## VETERINARY PRACTITIONER PROGRAM - JANUARY 31 - FEBRUARY 2, 2020

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VETERINARY PRACTITIONER
PROGRAM

PROCEEDINGS

January 31 - February 1, 2020
Canine Cardiac Diseases

Rebecca Gompf, DVM, MS, DACVIM (Cardiology) – UTCVM Cardiology

I. CANINE CHRONIC VAVULAR HEART DISEASE (CVHD) (Endocardiosis) (Chronic degenerative valve disease, CDVD)

A. Background

1. 10% of dogs have heart disease.
2. 75% of the dogs with heart disease have CVHD.
3. Mitral and tricuspid valves are commonly affected, but mitral valve is the most commonly affected. It can also affect the aortic valve.
4. Most dogs are ≤ 20kg (45 pounds).
5. Slowly progressive and very unpredictable. Most dogs that develop murmurs take 2-3 years for the heart to enlarge to the point of either needing medication or having heart failure.
6. May progresses more rapidly in large breeds.
7. Cavaliers get it at a young age.
8. Inherited component in Cavaliers and dachshunds. Environment may play a role in the severity of the disease.
9. While it is the most common heart disease, most dogs die of other problems and not from heart failure.
10. These are the same dogs that get respiratory problems (chronic bronchitis, collapsing tracheas, etc.). Therefore, if a dog is coughing or is dyspneic and does not have a murmur, his underlying problem is respiratory, not cardiac.

B. Pathophysiology

1. Mitral valve becomes deformed so that regurgitation occurs from the left ventricle into the left atrium. The left atrium gets an increased volume so it dilates.
2. Mitral regurgitation is a volume overload of the left side of the heart.
   a. It causes left atrial dilation. As the severity of the regurgitation increases, so does the left atrial pressure and the left atrial size.
   b. Due to the increased left atrial pressure and increased left ventricular volume:
      1) The left ventricle dilates and later hypertrophies (eccentric hypertrophy).
      2) Pulmonary veins, then capillaries, and finally pulmonary arteries have increased pulmonary pressure (secondary pulmonary hypertension).
   c. The left atrial enlargement causes compression of the left main stem bronchus which may result in coughing. This is the most common cardiac cause of coughing (not left heart failure) in dogs with chronic valvular heart disease.
3. Arrhythmias may develop and can further decompensate the heart.
   a. Atrial premature complexes, atrial tachycardia, and atrial fibrillation are due to the markedly dilated left atrium.
   b. Ventricular premature complexes and ventricular tachycardia are due to the hypoxia of the cardiac muscle when the heart fails.
4. Affected dogs are not more prone to developing bacterial endocarditis of these valves.
5. Prevalence of CVHD increases with age.
6. Factors that determine whether or not the dog will become symptomatic from his CVHD have not been identified.
7. Eventual outcomes:
   a. 70% are incidental findings and dogs die of other problems.
   b. Coughing due to left atrial enlargement
   c. Left heart failure (with dyspnea)
   d. Arrhythmias causing syncope

C. Classes of CVHD dogs
1. Stage A: Dogs at risk of developing CVHD.
2. Stage B1: Asymptomatic dogs with no cardiac remodeling or those hearts are not big enough to fit the EPIC Criteria.
3. Stage B2: Asymptomatic dogs with left heart enlargement that fit the EPIC criteria.
4. Stage C: Dogs who have past or current signs of left sided congestive heart failure associated with structural heart disease.
5. Stage D: Dogs with end stage disease that is refractory to standard treatment.

D. Stage A CVHD dogs
1. Small breeds
2. Recommendations
   a. Yearly physical exam
   b. No drug therapy
   c. No dietary restrictions, well-balanced diet, and optimum body weight
   d. If dog is less that 6-8 years old when a murmur develops, do not breed that dog.
3. Once a murmur develops, they move into Stage B.

E. Stage B
1. Dogs now have a murmur of mitral regurgitation (MR)
2. Recommendations
   a. Do thoracic radiographs yearly to monitor the progression of the disease.
   b. Check blood pressure yearly.
   c. Minimum lab work: PCV/TP, creatinine urinalysis
   d. Do an echocardiogram if:
      1) There is moderate to severe cardiomegaly,
      2) The cause of the murmur is not apparent,
      3) The severity of the problem cannot be determined by radiographs.
      4) It is a large breed dog.
3. Stage B1 (dog with just a murmur and no significant remodeling)
   a. No drug or dietary therapy is needed.
   b. Recheck small dog every 12 months.
   c. Recheck large breeds every 6 months.
   d. If Pimobendan is started, it causes thickening of the chordae tendineae and may cause ruptured of the chordae resulting in increased mitral regurgitation and potentially heart failure.
   e. If dog needs a dental or anesthesia for any problem, it has no greater risk under anesthesia than a normal dog as far as the heart is concerned.

4. Stage B2 (dog with a murmur and significant cardiomegaly)
   a. Radiographs
      1) Moderate left ventricular and left atrial enlargement—will meet the EPIC criteria on echo
         a) If the left atrium is not big or only mildly big, an echocardiogram has to be done to stage the dog's disease.
         b) Both VD (or DV) and right lateral radiographs have to be done in order to diagnose left atrial enlargement as VHS scores are not 100% accurate by themselves.
      2) Asymptomatic dogs with huge hearts on radiographs definitely need pimobendan and do not require an echocardiogram.
   b. Epic Trial—dogs with moderate heart enlargement
      1) 360 dogs at 36 centers
      2) If meet these criteria
         a) Vertebral heart score ≥ 10.5
         b) Left atrial dilation on 2D short axis view or echocardiogram with LA:AO ≥ 1.6
         c) Corrected left ventricular size (correlated to weight) ≥ 1.7.
      3) Pimobendan--Prolonged the time until dogs went into left heart failure by 15 months.
      4) Prognostic indicators
         a) The larger the left atrium, the poorer the prognosis.
         b) The higher the heart rate, the poorer the prognosis.
         c) The bigger the heart, the worse the prognosis.
         d) The higher the blood pressure (within normal limits), the better the outcome.
      5) Pimobendan also prolonged the life span after the dog went into failure.
   c. Severe cardiomegaly with no heart failure
      1) Severe dilated left ventricle and left atrium.
      2) Decreased left ventricular systolic function on echo
      3) Pimobendan
      4) Enalapril—may be of benefit also
Dental procedures or other anesthetic procedures for B2 dogs

1) Start the pimobendan and delay the procedure if possible for a couple of weeks
2) Avoid alpha 2 drugs as they will cause arteriolar constriction resulting in an increased work load of the left ventricle and increased mitral regurgitation.
3) Use fluid wisely.
4) Dogs with moderate heart enlargement have only a slight increased risk under anesthesia.
5) Dogs with severe left heart enlargement should ideally have an echocardiogram done as they as most likely borderline heart failure dogs. They will have a definite increased risk under anesthesia.

Stage C dogs (dogs that have documented heart failure or currently have failure)

1. Causes of prolonged coughing in an older, small breed dog with mitral regurgitation.
   a. Enlarged left atrium compressing the left main stem bronchus
   b. Primary respiratory disease (evident on radiographs)
   c. Pneumonias—fungal, viral, allergic (PIE), bacterial, parasitic (lungworms).
   d. Chronic bronchitis
   e. Tracheal collapse—either primary or secondary due to enlarged left atrium, mediastinal mass, enlarged lymph nodes
   f. Heartworms
   g. Pulmonary neoplasia—Primary or metastatic

2. Less common causes of prolonged coughing
   a. Left heart failure due to CVHD or congenital heart defects (large ventricular septal defect, patent ductus arteriosus)—dog also is dyspneic along with soft, moist cough
   b. Pericardial effusions
   c. Neoplasia involving the myocardium
   d. Dyspnea is increased rate and effort of breathing. Normal sleeping respiratory rate is less than 30 breaths per minute.

3. Diagnostics
   a. Thoracic radiographs are done when the dog is stable or if it is not responding to diuretic therapy. Pulmonary edema is in the hilar area but also the right caudal lung lobe in the DV view along with distended pulmonary veins.
   b. Echocardiogram is highly recommended when the dog is stable.
   c. Serum NT-pro BNP
      1) Due to stretch in the ventricles, BNP is elevated in the blood.
      2) If it is very high, then the dog has heart failure or soon will have it.
      3) If it is low, then the dog’s dyspnea is not due heart disease.
      4) If NT-ProBNP and ALT are elevated, the dog has a poor prognosis.
5) Problems
   a) There is a gray zone (no clear cut-off value), so values in the midrange do not tell you if the dog’s dyspnea is due to cardiac disease or not.
   b) Have to send it off and it takes two days to get results.
   c) Sensitivity and specificity decreased if it is used as a screening test. Therefore, just use it in dyspneic dogs.
   d) Must use the correct tubes and keep on dry ice to get accurate results.

4. Therapy
   a. Furosemide
      1) 2 mg/kg. IV, IM, or sub-q every hour until the respiratory rate decreases significantly or a total of 8 mg/kg has been given over four hours.
      2) Continue at 1 mg/kg/hr. CRI for severe pulmonary edema until the respiratory rate decreases significantly.
      3) Allow free access to water.
   b. Cage rest with oxygen
   c. Pimobendan: 0.25-0.3 mg/kg PO BID
   d. Remove ascites (abdominoacentesis) and/or pleural effusions (thoracentesis) to relieve dyspnea in right heart failure
   e. Good nursing care
      1) Monitor animal’s temperature and humidity in oxygen cage
      2) Elevate head on pillows
      3) Sedate if necessary butorphanol or buprenorphine
   f. Other acute therapy
      1) Sodium nitroprusside CRI for 48 hours in nonresponsive CHF
      2) Nitroglycerine ointment- No studies to show it helps, but also it has no side effects.
      3) ACE inhibitors- Better for chronic management, not acute
      4) Mechanical ventilation- Only considered if the heart is not huge and the dog has acute ruptured chordae tendineae on echocardiogram.
      5) With right heart failure, drain the ascites and/or thorax if the dog is dyspneic.
   g. Chronic therapy
      1) Furosemide to effect (1-2 mg/kg. q. 8-12 hours)
      2) Enalapril (0.5 mg/kg. q. 12 hours)
      3) Pimobendan (0.25-03 mg/kg. q. 12 hours)
      4) Spironolactone (1-2 mg/kg. q. 12 hours)
      5) Sotalol for ventricular arrhythmias (Start at 1 mg/kg. q. 12 hours and increase to 2 mg/kg. q. 12 hours after 3 days)
6) Atrial fibrillation therapy
   a) Beta blockers (atenolol or Carvedilol)
      1-2 mg/kg q. 12 hours
   b) Calcium channel blockers (diltiazem)—use sustained release Dilacor XR or Cardiozem CD
      1.5-5 mg/kg q. 12 hours or 10 mg/kg q. 24 hours
   c) Digoxin 0.01 mg/kg q. 12 hours if <20 kg, and 0.22 mg/m² q. 12 hours if >20 kg. (Subtract 10% for exilir)
   d) Digoxin and diltiazem are the most effective at decreasing the heart rate.

h. Other possible therapy
   1) Nitrol ointment should not be used long-term as dogs may develop a tolerance to it and ACE inhibitors are much more effective.
   2) Spironolactone- One study says that it is beneficial in dogs with left heart failure. It is definitely beneficial to use it with furosemide for right heart failure.
      a) Weak diuretic
      b) Blocks aldosterone which causes fibrosis in the heart
      c) Can elevate potassium levels
      d) May not be effective if there is renal disease or failure

5. Home program
   a. Monitor body weight
   b. Monitor appetite
   c. Monitor respiratory and heart rates—sleeping respiratory rates are good indication of early left heart failure (rate should be less than 30 breaths per minute)
   d. Cough suppressants- No consensus
   e. Bronchodilators- No consensus
   f. Dietary recommendations
      1) 60 kcal/kg body weight to prevent cardiac cachexia
      2) Weigh dog on each visit
      3) Avoid low protein diets-use heart diets, not kidney diets
      4) Modest decrease in sodium
      5) Treat anorexia
   g. Monitor potassium levels and supplement as needed.
   h. Monitoring of magnesium levels-no consensus
   i. Omega3-fatty acids- No consensus, but may be of benefit if dog has decreased appetite, muscle loss, or arrhythmias.

6. Anesthesia for procedures
   a. These dogs do have an increased risk but if their heart disease is stable, they have less risk than when it is unstable.
   b. Weigh risk versus benefits of the procedure. Consult with a board certified anesthesiologist for the best protocol for your individual patient.
G. Stage D (dogs with advanced CVHD that keep going back into heart failure)
1. On standard therapy of:
   a. Furosemide
   b. ACE inhibitor
   c. Pimobendan
   d. Arrhythmia medication
   e. Sodium restriction
2. Diagnostics are the same for Stage C.
3. Acute therapy
   a. Furosemide in IV boluses or constant rate infusion
   b. Drain pleural effusion and/or ascites
   c. Oxygen cage
   d. Reduce the afterload rigorously
      1) Sodium nitroprusside
      2) Hydralazine
      3) Amlodipine
      4) Continue the Pimobendan and ACE inhibitor along with one of the above.
      5) Avoid blood pressures under 85 mmHg systolic pressure.
      6) Measure creatinine before therapy and 72 hours later.
      7) Monitor ECG continuously.
   e. Sodium nitroprusside and dobutamine CRI- no consensus
   f. Sildenafil--no consensus; will reducing pulmonary hypertension benefit the animal acutely or at all?
   g. Bronchodilators-- no consensus.
4. Chronic therapy
   a. Increase furosemide (monitor renal function) or switch to torsemide (0.1-0.2 mg/kg q. 12-24 hours) which will:
      1) Increase urine volume
      2) Not decrease potassium
      3) Have an antifibrotic effect
      4) Not have tolerance develop
      5) Can severely dehydrate an animals so monitor closely.
   b. Same therapy as Stage C
   c. Start spironolactone if the dog is not on it.
   d. Thiazide--no consensus.
      1) A few cardiologist have seen renal failure and electrolyte problems in these patients.
      2) Used when nothing else works?
      3) Used with furosemide and in combination with spironolactone (AldaUse at lower dose than what is in the literature.
   e. Increase Pimobendan to TID--no consensus, as no studies to say it will help. The higher the dose of Pimobendan, the more likely it is that ventricular arrhythmias will occur.
   f. Sildenafil
      1) No consensus
      2) Have to document pulmonary hypertension on Doppler in order to use it.
g. Reduce the dose of beta-blockers if the dog is on them.

h. Cough suppressants—no consensus.

i. Bronchodilators—no consensus

j. Dietary therapy same for Stage C, but be sure to use low sodium diets in any dog whose heart failure is hard to control.

