed a hypercalcemia. A slightly enlarged popliteal lymph node was aspirated and the sample was submitted for analysis.</td>
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<td>LN CVC:</td>
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<td>Neutrophils</td>
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<tr>
<td>Lymphoid</td>
<td>%</td>
<td>Macrophages</td>
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<td>Plasma cell</td>
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<thead>
<tr>
<th>Case 028587</th>
<th>6 LN CVC: Inquinal LN aspirate</th>
<th>Cat, Tabbi, female (spayed), 8 years old</th>
</tr>
</thead>
<tbody>
<tr>
<td>The cat was presented because of weight loss and poor appetite. Physical examination revealed enlarged peripheral lymph node. One lymph node was aspirated and cytologic preparations were submitted for examination.</td>
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<tr>
<td>LN CVC:</td>
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<td>Neutrophils</td>
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<td>Lymphoid</td>
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<td>Macrophages</td>
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<td>Plasma cell</td>
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<thead>
<tr>
<th>Case 028260</th>
<th>7 LN CVC: Popliteal LN aspirate</th>
<th>Dog, Boxer, 7-yr-old, male (neutered)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A cutaneous mass on the left hind leg had been removed 10 days ago. The excised mass was not submitted for histopathologic examination. When the dog was returned for suture removal, an enlarged popliteal lymph node was found. An aspirate of the lymph node was submitted for analysis.</td>
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168
8 LN CVC: Prescapular LN aspirate Case 028445

Dog, Cairn terrier, 2-yr-old, female

The dog was presented because it was constantly scratching ears and neck. Physical examination revealed numerous fleas, red inflamed skin, and enlarged mandibular and prescapular lymph nodes. An aspirate of the lymph node was submitted for analysis.

<table>
<thead>
<tr>
<th>Lymphoid</th>
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<th>Neutrophils</th>
<th>%</th>
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<tbody>
<tr>
<td>Small lymphocytes</td>
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</table>
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) are commonly used in veterinary medicine due to their efficacy in managing pain of multiple origins and their overall safety. However NSAIDs are the drugs that are most commonly reported to the Food and Drug Administration (FDA) Center of Veterinary Medicine for adverse effects. The most common organ systems affected by adverse effects are gastrointestinal, followed by renal, then hepatic. Other adverse effects occur less commonly.

**Gastrointestinal adverse effects**

Gastrointestinal (GI) adverse effects are the most common adverse effects reported to the FDA and drug approval studies. Gastrointestinal adverse effects can range from vomiting and diarrhea to GI erosions and ulcers and even progress to perforated ulcers and death. The development of cyclooxygenase (COX) COX-2 preferential and selective NSAIDs have decreased the overall occurrence of GI adverse effects, but GI adverse effects are still the most common adverse effects. COX-2 selective or preferential NSAIDs are recommended to decrease the GI adverse effects of NSAIDs, but do not eliminate the risk. Both COX-1 and COX-2 are constitutively expressed in the canine gastrointestinal tract and inhibition of both isoforms (nonselective inhibition) results in the highest frequency of GI adverse effects. Prostaglandins produced by COX-1 (prostaglandin E, PGE) and COX-2 (PGE and PGI) provide GI mucosal protectant effects. Selectively inhibiting COX-2 still provides analgesic effects, but decreases GI adverse effects due to maintaining some PGE production by COX-1. However since COX-2 is still constitutively expressed in the GI tract, adverse GI effects still occur. COX-2 is also induced in injured (including surgical) and diseased GI tissues to promote and enhance healing. Therefore a COX-2 inhibitor will decrease the healing and have detrimental effects on damages and injured GI tissues.

There are conditions, diseases and drugs that NSAID use should be avoided. By far the biggest drug interaction is with glucocorticoids (prednisone, dexamethasone, methylprednisolone, et al.) and concurrent or even sequential use substantially increase the risk for GI adverse effects. Therefore NSAIDs and glucocorticoids should not be used together or sequentially. Although there are many recommendations of a “washout” time between use of NSAIDs and glucocorticoids there are no studies documenting an ideal period of time to minimize adverse effects. Conservatively, many people recommend a week, but again the ideal period of time is unknown. Concurrent use of multiple NSAIDs should be avoided as the risk of GI adverse effects may be increased. Although “washout” periods are often recommended, studies documenting the efficacy of different “washout” times are lacking. Many experts conservatively recommend a week for a washout period, but it is unknown if that is an appropriate time period. Similar to glucocorticoids, uncontrolled hyperadrenocorticism (Canine Cushing’s Disease) markedly increases the potential GI adverse effects of NSAIDs due to the high concentrations of endogenous cortisol. Dogs with uncontrolled hyperadrenocorticism are essentially on high doses of endogenous glucocorticoids and the risk of GI adverse effects of NSAIDs are increased. Animals that have gastrointestinal disease are also at an increased risk of GI adverse effects of NSAIDs. Inflammatory bowel disease, parasitism, erosions, foreign bodies, enterotomies and gastrotomies are all conditions in which NSAID use should be avoided as NSAIDs increase the damage and decrease the healing of GI tissues. Animals with renal disease also appear to be at a higher risk of NSAID GI adverse effects. Renal disease results in uremia which produces toxic effects on the GI mucosa and animals may have subclinical erosions and ulcerations of the GI mucosa. Administration of an NSAID will worsen the erosions and ulcers and should be avoided if possible in animals with renal disease.

There are several strategies for minimizing GI adverse effects. The approved dose of the NSAID may be higher than the specific patient needs to provide beneficial effects. The typical dose-response curve has a log-normal distribution and a dose to produce desirable effects in 90% of the population will be higher than needed in some patients. Decreasing the daily dose by 10-25%, even up to 50% may still produce beneficial effects in some patients. However some patients will lose beneficial effects, except at the highest approved dose. Limited data are available on the efficacy of GI “protectants” in combination with approved NSAIDs in dogs. Omeprazole and other proton pump inhibitors are the highest efficacy acid suppression therapies and are among the highest efficacy and best tolerated therapy to decrease GI adverse effects of NSAIDs in humans, but little data are available in dogs. Despite the lack of data, proton pump inhibitors are commonly recommended in dogs to minimize NSAID GI adverse effects. Histamine (H2) antagonists are also effective acid suppression therapy in dogs and have decreased GI adverse effects of NSAIDs in humans. Therefore drugs such as famotidine are also commonly recommended in conjunction with NSAIDs in dogs, but specific data are lacking demonstrating decreased NSAID GI effects in dogs when concurrently administered. Sucralfate is a GI protectant that has demonstrated decreased GI adverse effects of NSAIDs in humans, but specific data are again lacking in dogs. Misoprostol is a synthetic prostaglandin that has demonstrated decreased NSAID GI adverse effects in humans and dogs. Misoprostol does have more adverse effects such as diarrhea than the other protective therapies. However the biggest concern with misoprostol is that it can cause
abortion in humans (and animals) and as such may present a large liability risk. When misoprostol is prescribed, most experts recommend dispensing gloves to the clients to wear during drug administration to minimize inadvertent human exposure. Another limiting factor with misoprostol is that is the most costly of the GI “protectants” for minimizing NSAID GI adverse effects.

Renal adverse effects
Cyclooxygenase produces prostaglandins (PGE and PGI) which maintain renal blood flow during periods of renal hypotension and hypoperfusion. Although COX-1 produces renal prostaglandins in some species, COX-2 is up-regulated producing the beneficial hemodynamic effects during renal hypotension. Therefore the COX-2 selective and preferential inhibitors that produce less GI adverse effects have little to no beneficial effects for minimizing renal NSAID adverse effects.

Conditions resulting in renal hypotension including, but not limited to anesthetic hypotension, shock, dehydration and hemorrhage increase the risk of renal adverse effects of NSAIDs. COX-2 is typically upregulated in renal hypotension resulting in production of PGE and PGI causing localized renal vasodilation, counteracting the sympathetic mediated vasoconstriction to maintain critical blood flow to the kidneys. However administration of an NSAID inhibits COX-2 and the local vasodilation resulting in renal hypoperfusion, hypoxemia and subsequent renal injury. Therefore NSAIDs should be avoided when animals are hypotensive or have the potential to become and remain hypotensive.

Although little data are available, many experts recommend avoiding NSAIDs in patients with chronic kidney disease with the thought that NSAIDs may worsen or result in progression of CKD. However there are little data supporting this recommendation. A few studies have examined some specific NSAIDs which appeared to be tolerated in patients with CKD. However the majority of recommendations are to avoid NSAIDs in CKD when possible.

Although little data are available, many experts recommend avoiding NSAIDs in patients with chronic kidney disease with the thought that NSAIDs may worsen or result in progression of CKD. However there are little data supporting this recommendation. A few studies have examined some specific NSAIDs which appeared to be tolerated in patients with CKD. However the majority of recommendations are to avoid NSAIDs in CKD when possible.

Hepatic adverse effects
Hepatic adverse effects can be dose-dependent or dose-independent. Dose-dependent adverse effects typically occur with drug over dosages and can be avoided by administering appropriate dosages. However with the marketing of many flavored and chewable NSAID formulations inadvertent exposures may occur, therefore these formulations should not be stored in an area the animal may have access.

Dose-independent (aka idiosyncratic) hepatic adverse effects occur when appropriate dosages are administered, but hepatic adverse effects still occur. The exact mechanisms are not known, but are often hypothesized due to formation of reactive metabolites that are toxic to the liver. The occurrence of dose-independent adverse effects is rare, but the exact numbers are not known. Dose-independent hepatic adverse effects most often occur early in the course of NSAID therapy, often in the first 3 weeks. A strategy to minimize these adverse effects is to establish baseline hepatic serum chemistries and repeat around week after starting the NSAID. If marked increases in hepatic enzymes or bilirubin occur NSAID therapy should be immediately discontinued. Severe changes and damage require hospitalization and symptomatic treatment including fluids and hepatic “protectant” drugs such as SAMe and silybinin, although the efficacy of the protectants have not been validated in large controlled clinical trials.

Client communications – critical component of decreasing NSAID adverse effects
One of the best methods to decrease NSAID adverse effects are to have well informed clients about the benefits and risks of NSAIDs and appropriate at home monitoring. Clients should be informed to stop NSAIDs and notify their veterinarian if adverse effects are observed including: nausea, vomiting, diarrhea, lethargy, anorexia, depression, increased or decreased urination, discolored urine or discolored mucus membranes or sclera. Regardless of the adverse effect, the sooner it is identified, the NSAID is discontinued and appropriate diagnostics and treatments started as appropriate the better the overall prognosis. The FDA has available a free client handout detailing NSAID use and adverse effects which can be downloaded from their internet sight.

Disclaimer: The information is accurate to the best of the author’s knowledge. However recommendations change as new data become available and errors are possible. The author recommends double checking the accuracy of all information including dosages.
Veterinary Clinical Pharmacology Myths
Butch KuKanich, DVM, PhD, DACVCP
Kansas State University
Manhattan, KS

Morphine cannot be used in cats due to CNS excitement, aka morphine mania.
This is false. Morphine is commonly used in cats without producing morphine mania. Morphine mania was termed when CNS excitement was noted after doses of 5-20 mg/kg SC, which are at least 20 times higher than the clinically recommended dose. High doses or rapid administration to any species can result in CNS excitement and even seizures.

Morphine is slowly metabolized and eliminated in cats.
This is false. The pharmacokinetics of morphine in cats demonstrate it is rapidly metabolized and has a short elimination half-life (just over an hour). The myth came about because cats are deficient in some glucuronide conjugations enzymes which metabolize morphine in most species. However cats rapidly metabolize morphine through a different pathway, sulfate conjugation and as a result morphine has a short half-life in cats.

Morphine cannot be administered IV to dogs due to histamine release and severe hypotension.
This myth is false. Morphine can be administered IV to dogs, resulting in some histamine release, but hypotension does not occur at clinically relevant doses. The high end of clinically relevant IV morphine doses are 0.5 mg/kg as a bolus. Higher doses can cause more profound histamine release, but marked hypotension does not occur until around 3 mg/kg IV bolus in dogs. However the effect of IV morphine on histamine release and cardiovascular status have not been investigated in dogs with mast cell tumors. Other IV opioids may be better choices for dogs with mast cell tumors until further data are available.

Morphine and other opioids cause cardiovascular and respiratory depression in animals
This is partially true, but rarely clinically relevant. Morphine and other opioids at clinically recommended doses have minimal detrimental effects on cardiovascular function in animals. Even massive overdoses have minor cardiovascular effects in healthy animals.

Although opioids do cause dose dependent respiratory depression, the magnitude of the depression is small and plateaus at relatively minimal respiratory depression. If substantial respiratory depression occurs it is often due to other factors contributing such as other drugs (e.g. inhalant or injectable anesthetics), concurrent disease (pulmonary disease) or head trauma in which the respiratory centers are affected. If the animal is at great risk for respiratory depression, which is clinically very rare, than constant rate infusions can be administered. The CRI minimizes peak drug concentrations while maintaining effective concentrations resulting in little to no effect on the respiratory function if appropriate doses are administered.

Fluoroquinolones are broad spectrum antimicrobials
This is false. Fluoroquinolones have little to no activity against anaerobes (except pradofloxacin) and very poor activity against Streptococcus species. Therefore most fluoroquinolones are not broad spectrum, but have a limited spectrum that are effective against many gram negative and some gram positive aerobic bacteria.

Acepromazine lowers the seizure threshold
This myth appears false because of the way acepromazine is used in veterinary medicine. Phenothioazines administered at high doses for long periods of time decrease the seizure threshold in human psychiatric patients. However acepromazine is used as single doses or for very short periods of time in veterinary medicine, which does not appear to increase the risk of seizures. A retrospective study demonstrated potential anticonvulsant effects of acepromazine or at least no worsening of seizures in 36 dogs with a history of seizure activity.

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Drug interactions can occur due to multiple reasons. Drug metabolism may be inhibited or induced, and drug absorption may be increased or decreased. Drugs may exaggerate or decrease the effects of others drugs. Here are some common drug interactions veterinarians need to be aware.

**Drug metabolism inhibitors**
- Chloramphenicol decreases elimination resulting in enhanced effects of phenobarbital, propofol, methadone if dosages are not decreased.
- Ketoconazole (itraconazole to a lesser extent) decreases elimination resulting in enhanced absorption and decreased elimination of cyclosporine, digoxin.
- Enrofloxacin, marbofloxacin, ciprofloxacin decrease elimination of theophylline resulting in enhanced effects of theophylline.
- Cimetidine, although frequently mentioned as a drug metabolism inhibitor, the extent of inhibition in dogs is less than the other drug and as such does not cause many substantial drug interactions.

**Drug metabolism inducers**
- Phenobarbital results in increased metabolism and elimination of digoxin, chloramphenicol, glucocorticoids, ketoconazole, theophylline.
- Phenytoin induces its own metabolism (and other drugs), which is the reason it is not effective as an anticonvulsant in dogs.

**P-glycoprotein inhibitors**
- Spinosad results in increased drug penetration of ivermectin (deworming doses, not heartworm preventive doses) into the brain resulting in ivermectin toxicity.
- Ketoconazole results in increased drug absorption of cyclosporine and digoxin.

**Decreased drug absorption**
- Sucralfate, antacids, and iron supplements decrease absorption of doxycycline, minocycline and ciprofloxacin (not enrofloxacin) due to chelation.
- Omeprazole, famotidine and other acid suppressors decrease the absorption of ketoconazole.

**Pharmacodynamic**
- NSAIDs with glucocorticoids result in enhanced GI adverse effects.
- NSAIDs with furosemide and ACE inhibitors (e.g. enalapril) result in decreased activity of furosemide and ACE inhibitors.
- Opioids enhance sedation from sedatives and tranquilizers.
- Glucocorticoids decrease tolerance development to beta agonists (terbutaline, albuterol).
- Diuretics (furosemide et al) increase renal toxicity of aminoglycosides and NSAIDs.
- Tramadol, fluoxetine, selegeline, meperidine and clomipramine result in serotonin toxicity, which can manifest as autonomic dysfunction, nausea, vomiting, diarrhea, hypertension, arrhythmias, seizures and death.

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Antiemetics are for the symptomatic management of vomiting until an underlying condition is diagnosed and treated. It is important to differentiate vomiting from dysphagia and regurgitation. Antiemetics are not effective for dysphagia and regurgitation. The vomiting pathway is complex. It can be initiated from the gastrointestinal (GI) tract, pharyngeal stimulation, stimulation of the chemoreceptor trigger zone (CRTZ), vestibular system, intracranial and psychogenic causes. Depending on the source and cause of vomiting, some therapeutics may be effective and others ineffective.

Antiemetics

Maropitant. Maropitant is a neurokinin (NK1) antagonist that is a high efficacy antiemetic. The veterinarian must remember that maropitant can mask signs of severe or progressing disease due to its high efficacy. It can be effective for GI, pharyngeal, vestibular, CRTZ, and intracranial initiated vomiting. Maropitant is approved for use in dogs and cats and is available as injectable and oral formulations. SC administration results in high bioavailability and the oral bioavailability in dogs and cats is ~30 and 50%, respectively. Once daily dosing is typically effective. Maropitant undergoes saturable hepatic metabolism in dogs in which higher doses may result in greater than expected increases in plasma concentrations. Drugs such as ketoconazole, itraconazole, fluconazole, fluoxetine, and paroxetine may decrease metabolism whereas phenobarbital may increase metabolism. Adverse effects of maropitant can include pain and swelling at injection sight, lethargy, depression, weakness, ataxia, and sedation. Maropitant has cardiac potassium and calcium channel blocker effects which in healthy dogs are expected to produce minor adverse effects. However animals with decreased cardiac function may have worsening function and arrhythmias. Drug interactions including severe and potentially lethal arrhythmias could occur if maropitant is combined with antiarrhythmic drugs such as diltiazem, propranolol, atenolol, and sotalol among others, but studies documenting interactions are lacking. Additionally, the safety of maropitant has not been fully addressed when combined with doxorubicin.