H. Prognosis

1. Stage A
   Normal life span

2. Stage B
   a. B1: Dogs may never have a problem with their heart disease.
   b. B2: Pimobendan prolongs time to failure by 15 months (moderate heart size); huge heart, pimobendan prolongs the time to failure BUT most of these dogs go into heart failure within a year and then have 6-12 months to live after that.

3. Stage C
   a. Life span up to 1 year or longer (6-12 months) depending on the animal's heart size
   b. Depends on how big the heart is. The bigger the heart, the shorter the life span.

4. Stage D
   a. Very guarded prognosis
   b. 3-6 months up to a year

I. Chronic valvular heart disease of the tricuspid valve

1. Many times it occurs along with mitral valvular disease.
2. These animals usually present with signs of right heart failure.
3. Treat the right heart failure in the same manner as left heart failure but use spironolactone with the furosemide to control the ascites.
4. Drain the ascites and/or pleural effusion if the dog is dyspneic.

J. Cardiac cachexia—with either side of the heart failing but worse with right heart failure

1. The heart is a muscle—it needs protein so no K/D diets or other low protein diets.
2. Minimum of 60 Kcal/kg. per day
3. With right heart failure, multiple small meals instead of one big meal.
4. Puppy chow?
5. Low sodium diets
6. Entyce?
REFERENCES


• Gordon, SJ et al., Chronic valvular heart disease treatment in Veterinary Clinics of North America—Small Animal Practice 2017; 5: 955-


* Kittleson MD and Kienle RD: Small Animal Cardiovascular Medicine, VIN book library, Chaps. 19, 24


II. CANINE DILATED CARDIOMYOPATHY (DCM)

A. Primary or idiopathic DCM has an abnormality of the myocardial tissue that results in decreased contractility and dilatation of the left and right ventricles and the atria. It is uncommon to have dilation occur before decreased contractility occurs.

1. Chronic degenerative valve disease can be present but are not primary lesions.
2. Pump failure (systolic dysfunction) occurs due to poor myocardial function. The heart cannot pump the blood presented to it. Therefore, it must dilate to handle the blood volume not pumped out of the ventricle.
3. The papillary muscles are flat and atrophied.
4. Atrial fibrillation can occur and worsens the failure by decreasing the ventricular filling time and by losing the normal atrial input to filling.
5. Ventricular preventative complexes (VPCs) result from myocardial hypoxia.
6. Due to the myocardial dilation, the atrioventricular annulus can dilates so that secondary mitral and/or tricuspid regurgitation can occur.
   a. The murmurs are soft and do not correlate with the severity of the disease.
   b. The regurgitation(s) contributes to the volume overload by decreasing forward flow.
   c. When the heart cannot dilate further, heart failure occurs.
7. Poor cardiac output and venous congestion result in signs of left or right heart failure or both. Right heart failure alone is uncommon while left heart failure alone is common.

B. Secondary DCM is caused by other diseases

1. Only about 10% of all cases fall in this category in dogs.
2. In other species, the occurrence can be higher.

C. Natural history of DCM

1. Prevalence 0.5% of all cases in VMDB from Purdue University from 1986-1991(cats and dogs combined). Prevalence is low as compared to degenerative valve disease.
2. Breed Predisposition—mostly large to giant purebred dogs and more in males
   a. Doberman- Autosomal dominant trait
   b. Boxer (more prevalent in some lines) - autosomal dominant trait in one study
   c. American cocker spaniels and English cocker spaniels
   d. Newfoundland
   e. Golden retriever
   f. Labrador retriever
   g. Irish wolfhound
   h. German shepherd
   i. Dalmatian
   j. Scottish deerhound
k. Portuguese water dogs get early onset DCM inherited as an autosomal recessive trait. There is abnormal taurine metabolism leading to low plasma taurine levels in some but not all of affected puppies.

3. Age
   a. Prevalence increases with age
   b. Dobermans usually between 7-10 years old
   c. Great Danes at 4-7 years old

4. Etiology: Unknown
   a. Abnormalities in structure and function of several areas of the heart.
   b. The result is abnormal cardiac muscle with poor function.
   c. Many abnormalities have been documented but most are secondary to the disease process and not a primary abnormality.
      1) Decreased myocardial carnitine
      2) Decreased myocardial myoglobin
      3) Decreased electron transport with decreased ATP
      4) Increased lactate
      5) Decreased total CK and isoenzyme CK-MB
      6) Decreased sarcoplasmic reticulum calcium transport
   d. Viruses are NOT the cause
   e. Immune mediated diseases are NOT the cause

D. Other etiologies
   1. Taurine deficiency was a major cause of DCM in cats prior to 1987 but now it is supplemented in cat food and the incidence has fallen dramatically.
   2. Taurine deficiency can cause DCM in some breed of dogs
      a. American cocker, Irish wolfhound, golden retriever, Newfoundland
      b. Vegetarian and vegan diets may be deficient in taurine.
      c. Lamb and rice diets, unless supplemented with taurine, are deficient.
      d. Protein restricted diets can be deficient in taurine.
      e. Raw diets usually are not usually deficient but should be analyzed.
   3. Grain free diets high in lentils, peas, or potatoes can cause DCM by blocking taurine absorption from the GI tract or by the way they are processed can inactivate taurine. Supplementing taurine may not help as the supplement’s absorption is also blocked.
   4. Carnitine deficiency only rarely causes DCM in dogs.
      a. 50-90% of dogs with DCM have low carnitine levels but only a few ever respond to supplementation with it.
      b. Blood levels do not reflect muscle levels.
      c. Dogs under a year of age responded better to treatment if L-carnitine is added.
      d. May stimulate the dog’s appetite.
      e. One family of boxers responded to L-carnitine supplementation so all boxers with DCM should be started on it.
E. Clinical signs
   1. Usually occurs in large breed any time after 2 years of age but has been seen in dogs under a year of age.
   2. History
      a. Signs of heart failure such as dyspnea, coughing, orthopnea
      b. Sudden weight loss, especially loss of muscle mass (cardiac cachexia)
      c. Weakness
      d. Exercise intolerance
      e. Lethargy and anorexia
      f. Abdominal distension due to ascites
      g. Syncope occurs more in Boxers and Dobermans due to VPCs.
      h. Cool extremities
      i. A few are asymptomatic if they are detected early in the disease process.
      j. Sudden death can be the first sign and is due to ventricular arrhythmias.

F. Physical exam
   1. Dogs with early DCM that are not in heart failure have a normal physical exam (except a few might have arrhythmias such as atrial fibrillation or ventricular premature complexes that can be heard on physical exam).
   2. Weight loss can be severe.
   3. Pulse abnormalities include a hypokinetic pulse. Pulse deficits due to arrhythmias (atrial fibrillation, VPCs, ventricular tachycardia) can also be present.
   4. Dyspnea or coughing can occur due to pulmonary edema, ascites, and/or pleural effusion.
   5. Decreased pulmonary and heart sounds can be due to the presence of pleural effusion. Increased lung sounds can indicate pulmonary edema.
   6. The heart may sound normal or may have an S3 gallop, a soft murmur of mitral or tricuspid regurgitation, or an arrhythmia.
   7. An erratic heart rhythm with pulses deficits can be heard with atrial fibrillation (tennis shoes in the dryer).
   8. An enlarged liver or spleen may be felt in the abdomen or the abdomen may be distended with ascites.
   9. Distended peripheral veins occur if the right heart has failed.
   10. A fluid line can be percussed in the thorax if pleural effusion is present.

G. ECG
   1. The response of the body to decreased cardiac output due to heart failure is a sinus tachycardia.
   2. About 85% of the dogs will have atrial fibrillation.
   3. Some dogs, especially Boxers and Dobermans, will have ventricular arrhythmias.
4. A 24-hour Holter monitor is a good way to screen a dog for subclinical DCM.
   a. Some dogs develop ventricular arrhythmias prior to the time that systolic dysfunction is seen on the echo.
   b. Dobermans with greater than 50 VPCs in 24 hours have DCM.
   c. Ventricular arrhythmias are common in dogs with DCM and the Holter is better at detecting them.
   d. Complex ventricular arrhythmias and runs of ventricular tachycardia on a Holter predict a higher risk of sudden death.

H. Radiographs
   1. Generalized cardiomegaly that is mild to severe depending on the stage of the disease and the breed.
   2. Pulmonary congestion and edema occur in early cases. Pleural effusion, ascites, and increased caudal vena cava size occur in later cases.
   3. The Doberman heart does not appear globoid as in other breeds.

I. Echocardiography
   1. Dilation of the atria and ventricles with thin muscle mass is present on the echo (can be one or both sides of the heart involved).
   2. Decreased myocardial systolic dysfunction is evident.
      a. Decreased left ventricular fractional shortening in the teens is common (normal is 30-45%). This is just one measure of contractility.
      b. The ejection fraction is decreased below 40%.
      c. The right ventricular size and function can only be estimated and cannot be objectively assessed.
   3. Doppler will show mitral and/or tricuspid valve regurgitation due to:
      a. Stretching of the mitral or tricuspid annulus due to dilation of the ventricle
      b. Position of the papillary muscles changes due to ventricular dilation.
      c. It is uncommon for the dog to have both DCM and chronic valvular heart disease resulting in heart failure. (The mitral valve changes may be incidental.)

J. Laboratory results
   1. Prerenal azotemia is common with severe DCM and represents poor cardiac output with decreased tissue perfusion.
   2. Mildly elevated liver enzymes are usually present due to liver congestion.
   3. Ascites or pleural effusions are modified transudates (protein rich transudates) that can have a lot of protein present so that the animal may have a peripheral hypoproteinemia but an albumin less than 1 mg/dl is uncommon.
4. Electrolyte imbalances
   a. Hyponatremia can be due to water retention and carries a poor prognosis.
   b. Hypokalemia can be due to anorexia or diuretic use.
5. Cardiac troponin I increases slightly with disease and heart failure but is not good for screening for subclinical DCM.
6. NT-proBNP increases with severe heart disease and heart failure and is fairly good for screening for subclinical disease. In addition, it helps differentiate between dyspnea due to heart failure and that due to lung disease.
7. Plasma taurine levels should be measured in cats, American cocker spaniels, Golden Retrievers, Portuguese water dogs, dogs on homemade diets, dogs with cystinuria, or dogs that are of atypical breeds for the development of DCM or are on grain free diets.
8. Plasma blood levels of carnitine are not useful.
9. Hypothyroidism can be found in some of these dogs with DCM, especially in Dobermans and Cocker Spaniels.

K. Therapy
1. Subclinical cases (prior to failure)
   a. Treat ventricular arrhythmias
   b. Pimobendan delays the onset of clinical signs and prolongs the survival time in dogs (Dobermans) so it has been tried in other breeds.
   c. ACE inhibitors
      1) Recommended in people with DCM prior to failure
      2) Benazepril delays the onset of heart failure in dogs.
   d. Beta Blockers
      1) In people, beta-blockers improve ventricular function.
      2) Carvedilol was studied in dogs and did not improve survival in these dogs.
2. Heart failure therapy--acute
   a. Furosemide, cage rest, oxygen
   b. Pimobendan when the dog can tolerate oral drugs.
   c. Other positive inotropes if the dog is in severe heart failure
      1) Dobutamine
      2) Dopamine
   d. Vasodilators—be very cautious as hypotension will decrease cardiac output further and make the situation worse so their use is usually avoided.
      1) Nitrol Ointment- topical
      2) Nitroglycerin or sodium nitroprusside IV.
   e. Drain ascites and pleural effusions if they are contributing to the animal’s dyspnea and/or discomfort.
f. Control the supraventricular arrhythmias by using digitalis and diltiazem together as they give better control than when used individually.

g. Ventricular arrhythmias
   1) Lidocaine has no effect on contractility and is a good first line drug. Just watch your fluid volume.
   2) Mexiletine also has no effect on contractility but is usually only used if sotalol does not control the VPCs.
   3) Sotalol is a negative inotrope so use cautiously when in the dog is in failure but once the failure is controlled, sotalol does not tend to put the dog back in failure.
   4) Amiodarone is used when the VPCs are refractory to sotalol and mexiletine. 45% of the dogs with DCM on amiodarone developed signs of liver failure there were reversible when the amiodarone was stopped.

h. Additional therapy
   1) L-carnitine has been found to be deficient in the heart muscle of 50-90% of the dogs with DCM. However, supplementation in the majority of dogs only makes them feel better. However, dogs less than 1 year of age should be supplemented with it as they do better. In addition, one family of Boxers with DCM has improved with its use.
   2) Taurine therapy does not seem to be of benefit in large breeds. However, golden retrievers, Newfoundland, and cocker spaniels may respond to it and improve. In addition, dogs on grain free diets should be switched to another diet and placed on taurine.
   3) Coenzyme Q10 has not shown any benefits, but it also has no known side effects. Controlled studies have not been done with it.
   4) Low sodium diets may be of benefit if the dog will eat them.
   5) Fish oils have been shown to help the heart muscle to contract better and help to control ventricular arrhythmias. Omega-3 fatty acids are also antioxidants.
   6) Treat cardiac cachexia.
   7) New appetite stimulant which is grelinan (Entyce), is now on the market. It may help to get these dogs to eat.
   8) Recommended 60-100 Kcal/kg per day. Remember that puppy chow has lot of calories with less volume of food. Also, feed multiple small meals a day instead of one big meal.

L. Prognosis
   1. Subclinical period last 2-4 years prior to the onset of signs.
   2. The course of the disease is faster the younger the dog is when it goes into heart failure.
   3. About 50% of dogs with DCM who have gone into heart failure are alive one year after diagnosis (excluding Dobermans and Boxers).
   4. 9-12 months is the average survival time.
5. Severe cardiac cachexia is common after the right heart fails but also mild cachexia can occur with left heart failure.

6. Dobermans and Boxers have a poorer prognosis (3 months average).

7. Gastric torsions can occur in any large breed dog, including those with DCM. If the dog’s heart disease is well stable, the dog’s risk at surgery is only slightly higher than a normal dog’s.

M. Doberman dilated cardiomyopathy (DCM)

1. Autosomal dominant gene mode of inheritance (actin and desmin genes)

2. Males tend to get DCM more than females, and females tend to be older at the time of developing heart failure (Median age: 9.5 years for females and 7.5 years for males).

3. Normal Dobermans can have a fractional shortening as low as 25% on their echo, so Dobermans with DCM may have fractional shortening less than 25%, (most are in the teens). A fractional shortening between 25-30% is suspicious of DCM but is not diagnostic.

4. Three stages of the disease:
   a. Stage one
      1) No clinical signs
      2) All tests are normal
      3) Can last indefinitely
      4) 50% of “normal” Dobermans over ten years old have numerous VPCs and some echocardiographic changes. Are they carriers of this disease?
   b. Stage two—preclinical or occult stage
      1) No symptoms and can last 2-4 years
      2) Ventricular premature complexes
      3) Echocardiographic changes of decreased systolic function
      4) Can have both VPCs and echocardiographic changes
      5) About 20-30% die in this stage from sudden death due to the VPCs.
      6) Predictors of sudden death include
         a) Large hearts—the bigger the heart the more likely to have sudden death.
         b) Elevated – NT pro BNP levels that increase as the heart size increases.
   c. Stage three – Congestive heart failure.
      1) Often Dobermans appear to go into congestive heart failure suddenly.
      2) More males die of heart failure than females.
      3) Most symptomatic Dobermans die within three months of diagnosis.
      4) Dobermans with biventricular failure on presentation have a worse prognosis (median survival of 3 weeks)
      5) Dobermans with left heart failure alone survive about 7 weeks.
5. **Diagnosis of DCM**
   a. ECG or Holter for VPCs
   b. Doberman radiographs are not typical of other breeds.
      1) Their hearts are enlarged but not globoid (take radiographs of a normal Doberman and keep them for reference).
      2) Their pulmonary edema may be diffuse like cats and can be mistaken for pneumonia.
   c. Echocardiography for decreased systolic function and left heart size.
   d. NT pro-BNP may or may not be helpful, sometimes elevated in preclinical stage

6. **Treatment of Stage two (preclinical stage)**
   a. **Ventricular arrhythmias**
      1) Lidocaine boluses followed by CRI for severe arrhythmias.
      2) Sotalol
      3) Sotalol plus mexiletine
      4) Amiodarone
      5) Dobermans who do not get antiarrhythmic therapy for the VPCs have a higher incidence of sudden death (30-50%)
   b. **Decreased systolic function**
      1) Pimobendan delayed the onset of heart failure by 9 months and prolonged the time to death due to all causes.
      2) Enalapril showed some benefit in one study in delaying the onset of heart failure.

7. **Treatment of heart failure**
   a. Pimobendan
   b. Enalapril
   c. Furosemide
   d. Spironolactone

8. **Treatment of atrial fibrillation**
   a. Beta blocker (atenolol)
   b. Calcium channel blockers (diltiazem)
   c. Digoxin--Dobermans are sensitive to digoxin so use half the dose of other big dogs their size (Dobie dose is 0.125mg every 12 hours)

9. Dobermans tend to be hypothyroid and should be checked for this problem. If they are, then they should be treated, as normal levels of thyroid hormone are necessary for normal contractility of the heart.

10. **Current recommendations for breeding Dobermans**
    a. Yearly Holter monitor
    b. Yearly echocardiogram
    c. Genetic testing once at North Carolina State – one gene mutation has been identified.
N. Boxers with dilated cardiomyopathy
1. They also do poorly and live only about 3 months after diagnosis.
2. Like Dobermans, they tend to have more ventricular arrhythmias associated with the DCM and can die suddenly.
3. One family of boxers responded to L-carnitine therapy.

O. Cocker Cardiomyopathy (DCM in cocker spaniels)
1. Cockers are the only small/medium sized dog which gets DCM. The signs, physical exam findings, ECG, and echocardiogram can be the same as in large breeds.
2. Cockers, especially male Cockers, are also very prone to severe chronic valvular heart disease of the mitral valve. So, Cockers presenting with enlarged left hearts plus or minus heart failure, could have either disease and an echo would be needed to tell the two problems apart.
3. Treatment
   a. Primary treatment of the heart failure is the same as in large breeds.
   b. This problem can be improved so that the majority of dogs return to normal activity clinically but the echo does not return to normal. The current treatment to achieve this improvement is:
      1) Taurine 500 mg. PO q 12 hours
      2) L-Carnitine 1gm. PO q 12 hours
      3) These drugs must be continued indefinitely.
   c. All other cardiac drugs can be weaned off in 3 months after the above therapy. However, some dogs must be maintained on enalapril and/or furosemide and all of the drugs may need to be restarted if the dog develops heart failure in the future.
   d. Be sure the dog is on L-carnitine, as other forms of carnitine do not work.

P. Nutritional Related Dilated Cardiomyopathy
1. Carnitine deficiency only rarely causes DCM in dogs.
   a. 50-90% of dogs with DCM have low carnitine levels but only a few ever respond to supplementation with it.
   b. Blood levels do not reflect muscle levels.
   c. Dogs under a year of age responded better to treatment if L-carnitine is added.
   d. May stimulate the dog’s appetite.
   e. One family of boxers responded to L-carnitine supplementation so all boxers with DCM should be started on it.
2. Taurine
   a. Background
      1) An essential amino acid that is not bound to protein so is free in the blood
      2) High levels in heart, central nervous system, skeletal muscles, and platelets
      3) Necessary for normal myocardial function—may modulate calcium concentrations and availability to muscle, especially in heart
      4) Essential amino acid in cats as they do not synthesize it. Now that feline diets high in taurine, DCM is uncommon.
      5) Dogs can synthesize it from precursors.
      6) Dogs use taurine to conjugate bile acids.
   b. Recent upsurge in incidence of DCM in big dogs but also small dogs—some are on BEG diets (boutique, exotic ingredients, and grain-free diets)
      1) Is it a taurine deficiency? Dogs are on their diets long term.
         a) Many dogs responded to a diet change and taurine supplementation.
         b) Boutique manufacturers are ones who do not have veterinary nutritionists on their staff, do not do long term quality control, and do not analyze their diets routinely. Is something in the processing of the foods causing a problem or making taurine unavailable to be absorbed?
         c) The exotic proteins have not been studied as to their protein availability, digestibility, and interactions with other nutrients.
         d) Likewise, the use of legumes, peas, potatoes, lentils, fava beans, tapioca, barley, and chick peas have not been studied as to their long term interactions with other nutrients.
         e) Beet pulp does interfere with the absorption of taurine as it increases the excretion of fecal conjugated bile acids. Do high fiber diets do the same?
         f) Do some of the boutique diets contain products that have been exposed to insecticides, heavy metals, or other toxins that interfere with absorption of nutrients?
         g) Some dogs (Golden retriever, Newfoundland, American cocker spaniel, English setter, Saint Bernard, and Irish wolfhounds) are more prone to developing DCM with low taurine diets (gene predisposition?).
h) Certain diets (lamb and rice, low-protein diets, and high fiber diets) were found to be associated with taurine deficiency in some dogs.

i) Some dogs with DCM have low taurine blood levels and respond to a change in diet and taurine supplementation. Some dogs with DCM and normal taurine levels respond to a change in diet and taurine supplementation.

2) It may not just be taurine causing the problem.

c. Recommendations for dogs with DCM that are on BEG diets, homemade diets (unless a veterinary nutritionist has analyzed the diet), raw diets, high fiber diets, low protein diets, vegetarian diets, and vegan diets:

1) Measure plasma and whole blood concentrations of taurine (UC Davis lab).
2) Switch diet—if owner insists on grain free diet; use a major company's diet (Purina, Hill's, etc.) which undergoes quality control and testing.
3) Start the dog on taurine along with routine medications:
   a) Dogs <10 kg. 250 mg. q. 12 hours
   b) Dogs 10-25 kg. 500 mg. q. 12 hours
   c) Dogs over 25 kg. 1,000 mg. q. 12 hours

d. Recommendations for dogs without apparent low taurine blood levels

1) Switch diet as there could be other interactions in the diet that are preventing absorption of other nutrients such as choline, copper, L-carnitine, magnesium, thiamine, or vitamin E and selenium
   a) Due to low levels of these substances
   b) Lack of absorption of nutrients due to interactions with other substances in the diet
   c) Adulterated ingredients could unintentional be present in the food and causing problems.
   d) Gut flora may be interacting with a dietary factor and altering its absorption.
2) Taurine supplementation is optional

e. Get a complete diet history including treats as there could be a link between certain treats and a problem (will help with the research). Report suspected cases to the FDA.

3. Fish oils

a. In a small study of dogs with DCM, fish oils increased contractility and decreased ventricular arrhythmias.

b. All fish diets in cats interfere with taurine absorption so find out in the diet history, what flavors of dog food the dog is on.
Q. Arrhythmogenic right ventricular cardiomyopathy (Boxer Cardiomyopathy) (ARVC)

1. The changes in the heart associated with this disease are:
   a. Fibro fatty replacement of normal myocardial cells in the ventricular and atrial myocardium that disrupts normal electrical and mechanical function. Since it has been found throughout the heart, the name may change to arrhythmogenic cardiomyopathy.
      1) Due to the disruption of the electrical current, ventricular arrhythmias are triggered.
      2) Most episodes of VPCs are self-limiting.
      3) Eventually, the VPCs/ventricular tachycardia cause up to 1/3 of the dogs to develop syncope. VPCs can result in sudden death in some dogs and may die.
      4) A few dogs can develop enough changes in the right ventricle that they go into right heart failure or left heart failure but this is rare.
      5) A few dogs also have enough changes in an atrium to cause supraventricular tachycardias (uncommon).
   b. Three types:
      1) Category 1: mild ventricular arrhythmias (subclinical)
      2) Category 2: severe ventricular arrhythmias with clinical signs (syncope)
      3) Category 3: right ventricular dysfunction (DCM) with ventricular arrhythmias (uncommon to rare)
   c. People with ARVC have a genetic mutation with changes in the ryanodine receptor which causes calcium release from the sarcoplasmic reticulum and with cytoskeletal proteins involved with desmosome cell-cell interactions. These are eight genes with 141 mutations.
   d. Autosomal dominant inheritance in people and seems to be autosomal dominant with variable penetrance in boxers.
      1) One gene mutation has been identified and a genetic test is available at North Carolina State.
      2) Striatin deletion has been identified as causing ARVC in Boxers.
      3) Dogs diagnosed with ARVC:
         a) 61% were heterozygous for striatin deletion.
         b) 23% were homozygous for the striatin deletion.
         c) Homozygous dogs are more severely affected than heterozygous.
         d) Heterozygous dogs have more VPCs on 24 hour Holter than unaffected dogs.
      4) The frequency and severity of the disease increases with age.
   e. ARVC is rare in cats and has not been reported in other species.
2. History  
   a. Usually occurs in dogs 6-11 years old and in both sexes.  
   b. The main problem is ventricular arrhythmias so dogs present for:  
      1) Syncope/collapse  
      2) Weakness/exercise intolerance  
      3) Rarely do these dogs have heart failure.  
      4) Occasionally sudden death.  

3. Physical exam  
   a. Normal except for the presence of an arrhythmia (erratic heart rate with pulse deficits).  
   b. Murmurs may or may not be present (of mitral regurgitation or physiologic murmurs).  

4. ECG  
   a. Ventricular arrhythmias are most common and they develop abruptly.  
      1) Morphology of complete left bundle branch block (LBBB) as most originate in the right ventricle. QRS complexes are positive in leads II, III, and AVF.  
      2) If present in the Boxer, this helps make the diagnosis.  
      3) Occasionally have supraventricular arrhythmias.  
   b. If the ECG is normal, a Holter monitor or Event monitor should be done.  
      1) If the dog has greater than 300 VPCs in 24 hours in the absence of other causes then is has ARVC.  
      2) 50 – 300 upright VPCs could be early ARVC.  
      3) Less than 50 single VPCs are normal.  
      4) There is an 83% variability in the number of VPCs in every 24 hour period so one Holter may not rule out or rule in this diagnosis.  

5. Radiographs are normal.  

6. Echocardiogram  
   a. Normal in many cases  
   b. Subtle changes in right ventricular function cannot be seen on echo  
   c. Cardiac MRI may show the decreased RV function and infiltration of fat.  
   d. Right ventricle and right atrium may be dilated in advanced cases.  
   e. Dogs with dilated left ventricles and decreased systolic functions die suddenly.  

7. Treatment  
   a. Treat the ventricular arrhythmia if there are greater than 300 VPCs in 24 hours, there is R on T, dog is syncopal, or VPCs are polymorphic.  
      1) Sotalol  
      2) Mexiletine plus atenolol  
      3) Sotalol plus Mexiletine  
      4) Amiodarone
5) Reduces the number and complexity of the arrhythmia and reduces syncope but cannot prevent sudden death that will occur in some cases as the disease progresses.