Ondansetron is a serotonin (5HT3) antagonist and is a high efficacy antiemetic for GI causes of vomiting including chemotherapy. It will have lower efficacy for pharyngeal, vestibular and CRTZ vomiting. As with maropitant, ondansetron may mask the signs of progressing GI disease due to its high efficacy. There are no veterinary approved formulations of ondansetron in the USA, but it is used in an extra label manner for dogs and cats. The oral bioavailability of ondansetron in dogs is very poor and variable due to first pass metabolism, therefore PO is not a recommended route of administration. It has a short half-life and requires q 6-8 hr administration for the most consistent antiemetic effect. Due to its specific action of 5HT3 receptors, ondansetron is well tolerated with few adverse effects. Constipation can occur. In humans, headaches and dizziness have been reported. High doses of ondansetron have also been demonstrated to produce blockade of cardiac potassium channels, therefore adverse reaction may occur if combined with antiarrhythmic drugs such as diltiazem, propranolol, atenolol, and sotalol among others. Other drugs in this class include dolasetron and granisetron, but they are not commonly used due to their much higher cost.

Metoclopramide is an antiemetic producing effects through inhibition of dopamine (DA2) receptor, gastrointestinal prokinetic effects and at high doses 5HT3 antagonist effects. In the USA, there are no veterinary approved formulations. However high doses increase the risk of adverse effects such as CNS excitement and gastrointestinal hypermotility and pain. Due to its prokinetic effects, metoclopramide is contraindicated with GI foreign bodies or blockages due to the risk of perforation. Metoclopramide can be effective for GI, CRTZ induced vomiting and may provide some effects for intracranial and pharyngeal vomiting. Metoclopramide may also be beneficial in cases in which ileus contributes to GI vomiting such as opioid induced ileus. Other adverse effects can include peripheral and pulmonary edema due to aldosterone release and metoclopramide decreases the seizure threshold. Metoclopramide is available as injectable (administered IM, SC, IV and IV CRI) and oral formulations. Administration as an IV CRI may be more effective than other administration techniques.

Antihistamines are limited in efficacy to vestibular induced vomiting such as vestibular disease and motion sickness. Diphenhydramine is the most common antihistamine used in veterinary medicine as an antiemetic, but others are available.

Butorphanol and fentanyl also produce central antiemetic effects. However if opioids are administered for long durations or at high doses, ileus may occur which can result in vomiting.

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Glucocorticoids
Prednisone is a commonly used glucocorticoid. Prednisone is a pro-drug, therefore it must be metabolized to prednisolone to elicit its pharmacologic effect. Cats are variable metabolizers of prednisone to prednisolone, so the effect will also be variable and less predictable in cats.

Prednisolone is recommended for use in cats as it is pharmacologically active and does not need to undergo metabolism to be effective. Prednisone/prednisolone has predominant glucocorticoid effects, but does have some mineralocorticoid effects as well. As such fluid and sodium retention occurs which can result in pulmonary edema in patients even with subclinical and undiagnosed cardiac dysfunction.

Dexamethasone is a glucocorticoid with essentially no mineralocorticoid effects, therefore the retention of fluid and sodium is much less compared to prednisone/prednisolone. Dexamethasone is the glucocorticoid of choice in most patients with cardiac dysfunction. Gastric adverse effects (vomiting, diarrhea, gastritis, erosions and ulcerations) appear to more frequent with dexamethasone compared to prednisone/prednisolone. It is unclear if the increased risk is inherent to the drug or due to incorrect dosages. Dexamethasone is approximately 10x more potent than prednisone/prednisolone, therefore an equivalent dose is 1/10. Additionally, the duration of effect of dexamethasone is longer then prednisone/prednisolone, therefore it needs to be dosed less frequently. For example, 2 mg of dexamethasone PO q 48 hours produces near equivalent glucocorticoid effects as 20 mg of prednisone/prednisolone q 24 hours in dog/cats.

Injectable dexamethasone formulations are often confusing in their use in veterinary medicine. Dexamethasone solution is a 2 mg/mL solution of dexamethasone (free base) dissolved in polyethylene glycol due to the poor water solubility dexamethasone (free base). Dexamethasone sodium phosphate is a water soluble formulation of dexamethasone solution in water. The onset of effect and duration of effect for IV administration of either formulation will be near identical if equal doses are administered. IM or SC administration of dexamethasone solution may have a slightly delayed absorption, but is unlikely to be clinically appreciated.

Repository formulations of glucocorticoids (methylprednisolone acetate, triamcinolone acetonide) should not be used systemically in dogs and should only be used as a last resort in cats due to the increased risk and severity compared to oral glucocorticoids. Oral glucocorticoids can be rapidly discontinued if adverse effects occur, but once a repository formulation is administered it cannot be discontinued.

Glucocorticoid physiologic replacement therapy
Glucocorticoid physiologic replacement therapy is used when endogenous glucocorticoids are insufficient to maintain normal processes. The primary indication is hypoadrenocorticism (Addison’s Disease). The recommended prednisone/prednisolone dose in dogs is 0.2 mg/kg/d. An equivalent dexamethasone dose would be 0.02 mg/kg q 48 hours.

Anti-inflammatory therapy
Anti-inflammatory dosages are used for inflammatory conditions such as atopy. Anti-inflammatory dosages start at 1 mg/kg/d (equivalent to 0.1 mg/kg q 48 for dexamethasone) and are decreased to every other day for chronic administration and titrated down to the lowest effective dose for the shortest duration when needed.

Immunosuppressive therapy
Immunosuppressive dosages are used to control immune mediated diseases such as autoimmune hemolytic anemia and immune mediated thrombocytopenia among others. Prednisone/prednisolone starting dose is 2 mg/kg/d (equivalent to 0.2 mg/kg q 48 for dexamethasone) and may be titrated to every other day administration and or doses decreased. Immunosuppressive doses are recommended for the treatment of anaphylactic shock and Addison’s crisis as well.

Shock therapy
A shock dose of glucocorticoids is only indicated for spinal trauma (methylprednisolone sodium succinate, 30 mg/kg IV) and data suggest may only provide a benefit within the first 3-8 hours after the trauma. Other glucocorticoids have not demonstrated efficacy for spinal trauma.

Current data suggest shock doses of glucocorticoids are detrimental for head trauma and increase death and disability in humans.

Current data do not indicate there is a benefit for shock doses of glucocorticoids for generalized trauma such as hit by car, sepsis or endotoxemia, or heat stroke. Glucocorticoids may be detrimental in heat stroke due to the damage in the GI tract from the
hyperthermia. Fluid therapy (isotonic crystalloids, hypertonic crystalloids, colloids) and analgesia (opioids are the treatments of choice for shock due to trauma and pain) and fluid therapy for sepsis endotoxemia and heat stroke.

As stated in the immunosuppressive therapy section, immunosuppressive doses of glucocorticoids can be beneficial for anaphylactic shock and Addison’s crisis, but not shock doses.

Disclaimer: The information is accurate to the best of the author’s knowledge. However recommendations change as new data become available and errors are possible. The author recommends double checking the accuracy of all information including dosages.
There are numerous drugs that were approved many years ago prior to the rigors that are required for FDA approval needed to achieve safe and effective dosing. Unfortunately, many of these drugs are still available despite incorrect label recommendations and dosages. In order to change the labels or dosages, drug companies would have undergo an entirely new approval process which would cost upwards of hundreds of thousands of dollars. Therefore there is little incentive for manufacturers to change or update the labels.

**Acepromazine**

Acepromazine is a phenothiazine tranquilizer. The label dose 0.5-1.1 mg/kg in dogs (IV, SC, IM) and 1.1-2.2 mg/kg in cats. Unfortunately this is much higher than appropriate. The current recommended doses in dogs and cats are 0.05 and 0.1 mg/kg. The higher dose results in increased adverse effects such as hypotension and prolonged durations of effect, but does not provide increased sedation.

**Prednisolone sodium succinate**

Prednisolone sodium succinate (Solu-Delta-Cortef®) is labeled for use in dogs in cats for “shock” at a dose of 2.5-5 mg/# (5.5-11 mg/kg). This is not an appropriate dose for any condition! (see glucocorticoids lecture) It is between an immunosuppressive and “shock” dose. Additionally, immunosuppressive glucocorticoids should not be used in septic patients, despite the label recommending use for conditions such as sepsis, pneumonia, peritonitis mastitis, etc. Most causes of shock are not responsive to glucocorticoids and the adverse effects of glucocorticoids are too severe to warrant use (e.g. trauma, pain, heat stroke, endotoxemia, septicemia). For example, shock doses of glucocorticoids increase the rate of death and disability in human head trauma patients. The label states that the benefit may be limited unless used with plasma volume expanders (e.g. IV fluids), but the reality is the animals will respond to analgesics (if needed) and fluids and addition of glucocorticoids only worsens the animals’ condition due to their adverse effects. Glucocorticoids worsen the progression of osteoarthritis (OA) due to their catabolic effects on joint cartilage. The use of glucocorticoids are not recommended for use in snakebites as there are no data supporting there use and may increase the risk of secondary infections (despite the label recommendations).

**Methylprednisolone acetate**

Methylprednisolone acetate (Depo Medrol®) is labeled for IM use in dogs and cats, but most experts do not recommend using it in dogs systemically due to high risk of adverse effects. Despite its recommendation for OA, glucocorticoids worsen the progression due to their catabolic effects on joint cartilage. It is labeled for use in severe infection, but is actually contraindicated in most infectious diseases. The use of glucocorticoids are not recommended for use in snakebites as there are no data supporting their use and may increase the risk of secondary infections (despite the label recommendations).

**Procaine penicillin G**

Procaine penicillin G is labeled for use in dogs for a variety of infections including otitis externa. Otitis external often involve *Staphylococcus* spp. which are most often resistant and *Malassezia* (yeast) which are not susceptible to penicillin. The dose listed 6000 IU per kg q 24h is too low and increases the risk of treatment failure and resistance. The current dosage recommendations are 20,000 – 40,000 IU/kg q 12-24 h IM for susceptible infections.

**Procaine penicillin G / benzathine penicillin G**

Procaine penicillin G / benzathine penicillin G is labeled for use in dogs and cattle as an extended release formulation of penicillin due to the slow release of penicillin form the benzathine component. However the problem is that the release is so slow, it does not provide high enough plasma concentrations to extend the dosing interval for most infections except maybe uncomplicated urinary tract infections. Additionally, the labeled dose is much lower than currently recommended for penicillin and as such increased the risk for treatment failure and selection for resistant bacteria. Many people refer to this formulation tongue in cheek as long residue penicillin in food animals.

Disclaimer: The information is accurate to the best of the author’s knowledge. However recommendations change as new data become available and errors are possible. The author recommends double checking the accuracy of all information including dosages.
Primary hemostasis
Primary hemostasis is the formation of a platelet plug at the site of endothelial damage. Damage to a blood vessel causes vasoconstriction and exposure of endothelial collagen. When platelets contact exposed collagen and collagen-bound von Willebrand Factor (vWF), they change their shape, become sticky and release a variety of chemicals that promote adhesiveness with other platelets. They adhere together to form a loose platelet plug. This platelet plug is then reinforced with fibrin formed by secondary hemostasis.

Treatment of impaired primary hemostasis
The treatment of a defect in primary hemostasis involves the removal of the underlying cause if possible. Transfusion of platelets is challenging due to their very reactive nature and special handling required. The drawing of blood and placing it into collection bags can activate platelets to form clumps. Therefore, filters should always be used for administration. Platelets also activate at cold temperatures. All platelet transfusions must be done with fresh blood, either fresh whole blood or platelet-rich plasma.

Fresh whole blood transfusions are a source of platelets, but whole blood provides fewer platelets than a platelet-rich product and can cause hypervolaemia. Recently, a frozen platelet concentrate (PC) has been produced and is commercially available for dogs (Midwest Animal Blood Services, Inc. - Stockbridge, Michigan, USA). This PC is prepared from a single donor by automated blood cell processors using apheresis technology, and is cryopreserved in 6% dimethyl sulfoxide (DMSO).

In human medicine, platelets have been cryopreserved with 6% DMSO, resulting in conservation for up to 3 years. However, this method of storage also resulted in loss of platelet viability, decreased aggregation and reduced clinical efficacy compared to fresh platelets. Our lab recently published a study which studied platelet function, but not clinical efficacy, of this commercially available canine frozen PC.

With all these difficulties or clinical unknowns, there is no universal recommendation for the transfusion of platelets in dogs. It is very difficult to give a platelet number-based transfusion trigger. As a basic rule, the risk for hemorrhage is inversely proportional to the platelet count, and bleeding times in humans are prolonged in a linear fashion as platelet count drops from 100,000 to 10,000/µL. The most common trigger for prophylactic transfusion is 20,000/µL in human medicine. In veterinary medicine, numbers of 5,000/µL in cats and 10,000/µL in dogs have also been published. Published platelet numbers adequate for surgery are between 30,000 to 80,000/µL.

The current recommendation from our service is to treat ongoing life threatening hemorrhage that is secondary to thrombocytopenia with fresh whole blood or fresh platelet rich plasma. As a rule of thumb in veterinary medicine, the recommendation is to transfuse platelet-rich products only in case of life-threatening bleeding, especially pulmonary or intra-cranial hemorrhage. Fresh platelet rich plasma is not commercially available and must be made from fresh whole blood just before administration.

Three products are available for platelet replacement: platelet concentrate (PC), platelet rich plasma (PRP) and fresh whole blood (FWB). These are suggested initial doses but the individual dose must be guided by the response to therapy.

- Fresh whole blood: 20 mL/kg within 4 hours of collection.
- Platelet concentrate: 1 unit/10 kg. The transfusion should be finished in an hour.
- Platelet-rich plasma: 10 mL/kg. The transfusion should be finished in an hour.

Fresh whole blood is the most commonly available blood product to be used in case of life threatening bleeding due to thrombocytopenia.

Platelet rich plasma is prepared by centrifugation of fresh whole blood at a relatively slow speed. The supernatant is therefore "rich" in platelets. It is a fresh product so needs to be processed right before administration. Due to the presence of some red cells, a cross match is essential before administration.

Platelet concentrate is prepared by platelet-apheresis, a process whereby blood is removed from the donor and separated by an automated device into plasma, platelets, white blood cells and red blood cells. The platelet portion is saved and forms one unit of PC and the remaining components are returned back to the donor. According to the manufacturer, one unit of PC can be stored for 6 months at -20°C. PC can also be prepared by centrifugation of platelet rich plasma from different donors (from 4 to 10), separation of the platelet-rich buffy coat and reconstitution in a sterile blood collection bag.

Secondary hemostasis
The main purpose of secondary hemostasis is the production of fibrin to stabilize the platelet plug. Initiators of secondary hemostasis include the platelet plug and endothelial damage. It ends in the formation of thrombin, which cross-links fibrin and strengthens the
clot. Thrombin also activates fibrinolysis, to limit excessive fibrin accumulation. Coagulopathies can be caused by a congenital defect or deficiency in any coagulation factor, lack of production of coagulation factors, excessive consumption of factors such as in the late phase of DIC, or by dilution.

Assessment of secondary hemostasis
Disorders of secondary hemostasis are recognized by hemorrhage into body cavities (e.g. hemothorax, hemoabdomen, hemomediastinum) or into organs (e.g. brain, urinary bladder, intestinal tract). Lower platelets counts generally can be found due to consumption, but they are rarely low enough (i.e. less than 20,000/µL) to suggest that they were the primary cause of the hemorrhage.

The main purpose of secondary hemostasis is the production of fibrin to stabilize the platelet plug. Initiators of secondary hemostasis include the platelet plug and endothelial damage. It ends in the formation of thrombin, which cross-links fibrin and strengthens the clot. Thrombin also activates fibrinolysis, to limit excessive fibrin accumulation. Coagulopathies can be caused by a congenital defect or deficiency in any coagulation factor, lack of production of coagulation factors, excessive consumption of factors such as in the late phase of DIC, or by dilution.

The following tests can only be used to assess hypocoagulability:

- Coagulation time
- Activated clotting time (ACT)
- Activated partial thromboplastin time (aPTT)
- Prothrombin time (PT)
- PIVKA (proteins induced by vitamin K absence or antagonism)

These coagulation tests are timed tests and are reported in seconds. Fast times of tests, such as the ACT, PT and aPTT, do not represent excessive or fast coagulation within the patient; they only represent the absence of hypocoagulability. An increase in the length of time to clot formation would indicate a hypocoagulable state. Often the increased result of a bleeding time test may not yet manifest on the physical exam. Some of these tests are more sensitive or specific than others. For instance the PIVKA has nearly a 98% specificity for an anticoagulant rodenticide intoxication when the result is >300 seconds.

Treatment of impaired secondary hemostasis
Since most of the above tests are abnormal due to a lack of sufficient coagulation factors, the goal of therapy is to restore coagulation factors to levels that normalize these tests and, more importantly, reduce the chance for hemorrhage to persist. In general, 10-20 mL/kg of fresh frozen plasma (see Table 1) will restore coagulation factors to a level to normalize the coagulation tests. This should be administered within 4 hours of the thaw at a rate at which the patient is not at risk for fluid overload.

Fresh plasma is obtained by centrifugation from FWB and separation into packed red blood cells (pRBC) and plasma within 6 hours of collection. After fresh plasma has been frozen, it is called FFP for up to 1 year. After one year of storage it is then referred to as Frozen Plasma due to the natural decrease in the labile factors (FV, FVIII) factors during storage.

The major indication is the treatment of coagulopathies, either acquired (e.g. rodenticide intoxication, DIC) or inherited (e.g. von Willebrand disease, hemophilies).

The required FFP dose in an individual patient is impossible to predict and must be based on response to therapy, availability of blood products and financial limitations. A general guideline is an initial dose between 10-20 mL/kg.

Fresh frozen plasma is not the fluid of choice for low albumin/low osmotic pressure in dogs and cats because it contains very low albumin (less than 5%, i.e. 5 mg/dL). It takes over 40ml/kg of plasma to raise albumin 1g/dL in the patient. Synthetic colloids can be used to increase the colloid osmotic pressure. Human serum albumin can be used to effectively increase albumin concentration in dogs and cats, but questions remain regarding safety of this product in our patients.