8. Prognosis
   a. Many dogs live for years with stable disease.
   b. 64% of ARVC dogs are alive at 9 years old regardless of number of VPCs. However, effects of treatment were not evaluated.
   c. About 33% of dogs with ARVC will die suddenly

References
Ettinger SJ and Feldman EC & Cote E., Textbook of Veterinary Internal Medicine, Eighth Edition Chap. 26, 28, 30, 55, 103, 104, 246, 247, 248, 252, 253, 256
Kittleson MD, Small Animal Cardiovascular Medicine or VIN 2nd edition, Chap 20, 21, 22, 31.
III. Feline cardiomyopathies

A. Classification is based on the gross and microscopic findings. The classes are:
1. Hypertrophic (HCM)
2. Dilated (DCM)
3. Restrictive (RCM)
4. Unclassified (UCM)
5. Mixed

B. Hypertrophic cardiomyopathy (HCM)
1. Occurs in 9-15% of cats
2. Genetic cause
   a. In people, there are multiple genetic mutations in the different genes associated with development of the contractile elements of the heart, which results in HCM.
   b. In cats, HCM has a simple autosomal dominant pattern of inheritance in Maine Coons, Ragdolls, and probably in DSH.
   c. Maine coon cats and Ragdolls have been found to have a mutation in the cardiac myosin binding protein C, which is part of the contractile elements
      1) Maine coon cats have mutations in the A31 gene that results in HCM. Prevalence of this gene is 15-35% in Maine coon cats.
         a) Variable penetrance
         b) 10% are homozygous and most of these cats get HCM during their life span and develop it before 6 years old.
         c) Of the cats with this gene who go into heart failure, 50% are homozygous.
         d) Some of the heterozygous cats will get HCM.
         e) However, some Maine Coon cats without this gene mutation will get HCM.
      2) In Ragdolls, there is a mutation in the A820W gene that causes HCM. Prevalence of this gene in Ragdolls is 17-23 %.
         a) Homozygous ragdolls are more likely to develop clinical HCM.
         b) Ragdolls that go into heart failure have more severe disease and a short survival time.
3. Primary disease of the left ventricular myocardium that results in hypertrophy of the ventricular wall, septum, papillary muscles.
   a. Hypertrophy of the left ventricular myocardium occurs because the genetic mutation causes abnormal sarcomeres, which do not contractile normally. This results in increased wall stress. The heart responds to increased stress by producing more sarcomeres to replace the abnormal ones, which results in hypertrophy.
   b. Usually symmetrical hypertrophy of septum and LV wall.
   c. Can have asymmetrical thickening. If the septum is thick, it can cause obstruction of flow of blood from the left ventricle and is called hypertrophic obstructive cardiomyopathy (HOCM).
   d. Due to thickening of the muscle wall, there is a reduced left ventricular lumen so blood accumulates in the left atrium, and it dilates.
   e. The concentric hypertrophy causes decreased ventricular compliance, and therefore increased diastolic pressure. The increased diastolic pressure causes the left ventricle to relax slower in early diastole so:
      1) Left atrium dilates and its pressure increases
      2) Left heart failure can occur
      3) Thrombi can form in the dilated left atrium.
   f. The systolic pressure is normal as the hypertrophied heart muscle can contract almost normally throughout the disease. As the disease gets more advanced, the myocardial fiber disarray may result in inefficient contractility.
   g. The heart’s weight and mass are increased due to hypertrophy. It is important to remember that when a cat (or any animal) dies, the heart contracts so that is appears to be thickened. The only way to diagnose that the cat had HCM is to weigh the heart!!!
   h. Thrombi form in the left atrium or left atrial appendage and break off, forming clots in the terminal aorta (saddle thrombi) or in other organs. 10-30% of cats with HCM form thrombi.
   i. Systolic anterior mothing (SAM) of the mitral valve can occur.
      1) The septal (anterior) mitral valve leaflet is pulled into the left ventricular outflow tract (LVOT) in systole and touches the septum.
      2) Abnormal papillary muscle orientation is one cause of SAM
      3) Venturi effect is another cause of SAM
      4) Results in mitral regurgitation that decreases cardiac output and enlarges the left atrium.
      5) Results in dynamic obstruction to left ventricular outflow resulting in hypertrophic obstructive cardiomyopathy (HOCM).
      6) SAM is the result of the HCM and not the cause of it!
7) SAM theoretically could worsen HOCM but this has not been documented to occur in cats.

4. Problems that lead to congestive heart failure
   a. LV decreased compliance in diastole
   b. Decreased LV chamber size so it does not fill well
   c. Mitral regurgitation due to SAM
   d. RAAS activation
   e. Tachycardias
   f. Iatrogenic fluid overload, steroids

C Dilated cardiomyopathy (DCM)
1. The left ventricle and atrium are dilated and have atrophied papillary muscles.
2. The right ventricle and right atrium also dilate.
3. The heart cannot pump the blood presented to it due to myocardial dysfunction. (systolic dysfunction)
   a. Pulmonary and hepatic congestion occur (pulmonary edema, pleural effusion, ascites)
   b. Diastolic function is decreased, as the ventricles remain filled with blood due to the poor contractility.
   c. Due to the dilatation of the ventricles, the A-V annulus dilates which causes mitral and/or tricuspid regurgitations.
4. Causes
   a. Idiopathic
   b. Long term taurine deficiency has been shown to cause this disease in cats. Cats with dilated cardiomyopathy should be checked for taurine deficiency or supplemented with taurine. In addition, dogs on long term grain free diets high in lentils, peas, or potatoes may be deficient in taurine.
   c. Drug/toxins
   d. Myocarditis
   e. Arrhythmia
   f. Genetic mutations (?)

D. Extra cardiac lesions with HCM, DCM, or RCM:
   1. Aortic thromboemboli (ATE)
   2. Renal infarcts
   3. Pulmonary edema
   4. Pericardial, peritoneal, and pleural effusion
   5. Hepatic congestion

E. Restrictive cardiomyopathy (RCM) is not commonly seen.
1. Severe endocardial thickening with fibrosis and adhesions occurs in the left ventricle, mainly in the inner lining of the wall (endocardium). The ventricle has decreased compliance due to the fibrosis so it does not fill well. Blood then accumulates in the left atrium just as it does with HCM.
2. Treated the same as in hypertrophic cardiomyopathy, but prognosis is guarded (3-6 months).
F. Unclassified cardiomyopathies
1. Those that do not fit into the other categories based on echocardiographic findings.
2. Harder to treat and have poor prognosis (3-6 months)

G. Clinical signs
1. The average age is 5-6 years old for hypertrophic cardiomyopathy, while dilated cats are older. However, HCM can occur at any age.
2. The diseases affect more males than females.
3. The cats are asymptomatic until late in the disease process.
4. Cats present with nonspecific signs such as depression, anorexia, crying, exercise intolerance, and/or hiding.
5. Dyspnea will occur when the heart decompensates.
6. Sudden rear leg or right front leg paralysis can occur due to thromboemboli.

H. Physical (if has decompensated heart disease)
1. Usually is depressed
2. Obvious respiratory distress occurs when the cat is in heart failure.
3. Tachycardias can occur but cats could have normal heart rates or bradycardias.
4. Arrhythmias such as atrial fibrillation (uncommon), atrial premature beats, ventricular premature complexes (VPCs) can occur. VPCs occur due to the hypertrophy of the left ventricle resulting in hypoxia and to the myofibril disarray.
5. Harsh lungs sounds or rales can occur if pulmonary edema is present.
6. Sometimes a murmur can be heard.
   a. Murmurs are the most common finding in asymptomatic cats.
   b. Murmurs are labile and can become louder with stress so a murmur increasing in loudness may not indicate worsening heart disease.
   c. However, about 15 to 21% of healthy cats can have murmurs but only 1/3 of the cats with murmurs had HCM. Therefore, 2/3 of cats with murmurs have no heart disease.
7. Gallop rhythms (due to the presence of an S4 gallop in HCM, S3 gallop in DCM) are more commonly associated with heart disease than murmurs.
8. Decreased capillary refill is evident on exam of the mucous membranes.
9. Hepatomegaly or splenomegaly can occur, but ascites is unusual in the cat.
10. Emboli can occur in the limbs.
    a. Causes lameness, but more commonly causes total loss of use of the limb(s), especially rear limbs
    b. Gastrocnemius muscle may be tense.
    c. Lose segmental reflexes causing:
       1) Ataxia
       2) Flaccid paresis
       3) Loss of sensation (at first may be painful)
       4) Loss of patella reflexes
d. No femoral pulses
e. Pale or bluish rear feet pads
f. No bleeding when the rear nails are cut beyond the quick.
g. The rectal temperature is usually normal, but the rear legs feel cool.

I. Differential Diagnosis
1. Asymptomatic cats with murmurs
   a. Young cats could have congenital heart defects.
   b. Old cats could have degenerative changes of valves.
   c. Any age cat could have bacterial endocarditis.
   d. Dynamic right ventricular outflow obstruction (DRVOTO).
   e. Physiologic murmur
2. Dyspneic cats
   a. Pulmonary edema is usually due to left heart failure but can also be caused by other problems such as electric cord bites, etc.
   b. Pulmonary contusions can occur secondary to trauma.
   c. Asthma can cause dyspnea.
   d. Any cause of pleural effusion, which includes both right and left heart failure can cause dyspnea in a cat.
   e. Any pulmonary disease can result in dyspnea.
3. Other causes of left ventricular hypertrophy
   a. Systemic hypertension
   b. Hyperthyroidism
   c. Aortic stenosis
   d. Acromegaly (growth hormone induces myocardial hypertrophy)

J. ECG
1. A sinus tachycardia may be present, although atrial premature complexes (APCs) are uncommon.
2. Sometimes atrial fibrillation may be present (uncommon) due to severe left atrial dilation. Atrial fibrillation increases the chances of thrombi forming and is a poor prognostic sign.
3. If the cat has ventricular premature complexes (VPCs), rule out HCM as the cause first before looking for other causes of the VPCs.

K. Radiographs- Do not stress a dyspneic cat, and treat it prior to doing further diagnostic tests!
1. Cannot differentiate between a normal cat and one with HCM unless there is left atrial enlargement.
2. Hypertrophic cardiomyopathy shows bialtrial enlargement with no visible signs of ventricular enlargement, so the heart appears to be valentine-shaped, on the DV or VD view. Diffuse pulmonary edema may be present as may pleural effusion.
3. Dilated cardiomyopathy shows generalized cardiomegaly so the heart appears almost globoid. Pleural effusion and hepatomegaly are also commonly found.
L. Echocardiography

1. Hypertrophic cardiomyopathy cats
   a. Global or regional hypertrophy of the left ventricular wall and/or septum, prominent papillary muscles, systolic left ventricular lumen obliterated or small and stiff so the left ventricle does not fill easily.
   b. Enlarged left atrium:
      1) The left atrium may be normal in early disease.
      2) May have swirling haze (spontaneous contrast; smoke) if left atrium is very big.
      3) May have a thrombus.
   c. SAM in some cats, especially with HOCM
   d. 91% of cats with HCM have normal to increased systolic function.
   e. All cats with HCM have diastolic dysfunction.
   f. Color flow Doppler confirms
      1) Turbulence in LVOT with increased velocity due to SAM (about 2/3 of cats with HCM have some degree of SAM)
      2) Mitral regurgitation
   g. In end stage disease, may have areas of thinning of the LV wall with a “moth eaten” appearance and decreased contractility.
   h. Abdominal ultrasound with Doppler may be able to visualize and quantify a saddle thrombus.

M. Laboratory data (not specific for cardiomyopathy)

1. The CBC has signs of stress.
2. Mild prerenal azotemia
3. Mild increases in liver enzymes will occur (alanine transaminase, alkaline phosphatase, and bilirubin) due to passive congestion or hypoperfusion.
4. CPK and LDH are elevated in the early part of the disease due to myocardial necrosis or skeletal muscle problems due to emboli.
5. Pleural effusions are modified transudates.
6. Glucose may be increased due to stress.
7. NT-pro BNP
   a. Usually does not help to distinguish normal cats from cats with subclinical HCM.
   b. However, it is better at distinguishing severe HCM from normal rather than mild HCM from normal.
   c. It does distinguish cat with dyspnea due to heart failure from cats with dyspnea due to respiratory disease with 85% sensitivity and 84-88% specificity.
   d. Pleural effusion can be used to determine NT proBNP levels accurately.
N. Treatment of Feline HCM

1. Treatment of asymptomatic cats
   a. There are no controlled studies on treating the disease at this stage and so far no drug has been found to slow the progression of the disease.
   b. In people with HCM, beta blockers and calcium channel blockers are sometimes recommended to try to slow the progression of the disease.
   c. In cats, no drug has been shown to slow the progression of the disease although some clinicians still treat with atenolol or diltiazem.
   d. Cats with significant LV outflow obstruction are usually treated by most cardiologist with atenolol to decrease the obstruction. However, the long term benefits of this therapy have not been proven and the presence of SAM has not been shown to have an adverse effect on cats’ longevity.
   e. Atenolol has not been shown to improve the biomarkers or survival times in asymptomatic cats.
   f. In people with heart disease, ACE-inhibitors and spironolactone help to slow cardiac remodeling. However, in cats with HCM, neither Ramipril nor spironolactone had any effect on echocardiographic measurements of hypertrophy or diastolic function.
   g. Antithrombotic therapy is started if the left atrium is moderately to severely dilated or if there is evidence of a procoagulative state.
      1) Aspirin
      2) Clopidogrel (Plavix)

2. Severe acute pulmonary edema due to HCM
   a. Cage rest with oxygen and no stress
   b. Furosemide
      1) Intravenous-About 5 minutes to onset of action with 1-hour duration of action
      2) IM (only if no immediate IV access) 15-30 minutes to onset of action, duration of action about 2 hours
      3) More rapid naturiuresis and diuresis than dog so require smaller doses than dogs!!!!
      4) Tolerated well clinically in cats.
      5) If have systolic dysfunction, will require higher doses.
      6) Avoid NSAIDs as they decrease renal perfusion and decrease effectiveness of furosemide and increase its toxic effects on the kidneys.
   c. Venodilator, e.g. topical nitroglycerine ointment
      1) Always used in combination with furosemide
      2) No controlled studies to prove efficacy but no side effects either and easy to use.
   d. Serially reassess respiratory rate and effort
e. Addition of other medications can wait until the patient can tolerate oral medications and until after the echocardiogram is done to access the underlying problem and its severity.

3. Pleural effusion- due to either right or left heart failure or both
   a. Thoracentesis—Do both sides and have cytology and BNP done.

4. Chronic heart failure due to HCM- Maintenance therapy for cats that have gone into CHF
   a. Furosemide orally
      1) Dose should be titrated up or down on an individual patient basis.
      2) Can get tolerance eventually.
      3) Liquid forms are alcohol based which cats detest.
      4) Avoid NSAID with furosemide as the NSAIDS decrease renal perfusion which decreases the efficacy of the furosemide and increases its toxicity, especially if the cat is also on an ACE inhibitor.
   b. Torsemide (oral from only)
      1) Potent loop diuretic
      2) Peak effective 2-4 hrs. lasts 12 hours
      3) No reported side effects
      4) ¼ to ⅛ of furosemide dose
      5) Less diuretic resistance
      6) Only comes in a few tablet sizes.
   c. Diltiazem
      1) Decreases the heart rate so heart can fill better.
      2) Improves early diastolic relaxation.
      3) May lessen edema formation in some cats.
      4) Can reduce wall thickness in some cats over time.
      5) May decrease SAM and thereby reduce mitral regurgitation.
      6) Sustained-release diltiazem require less frequent dosing. Must use Cardiozem CD (not Dilacor!).
      7) Dilates coronary arteries.
      8) Only prospective study done with HCM showed that cats with severe HCM benefited from its use.
      9) If cat develops atrial fibrillation, it is the drug of choice for controlling the cat’s heart rate.
      10) Delays recurrence of signs of heart failure in cats with HCM.
   d. Beta blockers (propranolol, atenolol)
      1) Slow the heart rate (negative lusitrope) which allows better filling of the ventricle and coronary arteries which decrease the myocardial oxygen consumption. Target heart rate is 140-160 BPM.
      2) Decrease the degree of LVOT obstruction and reduce mitral regurgitation due to SAM so are used with severe HOCM.
3) No prospective clinical studies on the effects of propranolol or atenolol have been completed.

4) Atenolol is a beta₁ specific antagonist and is a better choice if there is any possibility of feline asthma.

5) Be careful as atenolol may promote the redevelopment of heart failure so the cat must be stable to use it.

6) Antiarrhythmic - for VPCs and for control of SVT

e. ACE inhibitors

1) There are no studies showing that it benefits cats. One prospective study showed that there were no benefits from its use.

2) Many clinicians use it in cats with CHF as it theoretically can help by inhibiting the RAAS system.

3) Safe in cats.

4) Do not start if the cat is anorexic and or has significant azotemia, is hypotensive, or if the cat is on injectable furosemide.

5) Can make left ventricular outflow tract obstruction worse.

6) Enalapril or benazepril 0.25-0.5 mg./kg. q.12-24 hours

f. Pimobendan

1) Used if decreased contractility (decreased systolic function).

2) A recent student appeared to show that cats with CHF due to HCM improved with the use of pimobendan – study was inaccurate as it was a retrospective trial and only showed that cats tolerated pimobendan but did not prove it benefited the cats. A prospective study abstract was presented that stated it does make a difference but the work has not been published.

3) May improve atrial contribution to left ventricular filling

4) May limit platelet aggregation.

5) May improve left ventricular relaxation.

6) Cats do not need as much pimobendan as dogs as the elimination half time is 3 times longer than dogs and its peak serum concentration is 9 times higher. But the dose for cats is not yet published so use the dog dose as the cats will tolerate it ok.

7) Can worsen dynamic left ventricular outflow obstruction

8) Oral suspensions are not stable unless the suspension is oil based.
g. **Aspirin**
   1) Reduce risk of thromboembolic events in cats with a dilated LA.
   2) Low dose given every 3 to 4 days (twice weekly) ¼ of 81 mg. tablet q. 3 days

h. **Warfarin (Coumadin)**
   1) Major risk of hemorrhage
   2) **Not** recommended.

i. **Clopidogrel (Plavix)** ¼ of 75 mg. tablet q. 24 hours
   1) Proven to help prevent future thrombi in cats that have thrown a thrombus.
   2) Helps to open collateral circulation when cat has a saddle thrombus.
   3) Bitter so put in gel capsule.

j. **Spironolactone**
   1) Blocks aldosterone receptors so causes diuresis and decreases myocardial fibrosis.
   2) Positive and negative effects poorly documented.
   3) Helps in combination with furosemide or torsemide in cats with pleural effusion due to right or left heart failure.
   4) Severe facial dermatitis in Maine Coon cats but other breeds do not seem to develop this problem. The dermatitis is reversible once it is stopped.

O. **Prognosis of cats with HCM based on clinical presentation and echocardiographic findings**

1. **Subclinical, asymptomatic HCM cats** can live for years. Their median survival time is greater than 10 years.

2. **Asymptomatic, with mild to moderate hypertrophy and none to mild LA enlargement:**
   a. **Good short term**
   b. **Good long term prognosis,** but it depends on the progression of the hypertrophy

3. **Asymptomatic, severe wall thickening, mild to moderate LA enlargement**
   a. **Guarded prognosis for CHF in the future.**
   b. **Some risk for thrombotic event and sudden death.**

4. **Asymptomatic, severe wall thickening, moderate to severe LA enlargement**
   a. **At risk for developing CHF very soon**
   b. **At risk for thrombotic event**
   c. **At risk for sudden death**

5. **Cats presenting in CHF**
   a. **Prognosis varies and can be 6-18 months.**
   b. **Median survival time three months in one study.**
   c. **20% stabilize and do well for longer.**
6. Severe HCM and aortic thromboembolism  
   a. Median survival time two months up to 12 months if survive initial event  
   b. Up to 65% of cases are euthanized on presentation.  
   c. Low rectal temperature, bradycardia, and increasing BUN/creatinine are poor prognostic indicators  
   d. Cats who have a thrombus are more likely to have a second embolic event.

P. Dilated cardiomyopathy therapy in cats  
1. Pimobendan  
2. Furosemide or torsemide  
3. Aspirin and/or clopidogrel  
4. Enalapril  
5. Spironolactone along with furosemide or torsemide for pleural effusions  
6. Taurine  
7. Most cats only live about three months before dying or being euthanized.  
8. Prognosis: 3 months or longer if responds to taurine.

Q. Thromboembolic problems- 5-17% of cats develop thrombi  
1. Site of formation is the left atrium  
   a. Most common site of lodging is aortic bifurcation.  
   b. Also can lodge in right front leg.  
   c. Non limb infarction in only 2% of events- cerebral, renal, and mesenteric arteries have been reported  
2. Clinical signs  
   a. Acutely going down in rear  
   b. Crying in pain for 12-18 hours  
   c. No pain sensation in rear legs  
   d. No femoral pulses  
   e. +/- Normal temperature  
   f. Gastrocnemius muscle is tense.  
   g. Lose segmental reflexes  
      1) Ataxia  
      2) Flaccid paresis  
      3) Loss of sensation  
      4) Loss of patella reflexes  
3. Diagnosis  
   a. Laboratory tests  
      1) If BUN and/or Creatinine are markedly elevated then embolus is blocking the kidneys.  
      2) CK and other muscle enzymes could be elevated.  
      3) Lactates are elevated in the rear legs compared to the front legs.  
   b. Radiographs  
      1) Heart is enlarged as the cat has underlying heart disease and the heart is the source of the embolus.  
      2) Nonselective or selective angiogram can show the extent of the thrombus.
3) Saddle thrombi have also been seen with pulmonary neoplasia.

c. Echo is used to determine which heart disease is present and if a thrombus is present in the left atrium.

d. Doppler is used to trace the flow of blood in the aorta to see the extent of the clot. This is less invasive and safer than angiography. Also, it can tell if the renal arteries are involved.

4. Therapy of saddle thrombus

a. Preventative— aspirin, Plavix or both

1) No study done to determine which will prevent the primary thrombotic event

2) Fat Cat Study showed cats on clopidogrel (Plavix) were less likely to have a recurrent thrombotic event (49%) than aspirin (75%) and had longer median time to an event.

b. Acute Therapy

1) Supportive— keep animal warm, physical therapy for the legs, fluids (be cautious as 50% of cats with thrombi develop heart failure and fluids are contraindicated if the cat has heart failure), treat the underlying heart disease

2) Analgesics— fentanyl, buprenorphine

3) Anticoagulants— heparin, low molecular weight heparin, clopidogrel

4) If the cat’s potassium levels are high, treat with insulin/glucose or calcium, or sodium bicarbonate.

5) Surgery (NOT recommended)— the clot can easily be removed by surgery but the anesthesia is very risky as the cat is usually in heart failure. Also, reperfusion injury (inflammation and oxidative damage) can occur.

6) Catheter procedures— risk of anesthesia, limited experience, and reperfusion injury also are problems.

7) Thrombolytic therapy

a) Streptokinase— no longer available— second and third generation available (expensive)

b) TPA (tissue plasminogen activator) – cats do not tolerate it very well.

c) Only use thrombolytic therapy within the first 6 hours of the saddle thrombus occurring.

d) Clopidogrel (Plavix)— opens up collateral arterial circulation sooner

e) Heparin only stops the clot from getting bigger.

c. Chronic therapy

1) Antithrombotics— clopidogrel and aspirin

2) Treat the underlying heart disease as above

5. Prognosis

a. Cats with thrombi have a shorter survival time especially acutely as 65% are euthanized

b. Will have another event

c. Average survival was less than one year
References


Payne et al. Cardiomyopathy prevalence in 780 apparently healthy cats in rehoming centers (the CatScan Study). JVC 2015; 17; supplement; S244-S257.

Reina-Doreste et al. Case-control study of the effects of pimobendan on survival times in cats with hypertrophic cardiomyopathy and congenital heart failure. JAVMA 2014; 245: 534-539.


Diagnosis of Syncope

Rebecca Gompf, DVM, MS, DACVIM (Cardiology) – UTCVM Cardiology

I. Background

A. Definitions
   1. Syncope—sudden but brief loss of consciousness from which recovery is spontaneous and complete
   2. Pre-syncope (near syncope)—a brief, episodic rear limb or generalized weakness, ataxia, or altered level of consciousness
   3. Syncope=transient loss of consciousness (TLoC)

B. Syncope versus seizures
   1. Seizures are a generalized and possibly transient loss of consciousness.
      a. May have urination and defecation
      b. May have total body trembling
      c. Has a preictal period
      d. Takes time to recover to normal
   2. Syncope is always transient
   3. Syncope is due to
      a. Arrhythmias
         1) Bradycardias
         2) Tachycardias
      b. Neurocardiogenic—vagal induced (cardioinhibitory) or vasodepressor
      c. Primary cardiac disease
         1) Heart failure with hypoxia of cardiac muscle
         2) Arrhythmias

II. Seizures versus syncope diagnosis

A. Guidelines for the Diagnosis and Management of syncope (2009)—European Heart Journal
   1. Is there loss of consciousness?
   2. Is it transient?
   3. Is it rapid in onset?
   4. Is it of short duration?
   5. Is there spontaneous recovery?

B. Occurrence of syncope
   1. Large breed dogs—rapid ventricular tachycardia and reflex bradycardia
   2. Small breed dogs—bradycardia (heart blocks, sick sinus syndrome), situational syncope, pulmonary hypertension secondary to primary pulmonary disease
   3. Cats—tachycardias (ventricular or atrial fibrillation), complete heart block, hypertrophic cardiomyopathy
III. Neurally Mediated Syncope

A. Neurocardiogenic—reflex comes from the heart or pulmonary vessels and the stimulus is adrenoneuric

B. Vasovagal—when the reflex comes from the brain and is triggered by emotional shock, phobias, and pain.
   1. Common in people
   2. May occur in dogs and the only way to document it is Holter monitor.
      a. Occurs with stress
      b. Coughing episodes are linked to this but stimulus comes from lungs and goes to brain.

C. Situational syncope—when the reflex is triggered by the vagus nerve due to coughing, vomiting, or urination—only in dogs

D. Carotid sinus syncope—mechanical stimulation of the carotid sinus—not in cats or dogs

IV. Orthostatic Syncope—syncope due to orthostatic hypotension

A. Primary autonomic failure
   1. Disease of the autonomic nervous system
   2. Parkinson’s disease in people

B. Secondary autonomic failure
   1. Diabetes
   2. Uremia
   3. Amyloidosis
   4. Spinal cord injuries

C. Drug-induced orthostatic syncope
   1. Vasodilators
   2. Diuretics
   3. Phenothiazines
   4. Alcohol
   5. Antidepressants

D. Volume depletion
   1. Shock
   2. Bleeding
   3. Vomiting/diarrhea
V. Cardiogenic Syncope

A. Arrhythmias—most common cause
   1. Tachycardias
      a. Supraventricular
      b. Ventricular
   2. Bradycardias
      a. Vagal induced
      b. Sick sinus syndrome
      c. Heart blocks
      d. Drug induced

B. Structural disease induced syncope
   1. Valvular heart disease
   2. Dilated cardiomyopathy
   3. Hypertrophic cardiomyopathy
   4. Cardiac tumors
   5. Pericardial disease
   6. Congenital heart diseases—subaortic stenosis, pulmonic stenosis

C. Dogs
   1. Chronic valvular heart disease or dilated cardiomyopathy—arrhythmias
      a. Only with advanced disease—big atrium or atria
         1) Atrial premature complexes
         2) Atrial tachycardia
         3) Atrial fibrillation
         4) Treatment
            a) Beta blockers—atenolol
            b) Calcium channel blockers—diltiazem
            c) Digoxin
         5) Prognosis—6-12 months
      b. Heart failure causing hypoxia
         1) Ventricular premature complexes
         2) Ventricular tachycardia
         3) Treatment
            a) Lidocaine immediately
            b) Sotalol
            c) Mexiletine
            d) Sotalol plus mexiletine
            e) Aggressively treat the heart failure
         4) Guarded as any dog with VPCs can drop dead suddenly.
   2. Bradycardias
      a. Second degree heart block
         1) Low grade—only occurs occasionally
         2) High grade—frequent and can cause syncope
         3) Treatment
            a) Atropine challenge test, 0.04 mg/kg
            b) Low grade—monitor ECG frequently
            c) High grade—pacemaker
4) **Prognosis:**
   a) Low grade may never progress—unpredictable
   b) High grade will advance to complete heart block and only survive months without a pacemaker

b. **Third degree (complete heart block)**
   1) Heart rate is fixed so cannot exercise
   2) Treatment—pacemaker
   3) Prognosis—dogs
      a) If VPCs are present, the dog could die at any moment (40% of third degree heart block dogs and 32% of high grade second degree block)
      b) 24% die in 30 days and 40% die within 6 months if not treated with a pacemaker
      c) Only a few dogs die due to pacemaker complications and the majority die of other problems with their pacemaker functioning normally.