During the process of thawing fresh frozen plasma at 4°C, a white precipitate forms due to the run-off of thawed portion; that is the cryoprecipitate (CP), which can be separated and stored. The major indication for the use of CP is von Willebrand disease and Hemophilia A. The published dose is 10 mL/kg.
Primary hemostasis

Primary hemostasis is the formation of a platelet plug at the site of endothelial damage. Damage to a blood vessel causes vasoconstriction and exposure of endothelial collagen. When platelets contact exposed collagen and collagen-bound von Willebrand Factor (vWF), they change their shape, become sticky and release a variety of chemicals that promote adhesiveness with other platelets. They adhere together to form a loose platelet plug. This platelet plug is then reinforced with fibrin formed by secondary hemostasis.

Assessment of primary hemostasis

Petechiae and ecchymoses are found on the physical examination of the patient with a disorder of primary hemostasis. It is uncommon to have hemorrhage into large body cavities. Epistaxis and other mucosal bleeding are common.

Platelet function and number must be scrutinized upon suspicion of a bleeding defect. Platelets are formed from megakaryocytes in the bone marrow and are the smallest cellular component in the blood. Platelets are anucleate, disc-shaped, cytoplasmic fragments that play an essential role in primary hemostasis, the initiation of a platelet plug, and the preservation of vascular integrity. Their exterior surface is highly reactive to external stimuli, ready to undergo a shape change to facilitate hemostasis on the damaged endothelial surface. Placed near the site of initial response to vascular injury, platelets react to stimuli, alter their shape, spread and adhere to the endothelium (and each other), secrete their granular contents (e.g. ADP, serotonin) to amplify the response, and interact with the hemostatic system to bind fibrinogen (onto GP IbIIIa) and solidify into a fibrin clot.

Thrombocytopenia is a relatively common finding in veterinary patients; however, platelet dysfunction (thrombocytopenia) is much less common. In people, thrombocytopenia (reduced adhesion, altered aggregation, and poor clot retraction) is common secondary to neoplasia or dysproteinemias. In domestic species, the common causes of thrombocytopenia are renal or hepatic disease, zootoxins, and infectious or therapeutic agents. Decreased platelet function should be considered when superficial bleeding (i.e. petechiae, ecchymoses) occurs in the absence of profound thrombocytopenia.

For all patients suspected of having a coagulation defect, a standard blood smear should be evaluated under the microscope for the estimation of a platelet count in the monolayer. A single platelet found on a 100X field equates to ~15,000 platelets/µL in circulation. It is unlikely that spontaneous bleeding will occur until platelet counts drop below 20,000/µL. Platelet clumps will alter your interpretation of the estimated number of platelets. Also, platelet numbers that are found to be low on automated, in-house blood cell counters should always be checked against a manual estimation of platelet numbers using this blood smear technique. Discordant results are often found because the automated cell counters are unable to count platelet clumps as individual cells, artificially lowering the platelet count.

When decreased platelet numbers do not account for bleeding, a buccal mucosal bleeding test (BMBT) can be considered. This in vivo test is completed by the measurement of the time for a stable platelet plug to form from the time an incision is created on the upper lip of a dog or cat. The test uses a template device that creates 1 or 2 standardized superficial incisions (1mm deep by 5mm long). Normal BMBT results are less than 4 minutes. A prolonged result would be consistent with thrombopathia or von Willebrand disease. This test is highly operator dependent; variable results have been reported in animals and in humans. BMBT measurements are poorly standardized, labor intensive, subjective, and have not been shown to correlate with clinical outcomes. In fact, this test has been all but abandoned in human medicine due to the lack of specificity and sensitivity to detect or predict clinical perioperative bleeding.

The Platelet Function Analyzer-100® (PFA-100) is a bench-top instrument that evaluates platelet function in whole blood. The PFA-100 simulates primary hemostasis by aspirating citrate-anticoagulated blood under a high shear rate through a small aperture in a collagen membrane coated with platelet agonists (ADP or epinephrine). This design mimics the in vivo organization of the subendothelial matrix: the initial site of platelet deposition and aggregation. Closure time (CT) is the time it takes for a platelet plug to form and occlude flow. The CT is highly sensitive to qualitative and quantitative defects in platelet receptors that mediate adhesion (GPIb-V-IX) and aggregation (GPIIbIIIa).

The PFA-100 detects inherited, acquired, or induced platelet dysfunction. It has most commonly been used for analysis of coagulopathies (e.g. von Willebrand Disease) in dogs, horses, and humans as well as assessing aspirin therapy and affects of various fluids (saline, artificial colloids). Studies have shown that the PFA-100 can be used as an indicator of platelet function and dysfunction in many species that are not anemic or thrombocytopenic. In addition, the CT may be inaccurate when high hematocrits (>60%) or platelet counts (>500,000)/µL are present.

Turbidometric aggregometry was invented in the 1960s and is regarded as the gold standard for the diagnosis of primary hemostatic defects. It is able to detect many different aspects of platelet function and biochemistry through the use of agonists (ADP,
thrombin, or collagen) at various concentrations. Platelet rich plasma from citrated whole blood is used in parallel chambers through which light is transmitted during the test. The opaque solution is stimulated to aggregate by way of the introduction of an agonist. As the platelets aggregate in response to the agonist, the sample becomes clearer as the platelets aggregate. The clarity of the sample is detected as an increase in the transmission of light across the sample. The difference between baseline and after agonist addition and aggregation is used to calculate the response. The specialized aggregometers graphically display the response as a curve that can be further analyzed to detect speed of aggregate formation. The major drawback is that it does not mimic in vivo physiologic conditions of adhesion, activation or aggregation to endothelial damage. Besides the limited availability to comparative hemostasis laboratories, it also requires large volumes of fresh blood and technical expertise. Aggregometry has been validated for use with canine and feline platelets as well as canine platelet concentrate.

To overcome some of the technical problems with aggregometry, alternatives such as the cartridge-based system of the VerifyNow® have been developed for humans. This instrument measures platelet aggregation in whole citrated blood via changes in light transmission. The basis of this assay is that coated polystyrene microparticles will agglutinate in whole blood in direct proportion to the degree of platelet activation. Specific cartridges are employed to monitor for the effects on primary hemostasis by the following drugs: aspirin, P2Y12 inhibitors (clopidogrel), GP IIbIIIa antagonists (abciximab). These limitations and expense of the machine make it unlikely to be used in clinical veterinary medicine. This analyzer has received little use in research studies in domestic animals.

The cone and plate(let) analyzer technology was developed to test platelet function under near-physiologic conditions. The benefits of this system (Impact-R®) are that it employs a small blood volume, requires no blood processing, and is simple to operate. Basically, this system mimics an extracellular matrix over which the blood sample flows. Since platelets are the only cell to adhere to this matrix under these conditions, the elongated aggregates align in laminar flow lines. After simulation of blood flow conditions, the sample is stained and optically analyzed. The effects of variable hematocrit and platelet counts have been investigated in people. No published studies have been found that employed this technology in domestic animals.
Blood Products Demystified
Karl Jandrey, BS, DVM, MAS, DACVECC
University of California
Davis, CA

Component therapy has become standard of care in veterinary medicine due to increased product availability as well as an increased knowledge of their use. Each blood component/product has specific therapeutic indications. There are 3 main reasons to use blood products: to expand intravascular volume, to increase oxygen carrying capacity, and to treat secondary hemostatic defects.

Intravascular blood volume expansion in a patient with poor perfusion can be achieved with blood. However, this is often impractical due to the time it takes to acquire blood from a fresh donor. Stored whole blood (SWB) or packed red blood cells (pRBC) can be used, but the product may be too cold nor cross-matched for immediate transfusion. In the emergency situation when volume is the need and it takes too long for a blood product to be delivered safely, isotonic crystalloids are the preferred choice. The more blood found on a patient or in its body cavity due to trauma, the more quickly blood products should be considered. However, the patient must first be resuscitated with isotonic crystalloids or synthetic colloids due to the time lag until institution of safe blood component therapy. A typical cross-match takes 40-60 minutes for completion; intravascular volume resuscitation with isotonic crystalloids should be complete within 10-15 minutes.

The time taken to achieve a hemoglobin (Hgb)/HCT/PCV value is also an important factor in the determination of when to give red cell products. Animals with chronic disease may have suppression in the production of erythropoietin. This more chronic anemia will often go clinically undetected for weeks to months as the patient compensates. In patients with chronic anemia, three principal compensatory mechanisms occur: a decreased Hgb affinity for oxygen, a redistribution of blood flow, and an increased cardiac output. Animals with an acute anemia (i.e. from trauma/hemorrhage into body cavities) have little physiologic compensation for this abrupt change in oxygen carrying capacity. They will show clinical symptoms faster with less of a decrease in Hgb concentration.

Human patients are at risk of decrease oxygen delivery and organ failure with a Hgb concentration of 3-4 g/dL (HCT/PCV ~9-12%). Transfusion decisions, however, cannot be based only on the level of anemia due to the compensatory mechanisms for anemia. Thus, clinical signs and the underlying causes of anemia are also very important. One patient with a HCT of 20% may appear to have cardiopulmonary stability, whereas one with a HCT of 25% may appear severely affected by the anemia. A transfusion trigger needs to be individualized for each patient.

The threshold values for the clinical use of blood products to treat anemia are not well defined in the veterinary literature. For many years in human medicine, the transfusion trigger had been defined as a Hgb of 10 g/dL (HCT/PCV of ~30%). However, transmissible infections, immunologic risks, transfusion-related acute lung injury, the cost of blood, and component availability are current disadvantages of transfusions. In 1999, the Transfusion Requirements in Critical Care (TRICC) trial showed that maintenance of a Hgb between 7 and 9 g/dL in ICU patients is as effective with less adverse consequences as the maintenance of a Hgb above 9 g/dL. Based on that information, hemoglobin-based threshold values have recently been revised for humans and are currently between 6 and 8 g/dL of Hgb (HCT/PCV ~20%).

Other objective measures that will help to decide if a transfusion is warranted include: venous oxygen tension and lactate concentration. As oxygen delivery to the tissues falls but the tissue extraction remains the same, less venous oxygen is found when measuring PvO2. This however may reflect increased oxygen demand by the tissues. Alternatively, an increase in lactate is a readily available marker of tissue anaerobiosis or poor perfusion.

The transfusion should be considered as soon as the patient’s cardiovascular status is jeopardized by the blood loss. Clinical signs include:

- Perfusion parameters: poor perfusion: tachycardia, pale mucous membranes, prolonged CRT, weak pulses, cold extremities, altered mentation.
- Signs of anemia (pale mucous membrane color and narrow pulses) are difficult to differentiate from hypoperfusion/shock and need to be re-assessed after initial fluid resuscitation.
- Perfusion markers: increased lactate, decreased blood pressure and urine output.
- Respiratory function: increased respiratory rate and effort, blood gas analysis.

As a rule of thumb, 2 mL/kg of fresh whole blood will increase the PCV by 1% point. So, 20 mL/kg are used to increase the PCV by 10 percentage points.

In normovolemic, anemic patients, such as autoimmune hemolytic anemia, the volume required to increase the PCV may place the patient at risk of fluid overload. This is a particular concern in the patient with cardiac disease.

Packed red blood cells (pRBC) will have a very small amount of remaining plasma. The hematocrit of pRBC may exceed 80%. In that case, dilution with 0.9% NaCl can be helpful to avoid hyperviscosity. Fluids containing calcium, like LRS, should not be used in order to decrease the risk of citrate chelation and coagulation.
As a rule of thumb, 1 mL/kg of pRBC will increase the PCV by 1% point. The post-transfusion PCV goal is usually between 18 - 25%.

Coagulopathies can be caused by a congenital defect or deficiency in any coagulation factor, lack of production of coagulation factors, excessive consumption of factors such as in the late phase of DIC, or by dilution. Fresh frozen plasma (FFP) would be indicated for the treatment of most defects in secondary coagulation.

The main purpose of secondary hemostasis is the production of fibrin to stabilize the platelet plug. Initiators of secondary hemostasis include the platelet plug itself and endothelial damage. It ends in the formation of thrombin, which cross-links fibrin and strengthens the clot. Thrombin also activates fibrinolysis, to limit excessive fibrin accumulation.

The goal of therapy is to restore coagulation factors to levels that reduce the chance for hemorrhage to persist. In general, 10-20 ml/kg of fresh frozen plasma will restore coagulation factors to a level to normalize the coagulation tests. The improvement in clinical bleeding and coagulation test results seem to parallel. FFP should be administered within 4 hours of the thaw at a rate at which the patient is not at risk for fluid overload.

FFP is the product of choice for the treatment of secondary hemostatic defects since it is processed and frozen with a few hours. This allows for the highest levels of coagulation factors to be present. After FFP has been stored for greater than one year, it is called frozen plasma (FP). Frozen plasma has lost its labile factors (V, VIII, von Willebrand) over time. FP is still very commonly used to treat the most common bleeding disorder in the Emergency Room, anticoagulant rodenticide intoxication. FP has plenty of Factors II, VII, IX, and X to treat the anticoagulant rodenticide intoxicated patient. Plasma is purely a unit of FFP that has been stored for 5 years or longer. The labile and stable factors have denatured over time and the main residual benefit left in this component is albumin. Other more specific products such as cryoprecipitate can be purchased from a blood bank and used for patients with special coagulation issues.

<table>
<thead>
<tr>
<th>This blood product…</th>
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<tbody>
<tr>
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<td>Factors VIII, XIII, von Willebrand factor, fibrinogen</td>
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<tr>
<td>Platelet rich plasma (PRP)</td>
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</tr>
<tr>
<td>Platelet concentrate (PC)</td>
<td>Platelets, plasma, DMSO cryopreservative</td>
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As stated previously, it is not wrong to use blood products for volume resuscitation; however, it is negligent to postpone any therapy to improve circulating intravascular volume while awaiting the perfect component therapy in an emergency. Blood products are often used inappropriately due to misunderstandings of the inherent benefits or risks of each component. A lack of knowledge of the cellular response to storage may also be implicated. Also, a frequent misunderstanding is the ability of plasma therapy to raise the colloid osmotic pressure of the patient.

Primary hemostasis is the formation of a platelet plug at the site of endothelial damage. Damage to a blood vessel causes vasoconstriction and exposure of endothelial collagen. When platelets contact exposed collagen and collagen-bound von Willebrand Factor (vWF), they change their shape, become sticky and release a variety of chemicals that promote adhesiveness with other platelets. They adhere together to form a loose platelet plug. This platelet plug is then reinforced with fibrin formed by secondary hemostasis (see above).

Primary hemostatic defects may be due to thrombocytopenia, thrombocytopenia, and vasculitis. These are suspected on physical examination by the presence of petechiae and ecchymoses. Confirmation of a platelet count, either automated or manual blood smear assessment, is an essential first step in the diagnosis of primary hemostatic defects. Manual platelet counts may be ideal since one can individually inspect for platelet clumps that may be counted as larger cells using automated methods, thus producing a falsely low platelet count. If the platelet count is normal in a patient with petechiae and ecchymoses, a thrombocytopenia may be to blame. Other more advanced tests of platelet function can be used to identify the severity and extent of the platelet dysfunction.

The treatment of a defect in primary hemostasis involves the removal of the underlying cause if possible. Transfusion of platelets is challenging due to their very reactive nature and special handling required. The donation of blood and placement into collection bags can activate platelets to form clumps. Platelets also activate at cold temperatures; therefore, all platelet transfusion must be done with fresh blood, either fresh whole blood or platelet-rich plasma. Filters should always be used for administration.

Fresh whole blood transfusions are a source of platelets, but whole blood provides fewer platelets than a platelet-rich product and can cause hypervolemia. A frozen platelet concentrate (PC) is commercially available for dogs. This PC is prepared from a single donor by automated blood cell processors using apheresis technology and is cryopreserved in 6% dimethyl sulfoxide (DMSO). Clinical efficacy of this product has not been published. Laboratory investigations show that the platelets are activated at thaw, have...

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fewer numbers of platelets than expected, and have storage lesions. Lyophilized canine platelets are also commercially available, but published information is scant.

In human medicine, platelets have been cryopreserved with 6% DMSO, resulting in conservation for up to 3 years. However, this method of storage also resulted in loss of platelet viability, decreased aggregation and reduced clinical efficacy compared to fresh platelets.

With all these difficulties or clinical unknowns, there is no universal recommendation for the transfusion of platelets in dogs. My current recommendation is to treat on-going life threatening hemorrhage that is secondary to thrombocytopenia with fresh whole blood or fresh platelet concentrates (not quickly or widely available, however). Fresh platelet rich plasma is not commercially available and must be made from fresh whole blood just before administration. Due to the presence of some red cells, a cross match is recommended before administration.

Plasma colloid osmotic pressure (COP) of a patient is mainly due to the contribution of albumin. A low albumin usually is associated with a low COP. Globulins contribute a smaller portion in health, but can contribute to the COP to a greater degree when the patient is hyperglobulinemic or hypoalbuminemic. In practices that can measure COP, the choice of therapy to raise the COP in general is a synthetic colloid due to its higher COP and lower cost compared to plasma. However, the half-life of the synthetic colloids is far shorter than albumin. When COP is not measureable and colloid therapy is directed by albumin concentrations, many clinicians use FFP, FP, or plasma to raise the albumin concentration or to reverse the clinical signs that accompany a low COP (i.e. interstitial edema). In general 50-60 ml/kg of plasma is needed to raise the albumin concentration by 1 g/dL. This is not only costly, it is potentially very antigenic and a large volume load. Currently, I do not recommend the administration of plasma to patients with low COP for the sole purpose to increase COP or albumin concentration.
Safe Blood Product Administration
Karl Jandrey, BS, DVM, MAS, DACVECC
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Transfusion therapy & blood banking

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</table>

Donor selection and blood collection

Fresh Whole Blood (FWB) contains red blood cells, platelets, and plasma. It can be obtained relatively easily if a suitable donor is available. Donor dogs should be ideally large (30-50 kg), young (between 1-7 year old), and tolerant of restraint. They should be screened before blood collection to be DEA 1.1 and 1.2 negative, healthy and transmissible-disease free. Donor cats should be at least 5 kg, young, indoors, vaccinated and negative for FeLV and FIV. Like dogs a blood type, complete blood cell count and chemistry panel should be done prior to enrollment as a donor. Cats can be sedated for easier blood collection.

Proper collection bags and anticoagulants are commercially available. The actual collection should be done in an aseptic manner (i.e. shave, sterile prep, wear sterile gloves). Protocol for collection has been described elsewhere.

There are 8 major blood groups in the dog. The major antigens are DEA 1.1 and DEA 1.2. Dogs can be positive for either DEA 1.1 or 1.2 or are negative for both. Naturally occurring antibodies occur in 20% of DEA 3-negative, 10% of DEA 5-negative, and 20-50% of DEA 7-negative dogs.

Acute hemolytic transfusion reactions occur most of the time in DEA 1.1 and 1.2 negative dogs. As these dogs do not have naturally occurring antibodies, a reaction will only be seen after sensitization of the dog through exposure to DEA 1.1 or 1.2 positive blood (antibody production takes 7-10 days after exposure). Therefore, a crossmatch in a dog is not essential on the first transfusion. However, a crossmatch is strongly recommended if possible prior to transfusion of this initial transfusion of red cells to reduce the likelihood of a reaction. However, in cases of life-saving emergencies when blood needs to be administered without the information of a crossmatch, it is acceptable to transfuse the blood and watch carefully for adverse reaction.

There are 3 feline blood types (A, B and AB). Cats have naturally occurring allo-antibodies to the antigen they lack. Therefore, typing is essential before the first transfusion. Life-threatening adverse transfusion reactions will occur if a type B cat receives a type A blood. Blood can be cross-matched or typed by a veterinary lab. Typing cards can be used quickly for point of care identification of blood types but does not supplant the information gained from the crossmatch.

The percentage of cats that are type A or B is largely breed-dependent. There is an incidence of type B blood in 1-10% of Domestic Short Hair cats whereas the incidence rises to 20-45% for exotic shorthair cats or Devon Rex. There are geographical variations as well; the UK, Australia and many countries of the Pacific Rim have a much higher incidence of type B cats. The overall incidence of type A domestic cats varies between countries but is around 95% in the USA. AB cats are rare; they can receive either blood type. Because of these regional and breed variations, the standard of care for transfusion therapy in cats requires a cross match and card typing.

Adverse reactions

There are numerous causes of adverse reactions to blood product administration.
### Table 2: Acute immune-mediated transfusion reactions and their treatments

<table>
<thead>
<tr>
<th>Acute reaction</th>
<th>Hypersensitivity Type</th>
<th>Clinical signs</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemolytic reactions</td>
<td>Type II</td>
<td>Vomiting, hypotension, tachycardia, tachypnea, pyrexia</td>
<td>Discontinue (D/C) the transfusion, treat symptomatically, IV fluids to promote diuresis</td>
</tr>
<tr>
<td>Anaphylactic reactions</td>
<td>Type I</td>
<td>Urticaria, pruritus, often with plasma products</td>
<td>D/C the transfusion, administer anti-histamines or small dose of steroids</td>
</tr>
<tr>
<td>Anaphylactic shock</td>
<td>Type I</td>
<td>Cardiovascular collapse, dyspnea, seizures</td>
<td>D/C the transfusion, treat symptomatically with IV fluids, epinephrine</td>
</tr>
<tr>
<td>Leukocytes and platelet sensitivity reactions</td>
<td></td>
<td>Increase in body temperature of at least 1°C</td>
<td>D/C the transfusion, may be re-started at a lower rate</td>
</tr>
</tbody>
</table>

There are many non-immune-mediated transfusion reactions. Hemolysis may occur by destruction of the donor RBCs before transfusion, either from inappropriate collection, storage or administration. This is usually benign unless hyperkalemia is severe. It will decrease the efficiency of the transfusion. Hypothermia may occur if rapid transfusion occurs with an inappropriately warmed product. Citrate binds calcium. Massive transfusions have been reported to cause hypocalcemia. The clinical signs of muscle tremors or weakness associated with hypocalcemia should be treated with slow IV calcium gluconate infusion. Bacterial contamination of the product is uncommon with proper handling, but it has been reported in the veterinary literature. As mentioned previously, volume overload may occur, so close monitoring of the patient and use of appropriate component therapy will decrease the incidence.

**UC-Davis veterinary medical teaching hospital small animal ICU transfusion protocol**

**Pre-transfusion**

1. Blood transfusion can be done intravenously or intra-osseously in small patients
2. A crossmatch/blood type should be performed; ideally in dogs, always in cats.
3. If the blood or plasma needs to be warmed, FFP must be thawed at room temperature for 20 minutes before defrosting in warm water (Note: FFP can be defrosted without thawing first in emergent situations); FWB or pRBC can also be warmed in warm water if indicated.
4. Set up a Y-type administration set with a filter for the blood. Attach blood bag with one of the 2 ports, the 2nd one will be used for the 0.9% NaCl flush if indicated.
5. If administering the blood product via syringe, insert an injection port into the bag. Draw the blood product into a syringe; attach a filter between the syringe and extension set.
6. Place indwelling temperature probe into the patient. Obtain a baseline TPR and vitals.

**Transfusion**

- Transfuse the blood product at 2.5-10 mL/kg/h. Usually, the transfusion is given in 4 hours to decrease the risk of bacterial contamination using the lower rate at the beginning and increasing it if the patient tolerates the transfusion. In some emergency situations, the infusion of blood product can exceed these guidelines.
- Temperature monitoring is to be done continuously: respiratory rate/effort and mentation should be monitored every hour.
- Vital parameter should be monitored every 15-30 minutes for the 1st hour, and then every hour until transfusion is completed.
- When transfusion is completed, administration set should be flushed with 0.9% NaCl at the same rate until fluid line is mostly clear.

**Post transfusion**

1. Disconnect the blood administration set or fluid line from catheter and flush the catheter with heparinized saline.
2. Draw blood for PCV immediately, or up to an hour post-transfusion.
Annual Review of the Top 5 Coagulation Articles
Karl Jandrey, BS, DVM, MAS, DACVECC
University of California
Davis, CA

The wealth of information published in veterinary medical journals on the topic of coagulation and hemostasis has risen considerably over the past few years. The author has provided 5 of his favorite articles from the past year that have significant impact and application to daily practice for general practitioners and specialists alike. No attempt was made to search and score the medical literature as a whole; the information explosion in human medicine and the basic and translational research areas for coagulation and hemostasis is huge. Many of those studies are referenced in these articles. The interested reader is encouraged to independently investigate some of the best journals for this: Blood; Journal of Thrombosis and Haemostasis; Blood, Coagulation and Fibrinolysis; Current Opinions in Hematology.

Article #1
An ex vivo evaluation of efficacy of refrigerated canine plasma
- AUTHORS: Grochowsky AR, Rozanski EA, de Laforcade AM, et al
- HYPOTHESIS/OBJECTIVES: To determine thawing times of fresh frozen plasma (FFP), and to evaluate the activity of hemostatic proteins (coagulation factors V, VII, VIII, IX, X, and fibrinogen), clotting times (prothrombin time and activated partial thromboplastin time), and sterility of canine plasma stored refrigerated.
- STUDY DESIGN: Prospective, laboratory-based study
- RESULTS: Time to thaw for FFP units was 34.7 +/- 1.38 minutes. Refrigerated storage resulted in significant decreases in activity of all clotting factors and a subsequent prolongation in clotting times. However, no values were outside the reference interval. All bacterial cultures were negative.
- DISCUSSION/CLINICAL RELEVANCE: Refrigerated storage results in only minor loss of coagulation factory activity in canine plasma. The use of refrigerated canine plasma, therefore, may be a viable option in high-volume veterinary hospitals for rapid correction of coagulopathy in critical care patients.

Article #2
Evaluation of tranexamic acid and epsilon-aminocaproic acid concentrations required to inhibit fibrinolysis in plasma of dogs and humans
- AUTHORS: Fletcher DJ, Blackstock KJ, Epstein K, Brainard BM
- HYPOTHESIS/OBJECTIVES: To determine minimum plasma concentrations of the fibrinolytic agents tranexamic acid (TEA) and epsilon-aminocaproic acid (EACA) needed to completely inhibit fibrinolysis in canine and human plasma after induction of hyperfibrinolysis. It was hypothesized the minimum required concentrations of TEA and EACA to inhibit this hyperfibrinolytic state would be higher in dogs plasma than in human plasma.
- STUDY DESIGN: Prospective, laboratory-based study
- RESULTS: Minimum plasma concentrations necessary for complete inhibition of fibrinolysis by EACA and TEA in pooled canine plasma were estimated as 511.7 µg/ml (95% confidence interval [CI], 433.2 to 590.3 µg/ml and 144.7 µg/ml (95%CI, 125.2 to 164.2 µg/ml), respectively. Concentrations of EACA and TEA necessary for complete inhibition of fibrinolysis in pooled human plasma were estimated as 122.0 µg/ml (95% confidence interval [CI], 106.2 to 137.8 µg/ml and 14.7 µg/ml (95%CI, 13.7 to 15.6 µg/ml), respectively.
- DISCUSSION/CLINICAL RELEVANCE: Results supported the concept that dogs are hyperfibrinolytic, compared to humans. Higher doses of EACA and TEA may be required to fully inhibit fibrinolysis in dogs.

Article #3
Effect of duration of packed red blood cell storage on morbidity and mortality in dogs after transfusion: 3,905 cases (2001-2010)
- AUTHORS: Hann L, Brown DC, King LG, Callan MB
- HYPOTHESIS/OBJECTIVES: To determine if duration of packed red blood cell (PRBC) storage has an effect on morbidity and mortality in dogs after transfusion.
- STUDY DESIGN: Retrospective 10-year case review
RESULTS: A total of 3,905 dogs received 5,412 PRBC units. Longer duration of PRBC storage was associated with development of new or progressive coagulation failure (P=0.001) and thromboembolic disease (P=0.005). There was no association between duration of PRBC storage and survival for all dogs overall. However, a logistic regression model indicated that for dogs with hemolysis, 90% of which had immune-mediated hemolytic anemia, longer duration of PRBC storage was a negative risk factor for survival. For every 7 day increase in storage, there was a 0.79 lesser odds of 30 day survival (95% CI, 0.64-0.97; P=0.024).

DISCUSSION/CLINICAL RELEVANCE: Duration of PRBC storage does not appear to be a major contributing factor to mortality in the overall canine population. However, the longer duration of PRBC storage may negatively impact outcome in dogs with immune-mediated hemolytic anemia, thus warranting further investigation with prospective studies.

**Article #4**
Recurrent episodes of severe bleeding caused by congenital factor XIII deficiency in a dog

AUTHORS: Kong LR, Snead ECR, Burgess H, Dhumeaux MP
HYPOTHESIS/OBJECTIVES: To describe a dog with a congenital bleeding disorder due to factor XIII deficiency.
STUDY DESIGN: Case report
RESULTS: Previously during this dogs evaluations, all standard coagulation testing and factor analysis was normal: prothrombin time, activated partial thromboplastin time, buccal mucosal bleeding time, activated clotting time, von Willebrand factor concentration, platelet function testing, and plasma factors VII, VIII, IX, X, XI, XII. Rotational thromboelastometry revealed that clotting times were within reference limits, with abnormal clot formation times and clot firmness. The results of a factor XIII (FXIII) clot solubility assay confirmed FXIII deficiency.
DISCUSSION/CLINICAL RELEVANCE: This is the first case report to describe a dog with FXIII deficiency. FXIII deficiency should be on the differential diagnosis list for any dog with excessive bleeding episodes and apparently normal results on the common, standard coagulation tests.

**Article #5**
Effect of synthetic colloid administration on coagulation in healthy dogs and dogs with systemic inflammation

AUTHORS: Gauthier V, Holowaychuk MK, Kerr CL et al
HYPOTHESIS/OBJECTIVES: To compare the effects of an isotonic crystalloid and synthetic colloid on coagulation in healthy dogs and dogs with systemic inflammation.
STUDY DESIGN: Randomized, placebo-controlled, blinded, cross-over laboratory study
RESULTS: Administration of either fluid to healthy dogs and dogs with systemic inflammation resulted in similar increases in prothrombin time and activated clotting time. In comparison to saline administration, tetrastarch administration resulted in significantly decreased R (P=0.017) in healthy dogs, as well as significantly increased activated partial thromboplastin time (P<= 0.016), CL30% (P<= 0.016), and K (P< 0.001) and significantly decreased platelet count (P= 0.019), alpha (P<= 0.001), MA (P< 0.001), and von Willebrand factor antigen (P< 0.001), and collagen binding activity (P<= 0.003), in both healthy dogs and dogs with systemic inflammation.
DISCUSSION/CLINICAL RELEVANCE: Tetrastarch bolus administration to dogs with systemic inflammation resulted in a transient hypocoagulability characterized by a prolonged activated partial thromboplastin time, decreased clot formation speed and clot strength, ad acquired Type I von Willebrand disease.
Secondary hemostasis

The main purpose of secondary hemostasis is the production of fibrin to stabilize the platelet plug. Initiators of secondary hemostasis include the platelet plug and endothelial damage. It ends in the formation of thrombin, which cross-links fibrin and strengthens the clot. Thrombin also activates fibrinolysis, to limit excessive fibrin accumulation. Coagulopathies can be caused by a congenital defect or deficiency in any coagulation factor, lack of production of coagulation factors, excessive consumption of factors such as in the late phase of DIC, or by dilution.

Assessment of secondary hemostasis

Disorders of secondary hemostasis are recognized by hemorrhage into body cavities (e.g. hemothorax, hemoabdomen, hemomediastinum) or into organs (e.g. brain, urinary bladder, intestinal tract). Lower platelets counts generally can be found due to consumption, but they rarely are low enough (i.e. less than 20,000/µL) to suggest that they were the primary cause of the hemorrhage.

Treatment of impaired secondary hemostasis

Since most of the above tests are abnormal due to a lack of sufficient coagulation factors, the goal of therapy is to restore coagulation factors to levels that normalize these tests and, more importantly, reduce the chance for hemorrhage to persist. In general, 10-20 mL/kg of fresh frozen plasma will restore coagulation factors to a level to normalize the coagulation tests. This should be administered within 4 hours of the thaw at a rate at which the patient is not at risk for fluid overload.

Fresh plasma is obtained by centrifugation from FWB and separation into packed red blood cells (pRBC) and plasma within 6 hours of collection. After fresh plasma has been frozen, it is called FFP for up to 1 year. After one year of storage it is then referred to as Frozen Plasma due to the natural decrease in the labile factors (FV, FVIII, von Willebrand Factor) during storage.

The major indication is the treatment of coagulopathies, either acquired (e.g. rodenticide intoxication, DIC) or inherited (e.g. von Willebrand disease, hemophilias).

The required FFP dose in an individual patient is impossible to predict and must be based on response to therapy, availability of blood products and financial limitations. A general guideline is an initial dose between 10–20 mL/kg.

Fresh frozen plasma is not the fluid of choice for low albumin/low osmotic pressure in dogs and cats because it contains very low albumin (less than 5%, i.e. 5 mg/dL). It takes over 40ml/kg of plasma to raise albumin 1g/dL in the patient. Synthetic colloids can be used to increase the colloid osmotic pressure. Human serum albumin can be used to effectively increase albumin concentration in dogs and cats, but questions remain regarding safety of this product in our veterinary patients.

During the process of thawing fresh frozen plasma at 4°C, a white precipitate forms due to the run-off of thawed portion; that is the cryoprecipitate (CP), which can be separate and stored. The major indication for the use of CP is von Willebrand disease and Hemophilia A. The published dose is 10 mL/kg.

Treatment of anemia

Human patients are at risk of decrease oxygen delivery and organ failure with a hemoglobin of 3-4 g/dL (hematocrit around 9-12%). Transfusion decisions, however, cannot be based only on the level of anemia due to compensatory mechanisms for anemia. Thus, clinical signs and the underlying causes of anemia are also very important. The transfusion should be considered as soon as the patient cardiovascular status is jeopardized by the blood loss. Clinical signs include:

- Physical examination perfusion parameters: poor perfusion: tachycardia, pale mucous membranes, prolonged capillary refill time, weak pulses, cold extremities, altered mentation.
- Physical examination signs of anemia (pale mucous membrane color and narrow pulses) are difficult to differentiate from hypoperfusion/shock and need to be re-assessed after initial fluid resuscitation.
- Perfusion markers: increased lactate, decreased blood pressure and urine output.
- Respiratory function: increased respiratory rate and effort, blood gas analysis.

The variable clinical response to anemia in patients suggests different mechanisms of adaptation over time. Therefore, many parameters need to be determined prior to instituting red cell transfusion. A patient with an acute splenic rupture from abdominal trauma can manifest shock and severe blood loss with a small drop in hematocrit. Some patients walk in the Emergency Room with a hematocrit of 6% and appear clinically stable. When chronic anemia occurs, three principal compensatory mechanisms occur:

1. Decreased haemoglobin affinity for oxygen: A rightward shift of the oxyhemoglobin dissociation curve is caused by decreased pH (acidity), increased 2,3-DPG, increased temperature, and increased PCO2. Red blood cells produce more 2,3-DPG under conditions of chronic hypoxia (i.e. anemia); therefore, oxygen is more easily released at the tissue level.
2. Redistribution of blood flow: In anemia, selective vasoconstriction of blood vessels underserves certain non-vital areas (skin for example) and allows more blood to flow into critical areas like the heart or brain.

3. Increased cardiac output: The increased output is matched by decreased peripheral vascular resistance and decreased blood viscosity, so that cardiac output can rise without an increase in blood pressure. Generally, anemia must be fairly severe (hemoglobin < 7 g/dL) before cardiac output rises.

Thus, duration (acute versus chronic) of anemia needs to be taken into account because of normal adaptation of the body to the blood loss.