4) **Prognosis—cats**
   a) Majority of cats with complete heart block picked up as incidental findings when the cat comes in for other problems. The cats die from other disease first in most cases.
   b) If the cat is syncopal, it will require a pacemaker and has the same prognosis as dogs.

5) **Screening prior to pacemaker implantation**
   a) Hematology, biochemistry
   b) Thoracic and abdominal radiographs and imaging
   c) Infectious disease screening
   d) Echocardiogram
   e) Holter if has second degree heart block

6) **Pacemaker complications**
   a) Major ones—12-18%—lead dislodgement (2.4%), lead fracture or malfunction, infection (1.4%)
   b) Minor—seromas (10%), and thrombus along the lead
   c) Surgical check list has improved outcomes
   d) Procedures done after hours have more complications

c. **Sick sinus syndrome—small breeds**
   1) Sinus node is not working properly and neither is the AV node.
   2) Syncope is dramatic but rarely results in sudden death
   3) Can have periods of sinus arrest and periods of sinus or atrial tachycardia
   4) Treatment
      a) Beta blockers or calcium channel blockers for the atrial tachycardia
      b) Pacemaker for the sinus arrest—does not improve longevity but decreases the chances of euthanasia

3. **Ventricular premature complexes**
   a. Associated with many causes including heart disease and failure
   b. Premature, wide and bizarre complexes with depolarization one direction and repolarization in opposite direction.
   c. Can progress from single beats to ventricular tachycardia and ventricular fibrillation
   d. When to treat
      1) Polymorphic (multifocal)
      2) Fast
3) Symptomatic
4) R on T

e. Treatment
1) Lidocaine initially
2) Sotalol
3) Mexiletine
4) Sotalol plus mexiletine
5) Amiodarone
6) Always treat the underlying cause

4. Any animal with syncope that the cause cannot be detected on a routine ECG should have either a Holter monitor (24 hour recording) or event monitor done in order to rule out an arrhythmia as the cause of the syncope.
SMALL ANIMAL BEHAVIOR CLINIC
Dr. Julie Albright, UTCVM Veterinary Medical Center

Common Psychoactive Drug Doses (oral or orotransmucosal)

<table>
<thead>
<tr>
<th>Benzodiazepine</th>
<th>Dog</th>
<th>Cat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam (Xanax)</td>
<td>0.02-0.1 mg/kg q4h</td>
<td>0.0125-0.25 mg/kg q8h</td>
</tr>
<tr>
<td>Clonazepam (Klonopin)</td>
<td>0.1-0.5 mg/kg q8-12h</td>
<td>0.015-0.2 mg/kg q12</td>
</tr>
<tr>
<td>Diazepam (Valium)</td>
<td>0.5 mg/kg q4h</td>
<td>0.1-0.4 mg/kg q12h</td>
</tr>
<tr>
<td>Lorazepam (Ativan)</td>
<td>0.02-0.5 mg/kg q8-12h</td>
<td>0.03-0.08 mg/kg q12h</td>
</tr>
</tbody>
</table>

- Oral diazepam linked to idiopathic hepatotoxicity in cats
- Oxazepam, Lorazepam fairly low in potentially harmful metabolites
- Potential side effects include vomiting, diarrhea, oversedation, ataxia, paradoxical excitement, increased appetite, increased aggression, chemical dependency with prolonged usage
- Reversible with flumazenil

<table>
<thead>
<tr>
<th>SSRI</th>
<th>Dog (all PO QD)</th>
<th>Cat (all PO QD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine (Prozac, Reconcile*)</td>
<td>1.0-2.0 mg/kg</td>
<td>0.5-1.5 mg/kg</td>
</tr>
<tr>
<td>Paroxetine (Paxil)</td>
<td>1.0-1.5 mg/kg</td>
<td>0.5-1.5 mg/kg</td>
</tr>
<tr>
<td>Sertraline (Zoloft)</td>
<td>0.5-4.0 mg/kg</td>
<td>0.5-1.5 mg/kg</td>
</tr>
</tbody>
</table>

- Potential side effects including vomiting, diarrhea, constipation (cats), urinary retention, seizure, increased agitation/aggression/anxiety, decreased appetite, sedation
- Typically start at 1/2 dose for 7-14 days
- * = FDA approved to treat canine Separation Anxiety

<table>
<thead>
<tr>
<th>Tricyclic Antidepressant</th>
<th>Dog</th>
<th>Cat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline (Elavil)</td>
<td>1-6 mg/kg q 12h</td>
<td>0.5-2.0 mg/kg q 12-24h</td>
</tr>
<tr>
<td>Clomipramine (Anafranil, Clomicalm*)</td>
<td>1.0-3.0 mg/kg q 12h</td>
<td>0.25-1.3 mg/kg q24h</td>
</tr>
</tbody>
</table>

- Typically start at 1/2 dose for 7-14 days
- See SSRI for side effects, increased anticholinergic effects with TCA

Trazodone (SARI antidepressant):
Dog: 2-10 mg/kg PO PRN ~ 90 min before stressor exposure; also can be given q 8-12 hour maintenance
Cat: 25 – 50 mg/cat PO PRN ~ 90 min prior to stressful event
Potential side effects include vomiting, diarrhea, increased aggression/agitation

Alpha-2 agonists
Clonidine: 0.007-0.05 mg/kg PO PRN 60-90 min before stressor also can be given q 8-12 hour maintenance
Sileo* (dexmedetomidine orotransmucosal gel): 125 µg/mL dosing syringe [note injectable dexmedetomidine up to 40 µg/kg can be administered OTM mixed in gel or syrup, reversal recommended at higher doses]

Gabapentin: dog 3-10mg/kg PO BID-TID; cat 2-5 mg/kg BID; up to 40 mg/kg one time dose 90 min prior to stressor

NON-TRADITIONAL ANALGESICS IN VETERINARY MEDICINE

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Introduction

Opioids, nonsteroidal anti-inflammatory agents, and local anesthetics are the primary classes of drugs used to provide analgesia; however, with advancements in drug development and pain research, particularly in the area of human medicine, new options are becoming available. These adjunctive analgesics may include administering common-mainstream analgesics in a different manner, such as the intravenous administration of local anesthetics, or any of the new analgesic pharmaceuticals developed to combat pain, such as the anti-glial medications. Although many of these new therapeutics are used adjunctively to prevent or control acute pain (e.g., surgical or trauma-related), the primary efforts of the development of new pain therapies are focused on control and treatment of different forms of chronic pain. Use of adjunctive pharmaceuticals, together with mainstream analgesics, may result in more successful treatment of conditions that are less responsive or refractory to mainstream analgesics, or allow for a reduction in dosage and frequency of mainstream analgesics and therefore, a reduction in their adverse effects. Here are some of the most known adjunctive analgesics with current or potential clinical applications in veterinary patients.
ALPHA-2 ADRENOCEPTOR AGONISTS

Alpha-2 agonists, such as dexmedetomidine, detomidine, and romifidine, are commonly used as part of anesthetic-sedative protocols in small and large animals (Seddighi 2014). Although sedation is considered a dominant clinical effect of these drugs, they also provide effective and dose-dependent analgesia and muscle relaxation.

Clinically, the degree of sedation and analgesia produced by an alpha-2 agonist is related not only to the density, location, and type of alpha-2 adrenoceptors but also to the individual selectivity and affinity of the specific drug molecule for the alpha-1 and alpha-2 receptor binding sites (Sinclair 2003). Alpha-2 agonists are not only used as part of anesthetic protocols but are also used in the form of a single dose or continuous rate infusion (CRI) during the recovery period to provide analgesia (Valtolina et al. 2009; van Oostrom et al. 2011), especially in combination with opioids to provide a synergistic analgesic effect (Ambrisko et al. 2005).

ANTICONVULSANT MEDICATIONS

Gabapentin and pregabalin are among several anticonvulsant medications that are being used more commonly to control pain in animals and people (Procopio 2010; Aghighi et al. 2012; Crociolli et al. 2015; Love & Thompson 2014). By binding to the α2δ subunit of voltage-gated calcium channels, these drugs disrupt calcium influx and thus result in analgesia via a decrease in associated cellular activities, including neurotransmitter release, excitability, and gene expression (Cao 2006; Tran-Van-Minh & Dolphin 2010). Another mechanism involved in the analgesic activity of these drugs is upregulation of descending noradrenergic inhibitory pathways (Hayashida et al. 2008), the same mechanism involved in the analgesic activity of alpha-2 agonists. Gabapentin is a structural analog of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), and its use is associated with an increase in the brain’s concentration of GABA (KuKanich 2013).
Although these drugs are primarily used in the management of chronic and neuropathic pain, their use in the control of acute pain has also been reported. For instance, in a controlled study in 60 human patients undergoing hysterectomy, preoperative oral gabapentin (1.2 g) decreased pain scores and morphine consumption in the first 24 h postoperatively, but was also associated with a lower incidence of chronic incisional pain at 1, 3, and 6 months postoperatively (Sen et al. 2009). In veterinary patients, some studies have failed to demonstrate gabapentin’s efficacy in the control of acute pain associated with thermal stimulation in awake cats (Pypendop et al. 2010), and in dogs undergoing forelimb amputation (Wagner et al. 2010). However, in a study in dogs undergoing mastectomy, administration of gabapentin (10 mg/kg PO) perioperatively was associated with a significant decrease in the dose of rescue analgesia with morphine during the first 72 h postoperatively (Crociolli et al. 2015).

Gabapentin is currently available in the form of capsules (100 and 300 mg) and tablets (600 and 800 mg). An important consideration for gabapentin use in dogs and cats is the difference in its disposition in these species compared with humans. The terminal half-life of gabapentin in dogs (3–4 h) and cats (3 h) is shorter than in humans. The difference in the metabolism rate of gabapentin in dogs and cats necessitates doses of 10–20 mg/kg q 8 h to maintain therapeutic concentrations (KuKanich 2013).

In dogs, sedation and ataxia are occasional adverse effects of gabapentin, and these are more common when higher doses are used; therefore, dose adjustment may be necessary for individual animals, especially when gabapentin is used in combination with other drugs. In addition, abrupt discontinuation of gabapentin after chronic administration may result in withdrawal syndrome and seizure activity. Therefore, in chronic use, tapering the dose over the course of 1 week is recommended (KuKanich 2013).

**NMDA ANTAGONISTS**

N-methyl-D-aspartate (NMDA) receptors (NMDARs) are amino acid receptors predominantly located in the central nervous system (CNS) and are involved in perception and transmission of noxious
stimuli mediated by the excitatory neurotransmitter glutamate (Muir 2010). Multiple variants of NMDARs are required for normal brain function, and they play a central role in learning, memory, and the development of the CNS in hyperactive states (Petrenko et al. 2003). NMDARs contribute to the pathogenesis of wind-up in chronic pain and the development of primary and secondary hyperalgesia and allodynia. These manifestations commonly occur following a severe or chronic nerve or tissue injury in which stimulus-independent firing of the second-order neurons and increased production of glutamate receptors occur (Love & Thompson 2014). Therefore, blockade of NMDARs can enhance analgesia and produce antihyperalgesic effects, particularly in subjects suffering from chronic pain.

Multiple drugs with nonselective NMDAR antagonism are available, and those most commonly used in veterinary medicine include amantadine and ketamine. Methadone, a pure opioid agonist, has some NMDA antagonistic effects and is also discussed briefly in the following.

**Amantadine:**

Amantadine is primarily known as an antiviral medication; however, the NMDA antagonistic properties of this drug have expanded its use to control pain, particularly for the treatment of central sensitization. The pharmacokinetics of amantadine in dogs are not fully understood, nevertheless, administration of 3–5 mg/kg q 24 h is recommended for cats and dogs (Love & Thompson 2014; Robertson 2005). In dogs, the limited data indicate a short half-life of 5 h after a 30 mg/kg dose (Bleidner et al. 1965). In cats, amantadine has a high oral bioavailability, yet a similarly short half-life (5.5 h) is reported after a 5 mg/kg dose (Siao et al. 2011). In contrast, the half-life in humans is 15 h (Aoki & Sitar 1992); thus, a dose interval adjustment to q 12 h is recommended by others (KuKanich 2013).

**Ketamine:**

Ketamine is primarily considered a dissociative anesthetic that is most commonly used for induction of anesthesia. In hemodynamically unstable human trauma patients, ketamine is considered as a preferred
anesthetic induction agent due to its indirect sympathomimetic effects that typically result in increased blood pressure, pulse rate, and cardiac output. In addition, ketamine has amnestic, analgesic, and anxiolytic activities (Green et al. 2011).