The transfusion trigger

The threshold values for the clinical use of blood products to treat anemia are not well defined in the veterinary literature. For many years in human medicine, the transfusion trigger had been set at a hemoglobin (Hgb) of 10 g/dL (hematocrit [HCT] of 30%). However, transfusional infections, immunologic risks, transfusion-related acute lung injury, the cost of blood, and component availability are current disadvantages of transfusions. In 1999, the Transfusion Requirements in Critical Care (TRICC) trial showed that maintenance of a Hgb between 7 and 9 g/dL in ICU patients is as effective with less adverse consequences as the maintenance of a Hgb above 9 g/dL. Based on that information, hemoglobin-based threshold values have recently been reviewed for humans and are currently between 6 and 8 g/dL of Hgb (HCT or packed cell volume [PCV] around 20%).

The time it took to achieve that particular Hgb/HCT/PCV value is also an important factor in the determination of when to give red blood cells. Animals with chronic disease may have suppression in the production of, or an insensitivity to, erythropoietin. This more chronic anemia will often go clinically undetected for weeks to months as the patient compensates. Animals with an acute anemia, i.e. from trauma/hemorrhage into body cavities, have little physiologic compensation for this abrupt change in oxygen carrying capacity.

Other objective measures that will help to decide if a transfusion is warranted include: venous oxygen tensions and lactate. As oxygen delivery to the tissues falls but the tissue extraction remains the same, less venous oxygen is present when measuring PvO₂. This however may reflect increased oxygen demand by the tissues. Alternatively, an increase in lactate is a readily available marker of tissue anaerobiosis or poor perfusion.

Red blood cell dosage

As a rule of thumb, 2 mL/kg of FWB will increase the PCV by 1% point. So, 20 mL/kg are used to increase the PCV by 10 percentage points.

In normovolemic, anemic patients, such as autoimmune hemolytic anemia, the volume required to increase the PCV may place the patient at risk of fluid overload. This is a particular concern in the cardiac patient.

Packed red blood cells (pRBC) will have a very small amount of remaining plasma. The hematocrit of pRBC may exceed 80%. In that case, dilution with 0.9% NaCl can be helpful to avoid hyperviscosity. Fluids containing calcium, like LRS, should not be used in order to decrease the risk of citrate chelation and coagulation.

As a rule of thumb, 1 mL/kg of pRBC will increase the PCV by 1% point. The post-transfusion PCV goal is usually between 18 - 25%.
Case-Based Approach to Hemoabdomen
Karl Jandrey, BS, DVM, MAS, DACVECC
University of California
Davis, CA

Emergency management
A patient in shock in the ER often has abdominal effusion. If this effusion is found by palpation, radiography, or ultrasonography, a diagnostic abdominocentesis can be completed quickly to identify the fluid as blood. Due to the generally large amount of blood in the peritoneal cavity to cause these clinical signs, many patients present in severe shock. The patient will likely have vasoconstrictive signs on physical examination that can be resolved by improving the effective circulating blood volume. The first step is to provide isotonic crystalloids to resolve these vasoconstrictive signs (pallor, prolonged CRT, tachycardia, weak femoral pulses, mental dullness and cool extremity temperature). Blood product delivery, in an expedient time frame, is typically unavailable and the urgency necessitates acellular fluid therapy. It is true that the patient will become relatively hemodiluted. However, improved perfusion is essential while you seek a more appropriate blood product for the patient.

The blood product of choice could be plasma if the patient has anticoagulant rodenticide or post-operative bleeding from von Willebrand Disease. Fresh whole blood or packed red blood cells are more effective for patients with a splenic or hepatic bleed (traumatic or pathologic secondary to a neoplasm). All natural blood products will have a much more potent effect on improvement of perfusion; however, continued loss will continue until the bleeding is controlled regardless of which fluid is used.

Abdominocentesis
Indications for abdominocentesis are 1) radiographic loss of serosal detail, 2) abdominal injury without obvious peritoneal entry wounds, 3) shock, multiple injuries, or signs of abdominal injury after blunt trauma, 4) head or spinal injury precluding reliable abdominal examination, 5) persistent abdominal pain or fluid distention of unknown cause, 6) post-operative complications possibly caused by leakage from an enterotomy or anastomotic site. Periumbilical ecchymosis (Cullen’s sign) may indicate hemorrhage in the peritoneum or retroperitoneum. Contraindications to abdominocentesis include coagulopathy, organomegaly, or distention of an abdominal viscus. Intestinal or uterine penetration is rare unless the viscus is dilated and adherent to the abdominal wall. Complications include the introduction or spread of infection, laceration of a viscus and hemorrhage from a punctured vessel. Following the techniques described below will reduce the risk of complications.

FAST (focused assessment with sonography for trauma)
The focused assessment with sonography for trauma (FAST) protocol was studied in dogs to prove it is a rapid and simple technique to detect free abdominal fluid in the emergency room by veterinary clinicians with minimal previous ultrasound experience. This technique scanned four regions in longitudinal and transverse planes of the abdomen with dogs in lateral recumbency. These regions are areas where fluid accumulation more commonly occurs: caudal to the xyphoid process, midline over the urinary bladder, and each flank

Medical or surgical management?
After the patient is stabilized, further monitoring is essential to determine if the following management is to be surgical or medical. Continued and on-going bleeding and a return of shock would suggest severe and persistent bleeding that often necessitates surgery. However, a few more diagnostic tests may need to be completed to ensure a normal hemostatic axis. Other options to surgical therapy include: autotransfusion or an abdominal bandage. Surgery is typically indicated if the patient has poor response to fluid resuscitation, a rising intra-abdominal PCV, or continues to effuse into the peritoneum.
Treatment of impaired primary hemostasis
The treatment of a defect in primary hemostasis involves the removal of the underlying cause if possible. Transfusion of platelets is challenging due to their very reactive nature and special handling required. The drawing of blood and placing it into collection bags can activate platelets to clump. Therefore, filters should always be used for administration. Platelets also activate at cold temperatures. All platelet transfusions must be done with fresh blood, either fresh whole blood, platelet-rich plasma, or platelet concentrates.

Fresh whole blood transfusions are a source of platelets, but whole blood provides fewer platelets than a platelet-rich product and can cause hypervolemia. Recently, a frozen platelet concentrate (PC) has been produced and is commercially available for dogs (Animal Blood Resources, International; www.abrint.net, Dixon, CA). This PC is prepared from a single donor by automated blood cell processors using apheresis technology, and is cryopreserved in 6% dimethyl sulfoxide (DMSO).

In human medicine, platelets have been cryopreserved with 6% DMSO, resulting in conservation for up to 3 years. However, this method of storage also resulted in loss of platelet viability, decreased aggregation and reduced clinical efficacy compared to fresh platelets. Our lab recently published our findings on the product’s platelet function, but not clinical efficacy, of this commercially available canine frozen PC.

With all these difficulties or clinical unknowns, there is no universal recommendation for the transfusion of platelets in dogs. It is very difficult to give a platelet number-based transfusion trigger. As a basic rule, the risk for hemorrhage is inversely proportional to the platelet count, and bleeding times in humans are prolonged in a linear fashion as platelet count drop from 100,000 to 10,000/µL. The most common trigger for prophylactic transfusion is 20,000/µL in human medicine. In veterinary medicine, numbers of 5,000/µL in cats and 10,000/µL in dogs have also been published. Published platelet numbers adequate for surgery are between 30,000 to 80,000/µL.

The current recommendation from our service is to treat on-going life threatening hemorrhage that is secondary to thrombocytopenia with fresh whole blood or fresh platelet rich plasma. As a rule of thumb in veterinary medicine, the recommendation is to transfuse platelet-rich products only in case of life-threatening bleeding, especially pulmonary or intra-cranial hemorrhage. Fresh platelet rich plasma is not commercially available and must be made from fresh whole blood just before administration. Platelet concentrates are commercially available but have to be ordered at the tie of need and shipped directly due to their 5 day shelf life.

Three products are available for platelet replacement: platelet concentrate (PC), platelet rich plasma (PRP) and fresh whole blood (FWB). These are suggested initial doses but the individual dose must be guided by the response to therapy.

- Fresh whole blood: 20 mL/kg within 4 hours of collection.
- Platelet concentrate: 1 unit/10kg. The transfusion should be finished in an hour.
- Platelet-rich plasma: 10 mL/kg. The transfusion should be finished in an hour.

Fresh whole blood is the most commonly available blood product to be used in case of life threatening bleeding due to thrombocytopenia.

Platelet rich plasma is prepared by centrifugation of fresh whole blood at a relatively slow speed. The supernatant is therefore "rich" in platelets. It's a fresh product so needs to be processed right before administration. Due to the presence of some red cells, a cross match is essential before administration.

Platelet concentrate is prepared by platelet-apheresis, a process whereby blood is removed from the donor and separated by an automated device into plasma, platelets, white blood cells and red blood cells. The platelet portion is saved and forms one unit of PC and the remaining components are returned back to the donor. Fresh PCs are stored at 20°C on a gentle continuous rocker and have must be used within 5 days of processing. According to the manufacturer, one unit of frozen PC can be stored for 6 months at -20°C. PC can also be prepared by centrifugation of platelet rich plasma from different donors (from 4 to 10), separation of the platelet-rich buffy coat and reconstitution in a sterile blood collection bag.
Reproductive problems often arise after normal business hours, so it is not uncommon for them to fall into the domain of the emergency veterinarian. As most owners lack medical knowledge, they frequently look to the veterinarian to answer questions and to identify potential problems. The emergency clinician must therefore be familiar with normal reproductive behavior in addition to the common emergencies that may arise. With this goal, we will review the events surrounding normal parturition as well as the common complications that may develop during this period.

Normal reproductive physiology
Normal gestation length in the dog may range from 57-72 days from the time of first breeding, with an average length of 65 days.1-2 Because cats are induced ovulators, there is generally less variability in gestation length, which ranges from 63-65 days. Ovulation may not take place after the first breeding however, so in the event of multiple breedings, uncertainties with regards to gestation length may still be present in the cat. As the whelping date approaches, a number of clues may point toward impending parturition. Mammary development, vulvar enlargement, mucous vaginal discharge, and relaxation of the pelvic ligaments are early signs of approaching parturition. Onset of lactation may be noted in primiparous bitches within 24 hours of parturition, but in multiparous bitches may occur several days before parturition. A sudden drop in body temperature (≥2°F) is generally noted within 24 hours of parturition in dogs and cats as a result of decreases in progesterone levels, but this finding is not always reliable. In one recent study, nadir temperature occurred >48 hours before parturition in 24% of dogs, and an appreciable drop in temperature (>1°F) was not seen in 35% of dogs.4

Normal parturition proceeds in three stages. The first stage is characterized by subclinical uterine contractions and progressive dilation of the cervix. During this stage, which typically lasts for 6-12 hours, bitches may show signs of restlessness, apprehension, panting, nesting behaviors, hiding, and anorexia. Queens may be tachypneic, restless, and vocal, or may lay in their nesting boxes, purring. Active expulsion of the fetuses occurs during the second stage of labor. The first fetus is usually delivered within 1 hour of onset of stage 2 labor in cats, and within 4 hours in dogs, with subsequent deliveries every 15 minutes to 3 hours.5,6 Active straining generally results in expulsion of a fetus within 15 minutes. The entire process generally occurs over 2-12 hours, but may take as long as 24 hours with large litter sizes. The third stage of labor results in expulsion of the placenta. One placenta should be identified for each fetus delivered. Placentas are usually still attached to the fetus by the umbilical cord and emerge with the fetus, but may emerge within 15 minutes to several hours if they become detached. Lochia, a greenish vaginal discharge, indicates placental separation and may be seen during all stages of labor. Following parturition, the discharge gradually becomes red-brown, decreasing in volume over 4-6 weeks as uterine involution takes place.

Dystocia
Historical and physical exam findings that should prompt a clinician to suspect dystocia are as follows:1

- A definite cause is apparent (ie. fetus lodged in birth canal, pelvic fractures)
- Gestation is prolonged (>70 days) with no evidence of labor
- Temperature has dropped to <100°F and returned to normal with no evidence of labor within 24 hours
- Lochia is noted and 2 hours have elapsed without expulsion of a fetus
- Strong and persistent contractions fail to result in the delivery of a puppy within 30 minutes
- Weak and infrequent contractions fail to produce a fetus within 4 hours.
- More than 4 hours have elapsed since the birth of a puppy with no evidence of ongoing labor
- Signs of systemic illness or severe pain are present

Dystocia may result from either maternal or fetal factors that prevent delivery from taking place. Uterine inertia is the most common maternal cause of dystocia, seen when the myometrium produces only weak and infrequent contractions that fail to expel a normal fetus through a normal birth canal. Primary uterine inertia is considered complete when gestation that has exceeded its expected length with no evidence of progression into active labor. Primary uterine inertia is termed partial if the bitch initiates parturition and expels one or more healthy fetuses, but then subsequently fails to deliver the remaining fetuses as a result of myometrial fatigue. Uterine inertia may also be considered secondary if myometrial failure results from prolonged attempts to expel an obstructed fetus, and persists following relief of obstruction. Morphologic causes of dystocia are those in which an anatomic abnormality of the bitch or queen results in obstruction of the birth canal (eg. small birth canal, pelvic fractures)

Fetal factors that may result in dystocia include malpresentations, oversize, fetal malformations, and fetal death. Some of the commonly described malpresentations include transverse presentation, lateral or ventral flexion of the neck, anterior presentation with flexion of one or both forelimbs, posterior presentation with retention of both hindlimbs, and simultaneous presentation of two fetuses.
It should be noted that posterior presentations are considered to be a normal variation in dogs and cats, occurring in approximately 40% of deliveries. Fetal oversize is another potential cause of dystocia, most commonly seen with single pup pregnancies. Fetal death is an infrequent cause of dystocia, increasing the likelihood of malpresentation because of failure to rotate and extend the head and legs, which commonly occurs immediately prior to parturition. Fetal malformations are another potential cause of dystocia, with anasarca (generalized subcutaneous edema), hydrocephalus, cerebral and cerebrospinal hernias, abdominal hernias, duplications, and rib cage malformations among the more commonly noted.

**Diagnosis of dystocia**

Workup of a patient that is presented for dystocia begins with a complete history and physical exam, including digital vaginal exam. If a fetus is lodged within the birth canal, digital manipulation should be attempted. The fetus may be grasped around the head and neck, around the pelvis, or around the proximal portions of the hind limbs, depending on fetal presentation. Excessive traction should never be applied to a single extremity because of the ease with which these may be avulsed. With the dam restrained in a standing position, traction is applied in a posterior-ventral direction. The fetus may be gently rocked back and forth, and twisted diagonally to free shoulders and hips “locked” in the pelvic canal. If flexion of head or extremities is preventing delivery, a finger may be used to extend them. One cannot overemphasize the importance of using copious amounts of sterile lubricant during obstetrical maneuvers, applied digitally or infused around the fetus using a red rubber catheter.

Radiographs should be obtained in any animal experiencing dystocia. Radiographs are accurate for assessing the number, size, location, and position of fetuses, as well as maternal pelvic morphology and general status of the abdomen. Fetal viability is more difficult to assess from radiographs, unless evidence of fetal decomposition is present. Signs of decomposition include intrafetal or intruterine gas patterns, awkward fetal postures, collapse of the spinal column due to loss of muscular support, and overlapping of the bones of the skull. Ultrasound may be a more useful tool for assessment of fetal viability, fetal malformations, and fetal distress. Normal fetal heart rates have been reported at 180-245 beats per minute in dogs and up to approximately 265 bpm in cats. Deceleration of fetal heart rates to less than 180 beats per minute and the presence of fetal bowel movements on ultrasound have been shown to correlate with severe fetal distress, and may indicate a need for rapid intervention.

Medical management should be considered if there is no evidence of obstruction, and fetal and pelvic size appear normal. Oxytocin is a peptide hormone that increases the frequency and strength of uterine contractions by promoting influx of calcium into myometrial cells. Oxytocin also promotes post partum uterine involution, aids in control of uterine hemorrhage, and assists in expulsion of retained placentas. The dose for oxytocin has traditionally been reported at 5-20 units IM in the dog and 2-4 units IM in the cat. However, with an increase in the use of uterine contraction monitoring (Whelpwise, Veterinary Perinatal Specialties Inc, Wheat Ridge, CO) in veterinary patients, there is a growing body of evidence to suggest that traditional doses may be too high, potentially causing uterine tetany, ineffective contractions, and decreased fetal blood flow. Recent data suggests that doses of 0.5-2 units are effective in increasing the frequency and quality of contraction. Calcium gluconate may be considered if weak, infrequent contractions are noted or when labwork reveals hypocalcemia. Retrospective studies have indicated that many patients who fail to respond to oxytocin alone may respond to a combination of calcium and oxytocin. The dose for calcium gluconate (10% solution) as a uterotonic agent is 11 mg/kg diluted in saline and given subcutaneously, or added to IV fluids and given slowly while monitoring an ECG for arrhythmias. If hypocalcemia is documented, a dose of 50-150 mg/kg intravenously should be used. Subcutaneous administration has been reported to result in irritation and potential granuloma formation, though this is an infrequent complication. Dextrose infusion should also be initiated if hypoglycemia is evident on labwork.

Surgical management should be considered for the following conditions:

- Complete primary uterine inertia
- Partial primary uterine inertia or secondary uterine inertia where large numbers of fetuses remain and response to drugs is unsatisfactory,
- Fetal oversize
- Gross abnormalities of maternal pelvis (fractures, masses)
- Fetal malformations
- Malpresentation that is not amenable to manipulation
- Past history of dystocia or c-section
- Fetal putrefaction
- Maternal evidence of systemic illness
- Suspicion of uterine torsion, rupture, prolapse, or herniation
- Evidence of fetal distress with poor response to medical intervention
An anesthetic protocol for caesarian section should be selected with the goal of maximizing survival of neonates and dam. Attempts should be made to minimize exposure of the fetus to anesthetics by keeping the time from induction to delivery as short as possible. Ideally, the dam should be clipped and prepped prior to induction, equipment should be out, and the surgeon should be scrubbed and ready. Induction agents should be given to effect. Regional techniques such as line blocks and epidurals may help to minimize the need for other drugs. A line block can be performed using 2 mg/kg lidocaine infused along the ventral midline. Alternately, epidural lidocaine may be administered in dogs at a dose of 2-3 mg/kg, not to exceed a total volume of 6 ml. Propofol (4-6 mg/kg IV) or mask inductions are most commonly used for caesarian section at this time, and have been associated with reduced neonatal mortality in dogs. Anesthetic agents that have been associated with increased neonatal mortality include thiopental, ketamine, xylazine, medetomidine, and methoxyflurane.

Neonatal resuscitation
A warm (90°F) incubator, hemostats, suture material, suction bulb syringes, emergency drugs, and an adequate supply of soft dry towels should be prepared beforehand. As each neonate is handed off, the umbilical cord should be clamped and ligated 1-2 cm from the umbilicus. Fetal fluids and amnion should be removed by rubbing briskly with a soft, clean towel. The oral cavity and nares may be suctioned with a bulb syringe. The old practice of “swinging” puppies to clear their airways is best avoided because of the potential for cerebral hemorrhage due to concussive injury. If vigorous rubbing is not successful at stimulating respiration, positive pressure ventilation may be initiated with a snug fitting mask, keeping the neonates head and neck extended to ensure adequate inflation of the lungs. Alternately, intubation may be accomplished using a catheter or small, uncuffed endotracheal tube. Because isoflurane is minimally metabolized, ventilation is the primary route of elimination. Thus, its depressant effects can not be reversed until the neonate breathes. Cardiac massage may be instituted if a heart beat is not detected once warming and ventilation measures have been instituted. Epinephrine (0.1 mg/kg) may be given intratracheally, intrasosseously, or intravenously if cardiac massage is unsuccessful. Naloxone (0.1 mg/kg) should be considered if the dam received opioid analgesics as part of the anesthetic regimen. Although doxapram (dopram) is routinely administered in many practices as a respiratory stimulant, it is not used for this purpose in the resuscitation of human neonates and there is no evidence to support its use in veterinary patients.

The prognosis for medical management of dystocia is guarded, with success rates of 20-40% in the veterinary literature. Additionally, stillbirth rates have been shown to rise when dystocia is allowed to continue for greater than 4.5-6 hours from the time of onset of second stage labor in the dog. For these reasons, the decision to proceed to caesarian section should not be delayed if response to medical management is poor or unlikely to result in successful delivery. In recent studies, neonatal survival rates following surgical treatment of dystocia have been reported at 92% at birth, with 80% still alive at 7 days post c-section.

Periparturient emergencies
Mastitis
Mastitis is a postpartum complication seen in both dogs and cats that results from bacterial infection of the mammary glands. Bacteria most commonly enter through the nipple as a result of nursing, trauma, or poor hygiene, but may also be spread hematogenously. In mild cases, discomfort, swelling, and inflammation may be seen, while in severe cases, signs of systemic illness such as fever, anorexia, and lethargy frequently develop. Dogs often refuse to allow their young to nurse and may be reluctant to lie down. Severe mastitis often progresses to abscession and necrosis.

Diagnosis of mastitis is generally based on history and clinical signs (fever and swollen, painful glands in the postpartum animal), but baseline CBC and chemistry as well as milk cytology and culture are useful for assessing severity of illness and appropriateness of antibiotic selection. Milk expressed from the gland may be purulent and cytology typically shows large numbers of white blood cells and intracellular bacteria. The most common bacteria isolated on culture include *E. coli*, *Staphylococci*, and *Streptococci*.

Treatment is initiated immediately with broad spectrum antibiotics. Amoxicillin-clavulanic acid or cephalaxin are good first choices and are safe for nursing neonates. Other measures that may be useful in the management of mastitis include warm compresses, hydrotherapy, and frequent milk stripping. If a fluctuant abscess pocket is identified on palpation, early lancing and flushing may limit the degree of skin necrosis that follows. Large, ruptured mammary abcesses may be successfully managed as open wounds with warm compresses, hydrotherapy, and systemic antibiotics, but in these cases mastectomy may provide a more rapid and cosmetic resolution of the problem.

Endometritis
Endometritis is a bacterial infection of the uterus that is generally seen within the first three days (up to one week) after whelping, though it may develop during pregnancy as well. Potential causes include retained fetuses or placentas, abortions, uterine trauma secondary to dystocia or obstetrical manipulation, and ascending infection from the vaginal canal. Typical signs include fever, lethargy, anorexia, vomiting, diarrhea, poor lactation, neglect of offspring, and foul-smelling vaginal discharge. Just as in the non-pregnant dog, any purulent vaginal discharge noted during or after pregnancy is abnormal and should prompt investigation.

Labwork abnormalities consistent with sepsis may be seen, including leukocytosis with a left shift or leukopenia, thrombocytopenia, elevated liver values, and hypoalbuminemia. Coagulation testing should be performed to rule out disseminated
Eclampsia or puerperal tetany is a life threatening condition that results from the development of hypocalcemia in the periparturient period. It is one of the more common complaints noted following parturition, accounting for roughly 1/4 of periparturient emergencies. Eclampsia is results from the loss of calcium through lactation and fetal skeletal mineralization, in excess of that entering the extracellular fluid through gastrointestinal absorption and bone resorption. Other factors such as inadequate diet or parathyroid atrophy resulting from oversupplementation of calcium may also contribute, though diet in affected animals has not been reported to be significantly different from non-affected animals. Increasing litter size to maternal body weight ratio has also been identified as a significant factor in the development of periparturient hypocalcemia.

Eclampsia is most commonly seen in small dogs, first-time whelpings, and dogs with large litter sizes. It typically develops 2-4 weeks after parturition but is occasionally seen in late gestation. Clinical signs in dogs most commonly include stiff gait, trembling, twitching, seizures, tachycardia, panting, and hyperthermia, but some dogs may present with atypical signs such as whining, vomiting, diarrhea, and behavior changes. If untreated, death may result from respiratory impairment, or from hyperthermia and cerebral edema. Cats may present with clinical signs similar to dogs, but unlike dogs, are more prone to hypothermia, and may present with hyperexcitability, hypersensitivity, or flaccid paralysis in place of clonic-tonic muscle spasms.

Diagnosis of eclampsia is made on the basis of history and physical exam findings in conjunction with low total or ionized calcium levels. Ionized calcium represents the physiologically active portion of calcium within the body, and is involved in muscular contraction, as well as neurologic and cardiovascular function. Ionized calcium levels are therefore believed to be a more sensitive indicator of extracellular calcium levels than total calcium, and typically fall below 0.8 mmol/L in dogs with eclampsia (reference range: 1.2-1.4 mmol/L). However, total calcium levels have been found to be decreased in all dogs with eclampsia, suggesting that total calcium levels may provide sufficient information in this disease if ionized calcium measurement is not available.

Animals presenting with eclampsia should have an IV catheter placed and intravenous fluids administered to address fever, dehydration, and tachycardia. Calcium gluconate (10%) should immediately be administered intravenously slowly to effect. Most animals will have tremors controlled at doses ranging from 0.5 to 1.5 ml/kg. An ECG should be monitored during calcium administration and the infusion stopped if bradycardia or arrhythmias develop. Ionized calcium levels should be rechecked post administration to make sure that ionized calcium levels remain within the normal range. Temperature should be carefully monitored in animals presenting with tremors, and active cooling measures (cool fluids, alcohol applied to footpads) should be instituted for patients with severe hyperthermia. Body temperature generally falls quickly once tremors are controlled, so active cooling measures should be discontinued once the temperatures falls below 103°F. Oral calcium carbonate (Tums) supplementation should be continued at a dose of 100 mg/kg/day throughout lactation. Up to 20% of dogs may have recurrence of eclampsia despite supplementation if puppies are allowed to nurse, so bottle feeding and early weaning of the puppies is recommended.

Supplementation of calcium prior to whelping is not recommended, as this may downregulate parathyroid hormone secretion, decreasing intestinal calcium absorption and increasing the risk of eclampsia during lactation. Instead, calcium administration (100 mg/kg/day divided) should be instituted following whelping in dogs at risk and dogs with a previous history of eclampsia.

References
Managing the Difficult Urethral Obstruction
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Overview and pathophysiology
Feline urethral obstruction is one of the most common emergency presentations in the cat, accounting for approximately 9% of feline emergency admissions. While there are many factors that may play into the development of lower urinary tract diseases in the cat, matrix-crystalline plugs and urolithiasis are the most common causes of obstruction. Cats with urethral obstruction may have signs localized to the lower urinary tract including dysuria, stranguria, pollakiuria, hematuria, vocalizing, and pain, or they may show signs of systemic illness such as vomiting, lethargy, or collapse. Cats with obstructive urinary tract diseases may or may not have demonstrated preceding signs of lower urinary tract disease.

Following the development of urethral obstruction, clinical signs of uremia typically develop within 24 hours. Dehydration occurs due to decreased water intake and ongoing fluid losses secondary to vomiting. Acid-base (metabolic acidosis) and electrolyte disturbances (hyperkalemia and hyperphosphatemia) develop due to impaired excretion. Accumulation of metabolic wastes leads to post renal azotemia. Bladder capacity is reached, leading to rising intravesicular pressure and subsequently falling glomerular filtration rate (GFR). Prolonged obstruction may result in intrinsic renal failure. Damage to the urothelium and detrusor muscle may also develop during this time. If left untreated, death secondary to cardiopulmonary failure or hyperkalemia may occur within 3-6 days. Damage to bladder mucosa or urethra may shorten survival times.

Diagnosis of urethral obstruction
Diagnosis of urethral obstruction is generally made on the basis of history and physical exam findings. Abdominal palpation typically reveals a turgid, painful bladder, though in rare cases, the bladder may be moderate in size if the cat is presented to the veterinarian shortly after clinical signs develop. Blood and/or crystalline debris may be visualized at the urethral orifice. The presence of bradycardia frequently indicates hyperkalemia, and severe systemic signs in conjunction with free abdominal fluid should prompt consideration of bladder leakage or rupture. In contrast, cats that present with stranguria but appear systemically healthy and have palpably small bladders typically have non-obstructive lower urinary tract disease.

At the time of presentation, a peripheral IV catheter is placed and blood is collected for complete blood count, serum biochemistry panel, and venous blood gas/electrolyte panel. The blood gas/electrolyte panel is particularly helpful as it provides rapid information on parameters such as potassium concentration (as well as acid-base status and renal values) that may affect initial interventions. Electrocardiography can also be helpful in the initial evaluation of the patient with urethral obstruction. Early ECG changes suggestive of hyperkalemia include bradycardia, dampened P-waves, tented T-waves, and prolongation of the P-R interval. As hyperkalemia worsens, loss of P-waves (atrial standstill) and widening of the QRS complex may develop. Electrocardiographic changes typically do not develop until potassium levels are greater than 7 mEq/L, but there is a great deal of individual variation in terms of patient response to hyperkalemia. Metabolic acidosis, hyponatremia, and hypocalcemia may contribute to the likelihood of hyperkalemic cardiotoxicity.

Once the animal has been medically stabilized and deobstructed, urine is submitted for urinalysis and culture. Because crystalline and cellular composition of the urine may change over time, evaluation of a fresh, undiluted sample is preferred. Diagnostic imaging should be performed to rule out cystic or urethral calculi. If a urolith or crystalline-matrix plug is retrieved at the time of deobstruction, composition should be determined as this may impact future therapies.

If free abdominal fluid is identified, fluid chemistry may be helpful in determining whether urinary tract rupture has occurred. An abdominal fluid:serum creatinine ratio of 2:1, or abdominal fluid:serum potassium ratio of 1.9:1 (cat) or 1.4:1 (dog) is predictive of uroperitoneum. Cytology of the fluid sample should also be performed to rule out urosepsis. Contrast cystourethrography is used to determine location and severity of the rupture.

Treatment of urethral obstruction
Fluid therapy
Initial management of urethral obstruction in the cat should focus on correction of hypovolemia, hyperkalemia, and other acid-base and electrolyte disturbances. In most cases, appropriate fluid therapy followed by restoration of urine flow will effectively correct these abnormalities. A peripheral IV catheter should be placed and fluid therapy instituted immediately using 0.9% sodium chloride or balanced electrolyte solution such as lactated Ringer’s solution (LRS). A shock rate of fluids (66 ml/kg/hour in the cat) is calculated and then administered to effect in increments of approximately ¼ of the calculated dose, reassessing major body systems after each bolus. For example, the calculated shock rate in a 5 kg cat is approximately 330 ml, and should be administered in individual boluses of 50-100 ml every 10-15 minutes until cardiovascular status is restored. The goal of fluid therapy should be normalization of vital signs such as heart rate, level of consciousness, pulse quality, blood pressure, and capillary refill time. The specific type of intravenous
Techniques for urethral deobstruction

During the initial exam, the urethra may be gently massaged, followed by careful palpation of the bladder to potentially dislodge superficial plugs. Extreme care should be taken to avoid accidental bladder rupture. While this technique is rarely effective, it is a simple extension of the initial physical exam and therefore may be worth trying in less severely affected cats prior to catheter deobstruction.

Although severely depressed patients may be deobstructed without the need for chemical restraint, sedation/analgesia is employed in the majority of “blocked” cats to improve patient comfort, facilitate deobstruction, and avoid urethral or bladder trauma secondary to patient struggling. Ketamine (100 mg/ml) may be combined with diazepam (5 mg/ml) in equal parts by volume and given at a dose of 1 ml/10 kg of the 50:50 mix. However, this combination should be avoided in cats with known or suspected hypertrophic cardiomyopathy, or when an undiagnosed murmur or gallop rhythm is present. In these cases, hydromorphone (0.05 mg/kg) in combination with diazepam (0.2 mg/kg) may provide a safer option.

Following sedation, the cat is positioned in dorsal recumbency with the legs pulled forward over the head. In this position, the prepuce may be retracted and the penis extruded by simply pushing the prepuce downward towards the anus. A further advantage to this technique is that it allows the urethra to be maximally straightened to facilitate deobstruction. The author’s preferred technique for deobstruction uses an olive tip catheter (FUS needle 21 g x 1”, Jorgensen Laboratories, Loveland, CO). This is a metal, bulb-tipped catheter that can be used to flush the urethra and either break down matrix-crystalline plugs or hydropulse thematraumatically into the bladder. Initially, the olive tip catheter is lubricated and inserted gently into the urethra to the site of the obstruction, approximately 1-2 cm. A 3 cc syringe is then used to lavage and break down the plug. Bits of the plug will often be seen emerging from the urethral orifice during the lavage. When the catheter is withdrawn, a strong stream of urine will frequently force the remainder of the plug from the urethra. Gentle bladder palpation may be used at this point to assist in the expulsion of the plug. To avoid urethral trauma, the catheter should not be forced past the obstruction. Instead, the lavage solution should be allowed to do the work. Additionally, acidic solutions should not be used for lavage as these have not been shown to be effective at plug dissolution and may further traumatize the urethral mucosa. If lavage alone is not successful at dislodging the urethral plug, the tip of the urethra can be pinched around the bulb tip of the catheter and hydropulsion used to push the plug back into the bladder.

Many clinicians use polypropylene “tomcat” catheters for the purposes of unblocking cats. These have the potential to cause additional trauma to the urethra when the rigid catheter is forced past the site of obstruction. If used, a number of steps may help to minimize iatrogenic urethral damage and maximize chances of success. (1) Completely straighten the urethra by pushing the prepuce dorsally towards to anus until the penis is parallel to the spine. (2) Use copious amounts of lubrication. (3) Hydropulse with sterile saline prior to advancing the catheter to assist in dislodging the plug. (4) Use a very light touch when advancing the catheter. Hold the catheter between index finger and thumb and twirl gently while advancing. Think about “picking a lock” when attempting to advance the catheter. Use finesse instead of force. (5) Once the catheter is well seated in the urethra, the penis may be allowed to retract into the prepuce. The prepuce may then be pulled caudally (toward tail tip) to further straighten the urethra while the catheter is advanced.

Some experienced clinicians advocate the use of cystocentesis prior to deobstruction to decompress the bladder and to potentially facilitate hydropulsion of urethral plugs. The author prefers to reserve this technique for use only as a last resort due to the number of fluid selected is of lesser importance than the administration of appropriate volume. Although 0.9% sodium chloride has traditionally been selected due to its lack of potassium, studies in both experimental and clinical cases have shown that potassium containing solutions (LRS, Normosol-R) do not adversely affect the rate of resolution of hyperkalemia in cats with urethral obstruction when compared with 0.9% saline. Additionally, the buffered solutions are more efficient at restoring electrolyte and acid-base balance in severely affected animals.

Hyperkalemia

Relative or absolute bradycardia should be immediately investigated by monitoring electrocardiography and serum electrolyte concentrations. Severe electrocardiographic changes such as atrial standstill, widened QRS complexes, or sine wave formation provide strong indication for the administration of calcium gluconate. Calcium gluconate (10%) is given slowly at a dose of 0.5-1.5 ml/kg IV while carefully watching the patient’s ECG for arrhythmias. Although calcium gluconate does not lower the serum potassium level, it has the immediate effect of buffering the myocardium from the toxic effects of hyperkalemia by restoring the normal difference between resting and threshold membrane potentials. Other intermediate to long-term interventions for hyperkalemia include the administration of regular insulin/dextrose and sodium bicarbonate, though these therapies are rarely warranted in animals with urethral obstruction as fluid therapy followed by timely restoration of urine flow are generally effective at reversing the hyperkalemia. However, if needed, 50% dextrose may be diluted 1:1 with saline and given at a dose of 1 gm/kg body weight to promote endogenous insulin release with subsequent potassium uptake by the cells through stimulation of sodium-potassium pumps. If regular insulin is used, it should be given at a rate of 1 unit insulin per 3 gm dextrose, though this is generally unnecessary and creates the need for careful blood glucose monitoring thereafter to avoid hypoglycemia. Sodium bicarbonate may also be given at a dose of 1 mEq/kg intravenously to facilitate intracellular potassium shifting in exchange for hydrogen ions.