In addition to its anesthetic effects, ketamine’s use as an analgesic and in the treatment of hyperalgesia has gained significant interest. In humans, ketamine improves perioperative opioid efficacy (Suzuki et al. 1999) and decreases opioid-induced hyperalgesia (Minville et al. 2010). In a literature review of analgesic effects of ketamine in people, a mean reduction of 40% in opioid consumption was reported when a low-dose infusion of ketamine (infusion rates of less than 1.2 mg/kg/h) was used perioperatively (Jouguelet-Lacoste et al. 2015). For animals undergoing surgical procedures using general anesthesia, particularly those with chronic inflammation and pain, ketamine may be incorporated in the anesthetic protocol for induction of anesthesia, as well as used as a CRI intra and postoperatively. In the author’s practice, ketamine is commonly used in combination with benzodiazepines for induction of anesthesia and is used in the form of a CRI (1–3 mg/kg/h) intraoperatively for its analgesic and particularly antihyperalgesic properties. Additionally, the author recommends administration of a ketamine CRI (0.5–1 mg/kg/h) in awake animals as a component of multimodal analgesia in animals that suffer from chronic pain, refractory to the traditional opioid-NSAID analgesic therapy.

SEROTONIN AND NOREPINEPHRINE-MODULATING AGENTS

Amitriptyline:

Amitriptyline was originally known as an antiviral medication. It is currently known for its efficacy in the treatment of neuropathic pain and has been evaluated in many placebo-controlled human trials. Amitriptyline improved pain and sleep disorders in fibromyalgia (Goldenberg et al. 1996) and was found superior in improving pain, fatigue, and quality of life compared to duloxetine, an SSNRI (Hauser et al. 2011).
Amitriptyline is available in tablet and injectable form and the common dose used in humans is 10–15 mg q 24 h (Chinn et al. 2016), but the daily dose to achieve results may vary from 75 to 150 mg (Gupta et al. 1999). In dogs, doses of 1–2 mg/kg q 12 h are recommended (KuKanich 2013); however, in a pharmacokinetic study in dogs, an oral dose of 3–4 mg/kg was associated with a short half-life of 5 h (Kukes et al. 2009). The latter results, therefore, may suggest the need for higher dose (3–4 mg/kg q 12 h) recommendation for clinical cases. In cats, the currently used dose of amitriptyline (1–2.2 mg/kg q 12 h) may also require adjustment, as these doses are associated with a short half-life and low plasma concentrations (KuKanich 2013). Nonetheless, to prevent adverse effects and reduce the risk of development of serotonin syndrome, gradual dose escalation is recommended, especially when mood-modifying drugs from different classes are co-administered (e.g., tramadol, amitriptyline, dextromethorphan, etc.) (Love & Thompson 2014).

Tramadol:

Tramadol is a synthetic codeine analog and is classified as an atypical opioid with weak opioid agonistic activity. In addition, tramadol has some similarities to TCAs in that it inhibits serotonin and norepinephrine reuptake, and may also facilitate 5-hydroxytryptamine release (Desmeules et al. 1996). Based on the literature and the author’s clinical experience, it seems that tramadol has limited efficacy, if any, in controlling acute pain. However, the use of tramadol, particularly if combined with other analgesics (e.g., opioids and NSAIDs), can provide an additional benefit in animals with chronic painful conditions. Based on a pharmacokinetic study in dogs, doses of 5 mg/kg q 6 h or 2.5 mg/kg q 4 h predicted tramadol and ODM plasma concentrations consistent with analgesia in humans (KuKanich & Papich 2004). Under clinical conditions, doses of 4 to 10 mg/kg PO q 8 h are recommended for dogs (KuKanich 2013). But when tramadol was used for several days (20 mg/kg PO for 8 days), the achieved plasma concentrations were reduced by 60% to 70% (Matthiesen et al. 1998). The latter may be due to either decreased drug absorption
or enhanced systemic metabolism. Nevertheless, this may dictate a need for dose adjustment in the longer-term use of tramadol in dogs. Doses of 2–4 mg/kg PO q 12 h are recommended for cats (KuKanich 2013).

The main adverse effects of tramadol may include sedation and dysphoria, especially in cats (Lamont 2008). Tramadol tablets have a bitter taste and can result in profuse salivation and retching in dogs and cats. Other adverse effects of tramadol overdose include restlessness, difficulty walking, salivation, vomiting, tremors, and convulsions. These excitatory effects are more likely if tramadol is co-administered with other serotonin and norepinephrine reuptake and monoamine oxidase inhibitors, such as selegiline (Lamont 2008). Diazepam may be effective in controlling tramadol-induced convulsions (KuKanich 2013). Higher risk of gastrointestinal (GI) adverse effects was reported in three dogs that received a combination of tramadol with deracoxib (Case et al. 2010). In humans, tramadol co-administration increases the potential for NSAID-associated GI adverse effects, and this is thought to be primarily due to serotonin-enhanced gastric acid secretion and decreased platelet aggregation (Torring et al. 2008). Therefore, concurrent administration of acid-suppressing agents (e.g., H$_2$ blockers or proton pump inhibitors) with tramadol may be beneficial in preventing adverse GI effects (KuKanich 2013).

**Prostaglandin Receptor Antagonists:**

Prostaglandin E2 (PGE2) is an important prostanoid with roles in homeostasis, pain, and inflammation. PGE2 binds to several receptors, of which, the EP4 receptor is responsible for mediating inflammation and pain in osteoarthritis. It is proposed that selective inhibition of EP4 receptors would maintain a more favorable homeostasis compared with nonselective PG inhibitors, and this is achieved by using a new class of drugs known as piprants (Shaw et al. 2015). Piprants were developed for the control of pain and inflammation associated with osteoarthritis in dogs and cats. The safety of long-term oral administration of the newly developed drug grapiprant has been reported in 36 beagles (Rausch-Derra et al. 2015). In early 2016, in the United States, galliprant (grapiprant tablets- Aratana Therapeutics) received approval from FDA as a new analgesic and anti-inflammatory medication for osteoarthritis (OA) in dogs.
To evaluate the effectiveness of Grapiprant in alleviating pain in dogs with OA, 285 client-owned dogs with OA were enrolled in a study and treated with either grapiprant (2 mg/kg) per OS or placebo (Rausch-Derra et al., 2016). Grapiprant treatment improved the pain interference and pain severity score in the grapiprant group compared to placebo. Grapiprant was generally well tolerated, but a higher percentage of treated dogs (17.02%) had occasional vomiting as compared to the placebo group (6.25%).

Based on these preliminary clinical reports and in view of FDA approval, grapiprant may be considered a valuable addition to multimodal approach to management of pain in dogs with osteoarthritis.

FUTURE ADJUNCTIVE ANALGESIC PHARMACEUTICALS

With simultaneous advancement in pain research and pharmaceutical technology, many other new analgesics have been developed, but yet require further research to prove their efficacy and potentially refine their pharmacological properties. In this section, some of these new drugs with potential for use as analgesics in future, are briefly discussed.

Anti-Glial Medications:

The crucial role of glial cells, astrocytes, and microglia in the maintenance of neuronal homeostasis in the CNS is well known. Upon activation, these cells release a number of signaling molecules with protective or pathological effects on the nervous system. The role of microglia in nociception and development of neuropathic pain via the release of pro-inflammatory immune factors in the spinal cord and dorsal root ganglia has been reported (Milligan & Watkins 2009). Glial activation opposes opioid-induced analgesia, reduces opioid efficacy, and creates dependence (Vallejo et al. 2010; Mika et al. 2013). Therefore, it has been proposed that pharmacological attenuation of glial cell activation would have a therapeutic effect in the treatment of chronic and neuropathic pain. Ibudilast (development codes AV-411 or MN-166), an inhibitor of glial activation and cyclic nucleotide phosphodiesterases, is in clinical use in Asia as a bronchodilator for the treatment of asthma. However, with its antiglial activity, this drug has a potential for
treatment of neuropathic pain and opioid withdrawal. In vitro, ibudilast suppresses glial lipopolysaccharide-induced production of inflammatory mediators, such as tumor necrosis factor α, nitric oxide, IL-1, and IL-6, and increases the production of anti-inflammatory cytokines, such as IL-10 (Kawanokuchi et al. 2004; Mizuno et al. 2004). In a study on rats, ibudilast had an additive antinociceptive effect when combined with morphine and partly restored morphine-induced antinociception in morphine-tolerant rats, but did not attenuate the development of morphine tolerance (Lilius et al. 2009).

Overall, based on the available information, it seems that there is potential for future clinical application of anti-glial medications; however, further research is necessary to determine their efficacy in a clinical setting.

**TRPV1 Receptor Antagonists:**

The analgesic efficacy of capsaicin, the active gradient in chili pepper, has been known for many years; but its mechanism of action has only been recently recognized. Capsaicin exerts its effects via the vanilloid receptor-1 (VR1), a nonselective cation calcium channel, and a member of the ligand-gated ion channel receptors called transient receptor potential channel (TRP). These receptors are primarily located on small myelinated and medium unmyelinated sensory fibers in different areas of the brain and spinal cord; their activation results in calcium and sodium influx and thus, membrane depolarization and transduction (Gunthorpe & Szallasi 2008; Kym et al. 2009). In neurogenic inflammation, TRPV1 receptors are triggered by inflammatory mediators and have a pivotal role in intracellular signaling and peripheral and central sensitization (Cui et al. 2006).

TRPV1 agonists result in an initial excitatory effect, but prolonged stimulation will result in receptor desensitization. To avoid the excitatory effects, considerable interest has been focused on the development of TRPV1 antagonists (Norman et al. 2007). Efficacy of some TRPV1 antagonists in laboratory conditions has been investigated and resulted in favorable preliminary findings (Hodgetts et al. 2010; Voight et al.
2014). In contrast, in a randomized placebo-controlled study in dogs with hip arthritis, an experimental TRPV1 antagonist (ABT-116) was inferior to carprofen or tramadol (Malek et al. 2012).

In summary, based on the available information, TRPV1 modulators such as RTX (Resiniferatoxin), may be considered valid options in animals with chronic pain; however, further evaluations are warranted to determine their role in the multimodal analgesic treatment of complex, painful conditions that are nonresponsive to conventional therapies.

References are available upon request (mrsed@utk.edu).
A Tale of Two Kitties: Demystifying GI Lymphoma in Cats

Feline gastrointestinal lymphoma is the most common form of alimentary neoplasia in cats. It accounts for approximately 55% of all cases of gastrointestinal tumors according to an epidemiologic survey conducted in 2011. The most recent classification of feline gastrointestinal lymphoma takes into account cell size, immunophenotype and location within the GI tract as well as what layers of the GI tract are predominantly affected. Feline gastrointestinal lymphoma can be broadly divided into two separate disease entities - large cell (high grade; lymphoblastic) and small cell (low grade; lymphocytic) disease. Each has a unique presentation, treatment, and prognosis. The aim of this lecture is to demystify the two major forms of gastrointestinal lymphoma in the cat.

Feline Large Cell GI Lymphoma
Dr. Andrea Dedeaux, DVM, DACVIM (SAIM)

Large cell gastrointestinal lymphoma affects the stomach, small intestine, and large intestine. Affected cats are typically middle-aged to older and retrovirus negative. The most common clinical presentation is acute weight loss, anorexia, vomiting, and diarrhea of days to weeks duration. Physical exam may reveal a palpable mass, as well as hepatomegaly and icterus.

Abdominal ultrasound reveals transmural intestinal thickening with disruption of wall layering. Lymphadenopathy is commonly noted. Extraintestinal involvement of liver, spleen, and kidney may occur. Intussusception, intestinal obstruction, and intestinal perforation have been reported in association with large cell GI lymphoma.

Most cases of large cell GI lymphoma can be diagnosed via cytology of the intestinal mass, abdominal lymph nodes, liver, or other affected organs. On occasion, histopathology may be needed to confirm the diagnosis. Advanced diagnostics, such as IHC and PARR, are usually not needed to make a definitive diagnosis.

Large-cell lymphoma in cats is an aggressive disease that requires aggressive treatment. Surgical intervention is generally reserved for cases with evidence of obstruction or peritonitis. Surgery may also be recommended in order to obtain a diagnosis.

Chemotherapy is the most common treatment modality for large cell lymphoma, with numerous protocols published. A multidrug protocol such as CHOP is typically considered to be the “gold standard” treatment. CHOP consists of alternating cyclophosphamide, hydroxydaunorubicin (doxorubicin), oncovin (vincristine), and prednisolone. Traditionally, the CHOP protocol involves weekly treatments for the first 8 weeks and then every other week treatments for a total of 25 weeks. Shorter protocols may also be effective in cats. Vinblastine is sometimes used as a substitute
for vincristine in COP and CHOP protocols. A recent study suggests that vinblastine causes less gastrointestinal side effects while retaining similar anti-tumor efficacy to vincristine when used as part of a multi-agent protocol. At UT, we sometimes use a modified CHOP protocol in which vincristine (0.025 mg/kg IV) and cyclophosphamide (10 mg/kg IV) are given concurrently once every 3 weeks for 3 treatments, followed by doxorubicin. This is repeated for up to 1 year as long as disease is not progressive. Anecdotally, cats seem to response similarly to this protocol. The decreased frequency in veterinary visits lowers treatment costs and is a good option for fractious cats or owners with logistical constraints. Oral CCNU is typically reserved as a rescue therapy but may be used first line in fractious cats. This is given by mouth (10 mg PO per cat) once every 4-6 weeks. CBCs should be checked weekly after the first dose to determine when the neutrophil nadir occurs. Gastrointestinal side effects from the drug are rare. The downside of this therapy is that if given first line further treatment has to be delayed (possibly for weeks) until the neutrophil count recovers. Prednisolone is used in conjunction with all of the above protocols at a dose of 5-10 mg/cat/day orally unless glucocorticoids are contraindicated in the patient (i.e. diabetic cats). This may be tapered depending on response to treatment.