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cats presenting to the emergency service with uroperitoneum and apical bladder tears following cystocentesis of overdistended bladders. However, it should be noted that our institution may see a biased population of more severely affected animals.

Cats that are critically ill, and those demonstrating large amounts of “sandy” crystalline debris in the urine, blood clots, uroliths, plugs hydropulsed into the bladder, bladder atony, or urethral narrowing are particularly at risk for reobstruction post-unblocking. For this reason, a soft, indwelling, 3.5-5 French red rubber catheter is placed following deobstruction to facilitate urine drainage overnight and to assist in quantitation of urine output. Indwelling catheters should be placed using liberal clipping and scrubbing of the perineum and aseptic technique to minimize risk of catheter-induced urinary tract infection. The tip of the catheter should sit just past the bladder neck to reduce risk of kinking or knotting. The catheter should then be connected to a sterile, closed collection system. To decrease the likelihood of premature catheter removal, careful attention should be given to suture placement. A piece of butterfly tape is placed around the catheter and appositional sutures are placed at the margin of the butterfly tape to prevent kinking of the catheter. The catheter body is then taped to the tail. An Elizabethan collar should be placed prior to anesthetic recovery.

**Hospital management**

**Fluid therapy**

Following initial stabilization and correction of hypovolemia, fluid rates should be adjusted to account for remaining fluid deficits, daily maintenance requirements, and ongoing losses. Deficits can be estimated as follows based upon clinical signs of dehydration: mild (5-6%), moderate (7-8%), and severe (8-10%). Multiplying the estimated percent dehydration by body weight gives the fluid deficit, which may then be replaced over the next 24 hours. For example, a 5 kg cat estimated to be 8% dehydrated would have an estimated deficit of 400 ml. To this value must be added maintenance needs (approximately 60 ml/kg/day) and ongoing losses. Ongoing losses following “unblocking” result from post-obstructive diuresis and can be estimated most easily by quantitating urine output. Normal urine output is approximately 1-2 ml/kg/hour (5-10 ml/hour in the average 5 kg cat). Urine output in excess of this amount typically results from post-obstructive diuresis. During the first 24 hours of therapy, a fluid rate should be selected that accounts for these ongoing losses. In other words, the intravenous fluids administered should slightly exceed measured urinary losses. Urine output is quantified every four hours. Inadequate urine production (<1 ml/kg/hr) indicates inadequate fluid administration or urinary catheter occlusion with debris. After troubleshooting the catheter, a fluid bolus followed by an increase in fluid rate is indicated if urine output remains low.

Fluid therapy is typically tapered over the next 24-36 hours. Daily monitoring of electrolytes and renal values should be performed to ensure that azotemia resolves and electrolytes normalize. Potassium supplementation may be required during post-obstructive diuresis should hypokalemia develop.

**Urinary catheter care**

Indwelling urinary catheters and tubing should be cleaned externally once daily with a dilute chlorhexidine solution. Gloves should be worn and aseptic technique used when handling the catheters to avoid nosocomial infection. Bladder palpation should be performed every 4-6 hours to ensure that the bladder remains decompressed. When moving the patient, the urine collection system tubing should be clamped and the bag held below the level of the patient to prevent retrograde flow of urine into the bladder.

To minimize likelihood of catheter-induced urethral irritation or urinary tract infection, catheters should be removed as soon as possible. For most cats, the catheter is removed within 48 hours, but the presence of excessive crystalline debris or blood clots in the urine may necessitate longer indwelling catheter duration to avoid reobstruction. Use of antibiotics during hospitalization is not recommended as this is unlikely to prevent catheter-related infection, but may contribute to antibiotic resistance of organisms protected by the catheter biofilm. Culture should be performed prior to catheter removal, with antibiotic therapy initiated as indicated based upon results of culture and sensitivity.

Following catheter removal, patients should be monitored for an additional 12-24 hours to ensure that the urethra remains patent. Cats will typically urinate small volumes frequently following catheter removal due to irritation resulting from obstruction and catheterization. Although they may appear to strain in the litterbox, the bladder should remain small on palpation. A progressively distending bladder post-catheter removal typically indicates reobstruction (firm bladder, difficult to express) or bladder atony (large, flaccid, expressible). Cats with suspected urethral spasm post catheter removal may benefit from a smooth muscle relaxant following catheter removal (prazocin 0.5 mg/cat q24h).

**Pain management**

Urinary obstruction and initial management are frequently associated with significant discomfort. In our practice, buprenorphine (0.01 mg/kg IV q6h) is commonly used to provide analgesia for the first 24-48 hours.

**Long term management**

Strategies for long-term prevention of recurrence focus primarily on environmental modification and dietary changes. Occasionally, pharmacologic intervention may be warranted. An ample number of litterboxes should be provided, particularly in multi-cat households, and litterboxes should be cleaned regularly to encourage more frequent use. Canned or moistened food may decrease frequency of lower urinary tract episodes by promoting a more dilute urine and increasing frequency of urination. Fresh water should
be available at all times. In cases where obstruction was caused by struvite-matrix plugs, an acidifying diet may be of benefit. Antibiotics, anti-inflammatories, and antispasmodics have not been associated with reduction in frequency of episodes and their routine use is not recommended.

**Perineal urethrostomy**
Perineal urethrostomy may be considered in cases where frequency of urethral obstruction is unacceptable despite appropriate medical management or when irreversible changes in the urethra (stricture, scarring, urolithiasis) cause recurrent or persistent obstruction. Perineal urethrostomy has been associated with significant short and long term complications including recurrent urinary tract infection and stricture, and as such should not be considered a first line recommendation for cats with urethral obstruction.

**References**
Diagnosing and Treating Pericardial Effusion

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Pericardial effusion is defined as the accumulation of fluid within the pericardial space. As the pressure within the pericardial space increases, right sided cardiac filling is impaired, resulting in decreased stroke volume with subsequent decreases in cardiac output and ultimately decreased oxygen delivery to the tissues (shock). These manifestations of pericardial effusion are referred to as cardiac tamponade. Successful emergency management of dogs with life threatening pericardial effusion depends on early triage, a thorough physical examination, point of care diagnostic imaging techniques, and subsequent pericardiocentesis or placement of an indwelling pericardial drain.

Key etiologic and pathophysiologic points

Pericardial fluid accumulation and cardiac tamponade in the dog most often occurs secondary to a neoplastic process. Hemangiosarcoma (HSA) is most commonly identified in the region of the right atrium or right atrial appendage while chemodectoma (common in brachycephalic breeds) is most often identified at the heart base. Mesothelioma and any metastatic tumor are additional neoplastic causes. Although location and breed are frequently suggestive of tumor type, definitive diagnosis is dependent on a biopsy specimen.

Idiopathic pericardial effusion tends to be an inflammatory process and is frequently recognized in similar breeds to those that frequently develop HSA. Significant efforts in recent years have been directed towards developing diagnostic tests to help differentiate malignant from benign pericardial effusion (idiopathic). Pericardial fluid pH was initially thought to aid in making this differentiation, however, pericardial fluid pH has now been clearly shown to be of little diagnostic value. Recent evidence suggests that blood concentrations of cardiac troponin I (cTnI) are significantly higher in dogs with masses consistent with HSA than in dogs without evidence of an underlying cause (idiopathic).

Vitamin K1 antagonists (anticoagulant rodenticides and coumadin) can also result in pericardial effusion. Therefore; it is the authors’ practice to always perform an ACT or other point-of-care coagulation assessment at the cage side prior to pericardiocentesis. If significant coagulopathy is present and patient condition permits, correction of coagulopathy with blood products (fresh frozen plasma or fresh whole blood) is indicated prior to pericardiocentesis. Subsequent institution of Vitamin K1 therapy for 4 weeks is indicated.

Left atrial tear is an uncommon consequence of chronic mitral regurgitation and left atrial dilatation, however, it has been recognized as a cause of acute pericardial effusion in the dog. An infectious cause of pericardial effusion is fungal disease (coccidiomycosis). Bacterial pericarditis and pericardial effusion secondary to trauma also occur, but are uncommon.

Numerous additional conditions such as congestive heart failure, uremia, decreased oncotic pressure, and a host of systemic inflammatory processes frequently result in small volume pericardial effusion accumulations without evidence of cardiac tamponade.

Key Clinical diagnostic points

Triage and physical examination in pericardial effusion

The most common presenting complaints from the owners of dogs with pericardial effusion and cardiac tamponade are lethargy, anorexia, collapse or syncope, abdominal distention, and dyspnea. Major body systems assessment of the dog with pericardial effusion will likely reveal compromise to one or all of the major body systems. Assessment of the cardiovascular system may frequently reveal the following:

- Pale mucous membranes: due to vasoconstriction and poor peripheral perfusion
- Slow CRT: due to decreases in cardiac output
- Increased heart rate: due to compensatory activation of the sympathetic nervous system
- Poor pulse quality: due to decreased stroke volumes and low blood pressure

Assessment of the respiratory system will frequently reveal increased respiratory rate and effort.

Assessment of the central nervous system will frequently reveal a decreased level of consciousness secondary to decreased oxygen delivery to the brain. Any one or combination of these findings should necessitate movement to the treatment area for further assessment including full physical examination, measurement of blood pressure, oxygen saturation, cardiac rhythm (ECG), and placement of an intravenous catheter from which a small blood sample for PCV / TS / Blood Glucose +/- Venous Blood Gas and Electrolytes can be rapidly acquired. If possible, blood for CBC, serum biochemical profile, and coagulation profile or ACT should also be collected. Concurrently, a second team member will be able to collect a full medical history.

Physical examination should still be centered on the major body systems, but subtle findings supportive of pericardial effusion may be noted including:

- Jugular venous distention: due to right sided congestive heart failure.
• Muffled heart sounds normal lung sounds: unlike pleural effusion which will frequently cause decreased heart and lung sounds, pericardial effusion will frequently only cause decreased heart sounds.

• Abdominal distention: ascites and hepatic engorgement may result from longstanding (days) pericardial effusion due to right sided congestive heart failure. Abdominocentesis will frequently reveal a relatively clear fluid with low cellularity and a protein concentration greater than 2.5g/dL but less than 3.5g/dL most consistent with a modified transudate.

• Pulsus paradoxus: An inspiratory fall of arterial systolic blood pressure of more than 10mmHg resulting in variation in pulse intensity with respiratory cycle due to increased venous return during inspiration, increased right sided filling, shifting of the interventricular septum to the left with decreased left sided diastolic filling and subsequent decreased left sided stroke volume.2

• Other physical examination findings specific to the underlying cause of the effusion such as fever in septic or fungal pericarditis.

Pericardial effusion causing cardiac tamponade should be HIGHLY suspected based on signalment, history, and physical examination findings, supported by diagnostic testing such as abdominocentesis and electrocardiography (+/- radiography) and confirmed through point of care diagnostic imaging techniques.

Diagnostic techniques
Abdominocentesis
See above.

Electrocardiography
Assessment of ECG in patients with pericardial effusion may reveal sinus tachycardia +/- ventricular arrhythmias. Ventricular arrhythmias may result from decreased myocardial oxygen delivery or aberrant conduction associated with the underlying cause of the effusion. QRS complexes <1mV in amplitude and the presence of electrical alternans (regular or irregular variation in QRS complex amplitude associated with the heart moving within the pericardium to and from the positive pole of lead II) are supportive of pericardial effusion.4

Echocardiogram
Echocardiogram is the diagnostic test of choice for confirmation of the presence of pericardial effusion in the dog. Many dogs with pericardial effusion have SEVERE cardiovascular compromise and can be on the verge of death. The stresses associated with radiographic imaging may put these patients at risk of decompensation. Consequently, in the ideal world, radiographic imaging should be avoided initially. The authors have found that the presence of a small, portable ultrasound machine with a mid-range frequency transducer placed at the primary treatment station in the emergency room / treatment area to be of great utility for identifying conditions like pericardial effusion, pleural effusion, and to assess patients with acute abdomen for the presence of abdominal fluid. Echocardiographically, pericardial effusion appears as a hypoechoic space located between the hyperechoic pericardium and the right ventricular wall when viewed through the right cardiac notch. The presence of pericardial effusion provides excellent contrast to aid in the diagnosis of cardiac masses, however, pericardiocentesis should NOT be delayed in a patient with signs of shock simply to aid the diagnosis.

Thoracic radiography
As previously mentioned, thoracic radiography can be an extremely stressful procedure for dogs with cardiac tamponade. However, not all practices are equipped with ultrasound capabilities. If thoracic radiography is performed in dogs with suspected pericardial effusion, ventrodorsal positioning should be avoided. A dorsoventral projection can be acquired with minimal stress. Lateral thoracic radiographs may also be performed. Supportive radiographic findings include an enlarged, globoid cardiac silhouette. Acute effusions may not cause severe enlargement of the cardiac silhouette because the pericardium has not had time to stretch. Concurrent pleural effusion may be present. The other primary differential for a globoid heart is dilated cardiomyopathy (DCM) or other underlying cardiac disease. Key findings to try to differentiate DCM from pericardial effusion include:

• Heart sounds: Heart sounds in dogs with DCM are frequently normal in contrast to the decreased heart sounds seen in pericardial effusion. A systolic murmur may be noted in dogs with DCM and is uncommon in dogs with pericardial effusion.

• ECG: Atrial fibrillation is common in dogs with DCM. Atrial fibrillation is uncommon in dogs with pericardial effusion. Electrical alternans may be seen in dogs with pericardial effusion.4

• Cardiac Silhouette: The silhouette of the heart on thoracic radiographs of dogs with pericardial effusion tends to be extremely round with sharp borders. The silhouette of the heart in dogs with cardiomyopathy can be round, but often, there are still some dimples or “waist” associated with the divisions between the chambers and the borders of the cardiac silhouette tend not to be as sharp because of motion artifact.

• Pulmonary infiltrate: Pulmonary edema is common in DCM and uncommon in pericardial effusion.

• Pulsus paradoxus: Pulmonary edema is common in DCM and uncommon in pericardial effusion.
Key therapeutic points
Pericardiocentesis

Pericardiocentesis can be a stressful procedure. Use of cardiovascularly sparing sedatives (narcotics and benzodiazepines) may alleviate patient stress and facilitate safe pericardiocentesis. Numerous techniques have been described for pericardiocentesis in the dog including, but not limited to the use of a large-gauge over-the-needle catheter, through the needle catheter, and catheters placed using the Seldinger technique. Numerous commercial pericardiocentesis trays / kits are also available. The authors prefer to use a 14-16g, 5.5” over-the-needle catheter (Abbocath T, Hospira Inc. Lake Forest, IL) with two additional small side-holes or a commercial multi-lumen intravenous catheter placed using the Seldinger technique (Arrow Triple Lumen Central Venous Catheter, Arrow International, Reading, PA). The former is much less expensive while the latter may be left in place for ongoing drainage.

ECG should be monitored during and after pericardiocentesis for the presence of arrhythmias induced by catheter-associated irritation of the epicardium and decreased myocardial oxygen delivery experienced during cardiac tamponade. Lidocaine should be readily available, as should a defibrillator.

Pericardiocentesis is most often performed from the right hemithorax because injury to the left coronary artery is unlikely, and the cardiac notch is slightly larger. The patient can be positioned in sternal recumbency (preferred by most) or laterally. Full surgical preparation should be performed between the 2nd to the 8th ribs and from the mid-thorax to the level of the sternum. A fenestrated drape should be placed. Aseptic technique should be practiced at all times. The apex beat of the heart should be palpated (most often between the 4th and 5th ribs just above the costochondral junction) and lidocaine should be infiltrated locally off of the cranial edge of the rib (to avoid the intercostal neurovascular bundle). Ultrasound guidance can also be used to identify the optimal location for pericardiocentesis. A small skin incision (<5mm) should be made in the proposed insertion site and the catheter advanced through this incision (off the cranial edge of the rib). Upon the appearance of fluid in the flash chamber, the catheter and stylet should be advanced together for 2-3mm and the catheter fed over the stylet into the pericardium. Initially, a small fluid sample should be placed in an ACT or clot tube. A sample retrieved from the ventricle should clot (unless the underlying condition is anticoagulant rodenticide intoxication) while one that has been in the pericardial space for any appreciable period of time should not. A fluid sample should be saved for cytologic analysis and culture and the pericardium should be evacuated.

Monitoring
Patient response to decompression of significant pericardial effusion is often very rapid and very gratifying as vital signs and physical examination findings improve dramatically. Monitoring for recurrence of fluid accumulation by frequent reassessment of major body systems, physical examination and echocardiography is useful. Placement of a central venous catheter and monitoring of central venous pressure can also be a useful technique in that re-accumulation of pericardial fluid will result in a rise in central venous pressure.

Key prognostic points

Prognosis for dogs with pericardial effusion will depend on the underlying cause of the disease. Surgical removal of a mass on the right atrial appendage will at least temporarily alleviate signs of recurrent pericardial effusion. Surgical removal of right atrial / appendage HSA followed by chemotherapy will prolong life in dogs with pericardial effusion.7 Pericardectomy will temporarily palliate clinical signs of pericardial effusion for most neoplastic processes, and will most often be curative for idiopathic pericardial effusion. Thoracoscopic pericardectomy or creation of a pericardial window may have similar effects.10-12 Treatment with fresh frozen plasma, vitamin K1, and pericardiocentesis will be curative for dogs with anticoagulant rodenticide intoxication. Culture and sensitivity based antimicrobial therapy +/- surgical debridement is indicated for the management of infectious pericarditis. Dogs with left atrial tear secondary to chronic mitral valve regurgitation and left atrial dilation carry a guarded prognosis. Surgical repair of such a lesion has been described.13

Summary

Triage and careful attention to physical examination findings supported by ancillary diagnostic tests and point-of-care diagnostic imaging are the keys to the rapid identification of pericardial effusion in the dog. Rapid identification of problems and institution of treatment will maximize the likelihood of a positive outcome.

References/suggested reading


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Where’s there’s Smoke, there’s Fire: Emergency Treatment of House-Fire Victims
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The emergency clinician is frequently called upon to treat burn wounds secondary to thermal, chemical, electrical, or radiation injury. Most burn wounds seen in veterinary medicine are relatively minor, possibly because animals with severe burns and smoke inhalation are less likely to be rescued from the scene of a house fire. However, life threatening burns and inhalation injury are being seen with increasing frequency and the emergency clinician should therefore be familiar with their pathophysiology and management.

Classification of burns
Burns are commonly classified according to the extent of body surface involved and the depth of injury to the skin. Extent of injury is initially estimated in human burn patients using “the rule of nines”. This rule divides the adult human body into areas corresponding to 9% of the total body surface area, or multiples of 9%. For example, each forelimb comprises approximately 9% of total body surface area; each hind limb, 18%; head and neck, 9%; chest and abdomen, 18%; back, 18%; and perineum, 1%. Body surface area percentages vary in children, and as such, the rule of nines is not typically used in children less than 10 years of age. Although the rule of nines has been cited in veterinary texts, it seems similarly unlikely that these percentages accurately describe the majority of veterinary patients. Other methods of estimating extent of injury include serial halving (Do burns cover more than half the patient’s surface area? If not, do burns cover ¼-½ the surface area? and so forth), or measuring the burn area in centimeters and using a chart to calculate meters² from the patient’s body weight in kilograms.

Depth of injury may be described as first-, second-, or third-degree, or using the more recent terms, partial- and full-thickness. First-degree burns involve only the epidermis (like a sunburn), and are bright red, non-blistered, and painful. First-degree burns typically heal within 5 days without scarring, and are therefore not included in the calculation of extent of burn injury unless they exceed 25% of body surface area. Second-degree, or partial-thickness, burns involve all epidermal layers and extend to various depths within the dermis. Superficial partial-thickness burns involve the epidermis and less than ⅓ of the dermis, and are characterized by blisters, pain, blanching in response to pressure, and intact hairs. The surface may appear moist, red, or mottled. Injuries of this depth typically heal without serious scarring within 2-3 weeks. Deep partial-thickness burns involve destruction of the deep dermal layers and may appear dry, or blistered and moist. As skin thickness is not uniform, partial-thickness burns may interdigitate with full thickness burns, appearing mottled-red intermixed with whitish areas. Deep partial-thickness burns do not blanche, lose hair easily, and heal more slowly, producing scarring and loss of function. They may easily progress to full-thickness injuries as a result of edema, infection, thrombosis, or mechanical injury. Third-degree, or full-thickness, burns involve destruction of the entire dermis, usually extending into the subcutaneous tissues. They are dry, leathery, lack sensation, and appear white or charred. Healing of these injuries can occur only by contracture and epithelial migration from the periphery, or through excision and grafting. Burn injuries that extend into the muscle, fascia, or bone can be seen as well, and are termed fourth-degree burns. These appear similar to third-degree burns, but may result in severe systemic illness if unrecognized due to severe underlying tissue necrosis. Depth of injury can be difficult to assess initially, and usually requires repeated evaluation over the first 24 hours for accurate determination. Once this information is collected, burned patients may be divided into minor, moderate, or severe categories for the purposes of treatment planning.

Pathophysiology of burn shock
Following severe burns (>20% TBSA), a severe systemic inflammatory response may develop within minutes, leading to cardiovascular collapse and multiorgan system failure if not quickly addressed. These systemic manifestations are driven by loss of the protective skin barrier, as well as release of inflammatory mediators from within the damaged tissues. Release of prostaglandins, leukotrienes, and other vasoactive substances leads to a diffuse “capillary leak” syndrome, increasing in proportion to size of burn injury, delay in initiation of resuscitation, age of the patient, and the presence of inhalation injury. This increased vascular permeability results in marked decreases in effective circulating volume as well of the development of edema in injured and non-injured tissues. Edema is further exacerbated by the development of hypoalbuminemia, resulting from loss of albumin through “leaky” vessels, compounded by decreased hepatic albumin production in favor of acute phase protein synthesis. Extensive tissue edema leads to tissue hypoxia at the junction between burned and non-burned tissues (the “zone of ischemia”), and may have adverse effects on depth of burn injury. Thromboxane A₂ and B₂ prostaglandins, cytokines, and reactive oxygen species are produced at the burn site and are associated with local ischemia and further tissue damage. Cardiac output decreases within the first eight hours of burn injury secondary to hypovolemia and myocardial depression associated with release of inflammatory mediators. Arterial blood pressure may be misleading however, as burn patients may have normal or increased blood pressure despite significant hypovolemia due to vasoconstrictive substances released from the burn wound.
Following successful resuscitation, microvascular leak typically “seals” after 18-24 hours. Hypermetabolic response develops during this time with near doubling of cardiac output and resting energy expenditure. Increased gluconeogenesis, protein catabolism, insulin resistance, and weight loss may also be seen. These changes are believed to result from increased cortisol, glucagon, catecholamine, and cytokine release, GI mucosal barrier dysfunction, bacterial translocation, burn wound sepsis, and heat loss. The hypermetabolic response typically persists until all wounds are closed, and continues for some time afterwards.

Sepsis is one of the major causes of death among burn patients. In addition to wound infections, respiratory infections, and catheter-related infections, decreased gastrointestinal perfusion in the first 24 hours following burn injury leads to compromised integrity of the mucosal barrier and allows passage of bacteria and endotoxin. Peak endotoxin levels have been reported to develop as early as 12 hours post-burn,¹ and may contribute to the development of multiorgan failure. It has been reported that patients with extensive burns also have altered humoral and cell mediated immunity attributed to increased levels of cortisol and inflammatory mediators such as TNF, IL-1, and IL-6. This immunosuppression may further contribute to the development of septic complications in these patients.

Inhalation injury contributes significantly to morbidity and mortality in the burned patient. Smoke inhalation triggers release of thromboxane, causing pulmonary vasoconstriction and pulmonary hypertention. Chemical and thermal injuries directly damage the respiratory epithelium, leading to sloughing of the tracheobronchial mucosa, impairment of the mucociliary escalator, and formation of cellular casts that may obstruct the airways and promote bacterial growth. Disruption of respiratory epithelium and vascular endothelium leads to exudation of proteinaceous fluid into the terminal airways and further contributes to respiratory compromise, impaired surfactant production, and bacterial proliferation. Acute lung injury or ARDS may also result indirectly from systemic inflammation related to the burn wound or from sepsis arising from various sources including the lungs, burn wounds, GI tract, or catheters.

Prehospital treatment of the burned patient
The first consideration in treatment of the burned patient is to stop the burning process. Flames should be extinguished and any collars or harnesses that may become constrictive should be removed. Because the skin is slow to cool, the burning process may continue for some time after the patient is removed from the heat source. For this reason burned areas should be cooled with running water for up to 10 minutes. Alternatively, cool wet towels can be placed over the burn areas. Ointments should not be applied at this time as these may hinder the subsequent assessment of extent of injury. Cold water or ice should also not be used as this can rapidly decrease the patient’s body temperature and may contribute to increased wound depth by inducing vasoconstriction. To avoid hypothermia during transport, the patient should be wrapped in several clean, dry sheets or blankets.

Primary and secondary surveys
A primary survey should be performed to determine the extent of injury and to institute treatment as needed. Ensuring a patent airway and supporting breathing should be the first priority, followed by shock resuscitation. 100% oxygen should be administered to any patient suspected to have smoke inhalation injury to hasten the elimination of carbon monoxide. Intubation or emergency tracheostomy may be required if airway edema is severe. In the event of orotracheal intubation, tubes should be carefully secured, as worsening edema may make re-intubation more difficult.

Vascular access may be difficult in hypovolemic, burned patients. Ideally, short peripheral catheters should be placed in non-burned areas, though burned areas may be used in the first 24 hours. If burned sites are used for catheterization, the catheters should be removed within 24-48 hours due to bacterial colonization of these areas. Intraosseous catheters are another good alternative for patients in whom vascular access is limited. Central lines may be required in patients with large burns, those needing parenteral nutrition, or those requiring central venous pressure monitoring, but their use should be avoided whenever possible due to the risks associated with hypercoagulability in burned patients.

Following initial stabilization, a secondary survey should be performed to identify concurrent injuries. Patients should be assessed for neurologic injuries secondary to trauma, hypoxemia, or carbon monoxide poisoning. The abdomen should be assessed for compartment syndrome, gastric distension, or other traumatic injuries. The airways and thorax should be carefully ausculted for stridor, crackles, or wheezes, and adequacy of ventilation should be assessed. The face, oral cavity, and pharynx should be examined for the presence of burns or particulate debris that may indicate inhalation injury. Baseline radiographs should be obtained to evaluate for changes related to smoke inhalation or traumatic injury. Chest radiographs may be normal initially, or bronchial markings may be present. The development of pulmonary infiltrates or lobar consolidation may suggest pneumonia. Arterial blood gas evaluation is useful for determination of parameters related to oxygenation and perfusion. However, because both partial pressure of oxygen (pO₂) and oxygen saturation can be misleading in the presence of carbon monoxide (pulse oximetry will misread carboxyhemoglobin as oxyhemoglobin), cooximetry should also be performed if available to determine carboxyhemoglobin levels. Baseline complete blood count, serum biochemistry panel, and urinalysis should be obtained upon admission. The presence of myoglobinuria may indicate a need for higher fluid rates to avoid renal tubular damage. Coagulation testing should be performed, as burned patients may suffer from
hyper- or hypocoagulable states. Blood typing may be indicated if surgery is anticipated for large burns, as these procedures frequently result in significant blood loss. The eyes should be evaluated for the presence of conjunctivitis, particulate material, or corneal ulceration. Corneal ulcers are common secondary to thermal injury or abrasion by particulate material, so fluorescein staining should always be performed. A topical anesthetic such as proparacaine may be used to facilitate examination behind the third eyelids for foreign material, and the eyes should be copiously flushed with sterile saline. Corneal ulcers may be treated with triple antibiotic ophthalmic ointment and atropine ophthalmic drops.

**Fluid therapy**

The goal of fluid therapy in the burn patient is to restore and maintain perfusion to the tissues while keeping edema fluid to a minimum. The greatest amount of fluid loss in burn patients occurs during the first 24 hours as a result of increased microvascular permeability. Fluids given during this time rapidly leave the vasculature, with colloids having no benefit over crystalloids due to the leakiness of the endothelium. Crystalloids, such as lactated Ringer’s solution, are therefore usually the fluids of choice for the first 24 hours. Hypertonic saline, used in some human institutions to decrease crystalloid requirements, is also of questionable benefit and has been associated with adverse outcomes in burn patients. Fluid requirements can be estimated based on percentage of body surface area burned using the Parkland formula. LRS is given at 4 ml/kg \( \times \) TBSA, with one half of the calculated volume given within the first eight hours, and the second half given over the next 16 hours. The starting point is the time of injury, not the time of hospital admission. Urine output should reach 0.5-1 ml/kg/hr within the first three hours. If it falls below 0.5 ml/kg/hr, more fluid is needed. Lasix should not be used to increase urine output, as this will further deplete effective circulating volume as well as invalidate the use of urine output as an indicator of shock resuscitation. If total resuscitation needs are estimated to exceed 6 ml/kg/% TBSA, central venous pressure (CVP) measurement should be performed to assess intravascular volume. If blood volume is assessed as adequate, dopamine (5-15 ug/kg/min) or dobutamine (3-10 ug/kg/min) may be added to maintain cardiac output and arterial blood pressure.

Many resuscitation formulas recommend adding colloids at 0.5 ml/kg/day \( \times \) TBSA after 24 hours, as colloids are more likely to be retained within the vasculature at that time. (Note: some formulas advocate colloid supplementation as early as 8 hours post-burn). Hetastarch, fresh frozen plasma, or albumin may be used, though it is interesting to note that albumin supplementation in burn patients has not been associated with decreased mortality nor mobilization of tissue edema within the first week. Crystalloids are continued only at doses needed to maintain urine output, approximately 1.5 ml/kg/day \( \times \% \) TBSA.

It is important to emphasize that these fluid formulas should be used only as guidelines, and should be frequently reevaluated and adjusted based on physiologic parameters. Additionally, because these formulas have been derived from experiences with human patients and experimental models in animals, they should be applied cautiously in clinical veterinary patients, and dose reduction may be appropriate in cats.

**Wound care**

Patients with small burns rarely develop overwhelming wound sepsis, and medical management for several days usually allows better determination of wound depth and extent. Wounds should be gently clipped of hair and then rinsed or soaked in dilute povidone-iodine solution. Animals with thick coats may hide more extensive wounds than initially suspected, so liberal clipping should be performed in these cases. After the wounds are cleaned, topical agents may be applied to decrease pain, prevent desiccation, and delay bacterial growth. Silver sulfadiazine is used most commonly as it has broad antibacterial activity, is soothing, and has no systemic effects. Eschar penetration is poor however. In contrast, mafenide acetate has excellent eschar penetration and similarly broad antibacterial effects, but can be painful when applied. Topical agents can be applied directly to wounds with a clean tongue depressor, or the burn can be covered with impregnated dressings. Gloves should be worn at all times during wound care to avoid spread of resistant organisms.

The choice of dressing is a much-debated topic. Of critical importance is the maintenance of a moist environment to promote rapid wound healing. This may be accomplished through the use of semi-occlusive dressings, or with various types of hydrogel shown to speed healing and to decrease scarring of partial thickness wounds. Wounds with heavy exudation may be managed with dry, absorbent bandaging material applied in layers. Following application of silver sulfadiazine, a non-adherent and porous inner layer is applied, allowing passage of fluid and exudates. Absorbent padding or gauze should then be applied, followed by an elastic outer layer. Bandages should be loose enough to avoid putting additional pressure on the wounds.

Patients with more extensive burns generally do better if full thickness wounds are excised within the first week, starting 24-48 hours following burn injury. Early wound excision has been shown to circumvent the development of wound sepsis and SIRS, attenuate the hypermetabolic response, and reduce morbidity and mortality, length of hospital stay, and pain in patients with large burn wounds. Burns >20% total body surface area may require staged procedures, and burns > 50% TBSA make closure with autograft impossible. Once autograft closure is no longer feasible, temporary closure may be performed using cadaver allografts, porcine xenograft, or synthetic skin substitute, though these procedures are not routinely performed in veterinary medicine. Research is currently underway to evaluate the use of synthetic membranes such as Integra (Integra Life Sciences, Plainboro, NJ) that mimic
vapor transmission characteristics of normal skin and allow fibrovascular ingrowth from the host, ultimately undergoing biodegradation.7

Prophylactic antibiotic usage is controversial as penetration of the eschar is unlikely and the potential for development of antibiotic resistance exists.8 As such, antibiotic therapy is generally reserved only for documented infections and should be based upon culture and sensitivity of full thickness eschar biopsies. Excision of eschar has been associated with bacteremia however, so intraoperative antibiotic administration has been recommended.

Inhalation injury
Management of smoke inhalation is typically supportive. The head should be elevated and excessive fluid therapy avoided to minimize development of edema. However, it should be noted that patients with inhalation injury typically have higher fluid requirements than those with burn injury alone due to increased severity of systemic inflammatory response. Bronchospasm may be treated with systemic β agonists such as terbutaline, or inhaled albuterol administered via spacer (Aerokat, Trudell Medical, London, Ontario). Prophylactic antibiotics have not been shown to reduce morbidity or mortality associated with smoke inhalation, and may contribute to resistant infections. Antibiotics should therefore be reserved for documented infections, and should be based on tracheal wash culture and sensitivity when possible.

Supplemental oxygen should be provided as needed, based on blood gas analysis. Carbon monoxide poisoning, if present, may be treated with hyperbaric oxygen therapy, but in most cases administration of 100% oxygen for 6 hours9 constitutes appropriate therapy without the increased risks and cost involved in transporting a critically ill patient to a facility with a hyperbaric oxygen chamber. Administration of 100% oxygen has been shown to shorten the half life of carboxyhemoglobin from several hours to approximately 74 minutes (range 26 to 148 minutes).10

If ventilation is required, lung protective strategies should be use to minimize ventilator induced lung injury. Peak airway pressures greater than 40 cm H2O and FiO2 greater than 0.60 should be avoided, using PEEP, faster rate, and permissive hypercapnea to maintain an oxygen saturation greater than 90% with a PCO2 less than 65 mmHg. Strict attention should be given to suctioning of airways, and aspesis should be maintained to minimize the likelihood of nosocomial infection.

Nutritional support and the hypermetabolic response
Nutritional support is an important component of burn care, and should ideally be provided as soon after resuscitation as possible. Enteral nutrition using a nasogastric or esophagostomy tube is ideal, as this is believed to decrease gut atrophy, possibly decreasing bacterial translocation and subsequent sepsis. Resting energy requirements may be calculated using the formula [RER= Weight (kg) x 30 + 70]. Although the use of an illness energy requirement calculation (IER) has largely fallen by the wayside in veterinary medicine, multiplying resting energy requirements by an IER of 1.3-1.7 may be appropriate in the burned patient to compensate for the anticipated hypermetabolic response. The use of such formulas has been shown to correlate poorly with actual energy requirements in both human and veterinary patients however, and as such, indirect calorimetry would be a more accurate method of determining resting energy requirements if available. Critically ill patients or those with very large burns may not tolerate their full nutritional requirements because of ileus or vomiting, and these patients may benefit from the supplementation of parenteral nutrition through a designated central line.

Pain management
Pain can be reduced initially using cool compresses and soothing ointments such as silver sulfadiazine. Once burn shock has been adequately controlled, narcotics may be administered. Pure agonists such as fentanyl (CRI: 3-5 ug/kg/hr), hydromorphone (CRI: 0.025 mg/kg/hr), or morphine (0.5-1 mg/kg SQ q4h) are recommended for patients with moderate to severe pain. Ketamine can be useful for the relief of somatic pain, and may be used in conjunction with narcotics at a constant rate infusion of 0.15-0.6 mg/kg/hr. Lidocaine may provide adjunctive analgesia in addition to free radical scavenging properties, and may also be added at a rate of 1.5-3 mg/kg/hr. If using constant rate infusions, a loading dose equal to the hourly rate should initially be administered.

References