Feline large cell lymphoma does not respond as well to chemotherapy as canine lymphoma. About 30% of cats will fail to respond to treatment. Most protocols have 50-60% response rate which includes both partial and complete responses. Median survival times range from 4-6 months. Cats achieving a complete remission may experience long-term survival (years), with 40% still in remission 1-year post-diagnosis.

The most consistent prognostic indicator in cats with large cell lymphoma is response to chemotherapy. Weight loss within the first month of treatment is also a negative prognostic indicator. Characteristics such as stage, substage, and immunophenotype (B vs. T) are not useful prognostic indicators in cats.

Radiation therapy may also play a role in treatment of large-cell GI lymphoma, either in combination with chemotherapy or as a rescue therapy for relapsed or chemotherapy-resistant disease.

**Feline Small Cell GI Lymphoma**

Dr. Olya Martin, DACVIM(Oncology)

Feline small cell GI lymphoma is predominantly found in the small intestine. This form of lymphoma is usually classified as involving the mucosa, although extension in to the submucosa and muscularis may occur. Although immunophenotype is not a prognostic indicator of outcome in feline lymphoma, it may be helpful to know for diagnostic purposes that~94% of mucosal small cell GI lymphoma is of T-cell immunophenotype. It is common for other organs such as liver and mesenteric lymph nodes to be involved.
Up to 53% of cats with small cell GI lymphoma had liver involvement and up to 33% - mesenteric nodal involvement in one report of 29 cases. The classic signalment for small cell GI lymphoma is an older, FELV negative cat.

Clinical signs range from weight loss (80-100%), and anorexia (66%) to vomiting and/or diarrhea (70-85%). The average duration of these signs is around 6 months. It is not uncommon for this disease to have a slow onset, with cats declining gradually rather than getting ill acutely. Abnormalities on abdominal palpation are reported in 70% of cats, but mostly consist of intestinal loop thickening and can be difficult to appreciate.

Diagnosis of small intestinal lymphoma can be a challenge. Clinical presentation and ultrasonographic abnormalities are often identical to inflammatory bowel disease (IBD). Diffuse thickening of the small intestinal wall is present in 50-70% of cats with small cell lymphoma and 10-50% of cats with IBD. Mesenteric lymphadenopathy is reported in 45-80% of cats with lymphoma and 15-20% of cats with IBD. Fine-needle aspirate cytology of the enlarged lymph nodes is rarely useful. Cytologic assessment is consistent with lymphoid hyperplasia in most cases. Definitive diagnosis can only be made on tissue samples utilizing histopathology, immunohistochemistry, and in some cases, ancillary means such as PARR analysis. Standard histopathology is reported to be 99% specific and 72% sensitive. Addition of immunohistochemistry brings the sensitivity up to 78%, and addition of PARR – to 83%. There is an ongoing debate in the oncology community about whether full-thickness biopsies are necessary. Some advocate endoscopic biopsies with immunohistochemistry and PARR. However, to date, full-thickness biopsy remains the standard of diagnosis.

Treatment is relatively straightforward for newly diagnosed patients. The preferred protocol consists of chlorambucil at either 20mg/m2 PO every 2 weeks OR 2mg PO EOD and prednisolone. The dosing of prednisolone in cats with small cell GI lymphoma has not been standardized. Some clinicians start with 1-2 mg/kg PO once a day reducing the dose to 0.5-1 mg/kg PO every other day for the long-term maintenance phase- typically one-year duration. Others recommend starting with 5-10 mg PO per cat once a day (5 mg for smaller, less clinically affected cats and 10 mg for larger cats or cats with severe clinical signs), reducing the dose to 2.5-5 mg PO per cat once a day indefinitely. Cats tend to tolerate long-term administration of steroids much better than dogs, but diabetes has been reported to occasionally occur with chronic treatment. The response rate to the chlorambucil/prednisolone protocol is reported to be greater than 90% with average survival of 2 years or longer. Rescue protocols for relapsed disease include injectable multi-agent (CHOP-like) chemotherapy, single agent cyclophosphamide, or single agent lomustine.
ULTRASOUND OF THE THORAX
IT’S NOT JUST FOR THE HEART!

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Resources

Introduction and Indications

Normal thorax:
• Evaluation of thoracic structures hampered by interposition of aerated lung tissue
• Can see thoracic wall, lung surface, intrathoracic fat, and possibly cranial mediastinal vessels

Abnormal thorax:
• Pulmonary consolidation, thoracic masses and/or pleural effusion may provide an “acoustic window”
Thoracic radiography should precede thoracic ultrasonography:
- Identify lesion
- Confirm presence of a suitable acoustic window
- Rule out entities precluding ultrasound examination (e.g., pneumothorax)
Technique

Ultrasound allows assessment of:
- Lesion location ("sliding", "extrapleural sign")
- Lesion extent/size and margination
- Lesion echotexture and echogenicity
- Bone involvement
- Presence of foreign material, gas and fistulous tracts

Examples: Neoplasms, abscesses, traumatic lesions...
Rib Mass

9-year-old English Bulldog
Chest Wall Mass

9-year-old English Bulldog
Chest Wall Mass
Thoracic Wall Abscess
Draining Tract

Rib Fracture

Pleura and Pleural Space
Pleural effusion:
• Amount
• Distribution
• Echogenicity
Pleural surface
Pleural thickening, masses and nodules
(Pneumothorax)
Mediastinum

Ultrasound most useful in evaluation of the cranial mediastinum
In some cases, evaluation of the caudal mediastinum possible (transhepatic approach)
Ultrasound facilitates differentiation between different etiologies of mediastinal widening on radiographs:
• Accumulation of fat
• Mediastinal effusion
• Cranial mediastinal mass
Helpful in evaluation of the cranial mediastinum in cases of concurrent pleural effusion

3-year-old FS DSH
Cranial Mediastinal Mass – Lymphoma

3-year-old FS DSH
Cranial Mediastinal Mass – Lymphoma
Sternal Lymphadenopathy

Cranial Mediastinal Mass Lesion (Cyst)

Caudal Mediastinal Mass
Other Mediastinal Abnormalities

Lung

Pulmonary mass lesions and nodules
- Solid lesions (usually hypoechoic) surrounded by normal lung
- Acute angle with thoracic wall
- Move with respiration

Alveolar infiltrates/consolidation
- Often hypoechoic, lung lobe usually normal shape

Abnormal position (?) and echogenicity
- Lung lobe torsion

Atelectasis (= Pulmonary collapse)
- Best evaluated if secondary to effusion, otherwise not seen
- Small, triangular portions of lung floating in effusion
15-year-old FS Dachshund
Pulmonary Carcinoma

Pulmonary Mass Lesions

Diagnosis: Histoplasmosis!
"Hepatization" of Lung

Abnormal Position (?) and Echogenicity

Atelectasis
Diaphragmatic Hernia
Rupture = traumatic diaphragmatic hernia
True (congenital) diaphragmatic hernia
Others

Diaphragmatic Rupture

True Diaphragmatic Hernia
A Case That Gave Me Nightmares...

...Should Have Read The Literature!

RADIOGRAPHIC DIAGNOSIS: INTRATHORACIC GALLBLADDER IN A DOG

Ultrasound Guided Procedures

One Last Clinical Case

12-year-old MC Labrador Retriever
Intermittent retching cough that has gotten worse for the past week
Ultrasound Findings

Conclusions

Ultrasound is a useful tool in evaluating the small animal thorax
An acoustic window has to be present
With few exceptions, ultrasound is used as an adjunct to thoracic radiographs
The Greatest Story Ever Told: The Story of Jeremiah; A Case-Based Approach to the Feline with Ventroflexion of the Neck

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The Problem-oriented Approach

Problem solving within veterinary practice can at times appear like magic to the casual observer. How the veterinary professional decides what is wrong with a pet and what course of action to take can appear to be somewhat of a black box process. In truth the process is fairly standardized and can be taught and practiced. Veterinarians use what has been termed the problem-oriented approach to veterinary medicine. The approach is defined but is flexible enough to be tailored to any practice environment. Some veterinarians even incorporate the approach into their record keeping by using the acronym SOAP. In the problem-oriented approach, the veterinary professional repeatedly defines and redefines problems and then uses the problem list and data about the case generated to assess each problem and to define a diagnostic, therapeutic, and client education plan necessary to solve each problem.

The problem-oriented approach begins by gathering a standard set of data. The data typically gathered initially includes; 1) the primary complaint of the owner, 2) the signalment (type of animal, breed, sex, and age) of the animal, 3) the past medical history, 4) the present medical history, and 5) the physical examination. The trained veterinary technician can be invaluable in these data gathering steps. Once the data is gathered a problem list is generated. The problem list becomes the back-bone around which the case is worked up and treatment decisions are made. Keeping in mind the defined problems the veterinary professional uses the data to make an assessment. The assessment might be a diagnosis, a list of potential diagnoses (differential diagnosis list or rule-out list), or might be an acknowledgment of the need for additional information. The assessment is used then to redefine the problem, in which case the process is repeated, or it is used to create a plan. The plan is always subdivided into diagnostic (gathering more data), therapeutic, and client education components.

Problem-oriented approach is often defined by the use of the term, SOAP. The S and O are the data arm, the A is the assessing arm, and the P is the plan:

- **S** Subjective data (that data usually the observations of the owner that is subjective in nature)
- **O** Objective data (that data, usually able to be quantified, that is generated by the observations of the veterinary professional)
- **A** Assessment
- **P** Plan (subdivided in a diagnostic, a therapeutic, and a client education plan)

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In this presentation the audience will be presented with a cat that is brought into a referral setting with a primary complaint of ventroflexion of the neck. The case will be followed as an example of the problem-oriented approach. Even though this is a fairly standardized process the ambiguity of practice is still significant and the results are often unexpected. This becomes obvious in this case. Not knowing precisely what each day may bring is one of the challenging aspects of veterinary medicine that makes the profession rewarding and fun. The following base of information will be used in the assessment of the cat’s problems and the development of a rational plan.

Thiamine Responsive Neck Ventroflexion (common)

Thiamine deficiency has been uncommonly diagnosed since the advent of readily available, nutritionally complete cat foods. Yet diseases that are thiamine responsive are still occasionally encountered. Thiamine deficiencies have been reported to cause weakness secondary to polyneuropathy and polymyopathy in man. While this has not been experimentally confirmed in the cat, clinical observations of thiamine responsive neck ventroflexion might suggest the existence of a similar disease process. Classical descriptions of thiamine deficiency in the cat have included dilated, slowly responsive pupils and rigid flexion of the neck with extensor rigidity of the forelimbs. Signs of vestibular involvement are also reportedly common. In my experience most cats that presented with ventroflexion of the neck and were responsive to thiamine therapy have not shown significant evidence of vestibular disease, nor have they been in extensor rigidity. Dilated, poorly responsive pupils have been a common but not consistent finding. Most of the cats were fed an adequate diet, implying that some cats may require higher levels of thiamine than are currently available in most commercial cat foods.

Since there is no readily available diagnostic test to rule out thiamine responsive disease, a therapeutic trial of thiamine is recommended in all cats that present with ventroflexion of the neck. Thiamine should be administered at a dosage of 25-50 mg IM once a day for the first two to three days. Improved or normal head carriage is usually noted within 24 to 48 hours. It is important that blood be drawn for CPK evaluation before the administration of thiamine, as the IM injections may increase CPK activity. The therapeutic trial can be attempted while waiting for serum chemistry and cholinesterase results.

Hypokalemic polymyopathy (Common; but less common since increased potassium has been added to feline diets)

A study by Schunk at Angell Memorial in Boston demonstrated that a high percentage of cats with neck ventroflexion and generalized muscle weakness were hypokalemic. Dow and coworkers from Colorado State University showed that renal potassium wasting associated with chronic renal disease appears to be the primary underlying etiology. Decreased dietary intake of potassium and metabolic acidosis is also important for most of the predisposed cats to become severely clinically affected. Diagnosis is dependent on demonstration of a low serum potassium (less than 3.5 mEq/L) and a high CPK in a cat with consistent clinical signs. Most of the cats will have generalized muscle weakness and ventroflexion of the neck without pain. About 25 percent of the cats will have muscle pain and a stiff or stilted gait. Electromyography will demonstrate abnormalities in multiple muscle groups but muscle biopsy fails to reveal...
histopathologic evidence of myositis. Azotemia and mild to moderate metabolic acidosis are also common findings. The pathophysiology of the disease is not completely understood but it is speculated that sarcolemmal hypopolarization and attenuation of muscle blood flow associated with hypokalemia produces the profound weakness.

Potassium administration should be initiated as soon as the diagnosis of hypokalemia is confirmed. Oral administration is recommended for all except the most severely affected cats. Parenteral administration of fluids, even those containing high concentrations of potassium may transiently decrease the serum potassium and worsen the clinical signs. Complete paralysis necessitating intubation and ventilatory support has been reported. Despite the potential dangers of parenteral potassium administration, parenteral therapy may be required in cats that are extremely weak, especially those in which respiratory paralysis appears imminent. Potassium gluconate tablets, gel, or powder (Tumil-K, Virbac Animal Health) is recommended as the most palatable available potassium salts. KCl can be used but is considerably less palatable and may worsen pre-existing metabolic acidosis.

The dose of oral potassium has been empirically determined to be 5 to 8 mEq divided twice a day in cats with serum potassium less than 3.0 meq/l. Improvement is usually seen in 24 hours with most affected cats being markedly stronger in 2 to 3 days. A maintenance dose of 2 to 4 mEq of potassium per day should be continued after the serum potassium levels have normalized. Feeding a diet containing greater than 0.6 percent potassium is recommended and may be sufficient as the sole potassium supplement in cats without severe renal disfunction.

**Hypernatremic Polymyopathy** (real zebra)

A cat with hypodipsic hypernatremia developed a polymyopathy that resulted in ventroflexion of the neck. The neck posture became normal with correction of the hypernatremia and returned to the ventroflexed position when the hypernatremia returned. High extracellular sodium concentrations have been shown to accelerate sodium-potassium exchange across the myocyte membrane causing high intracellular sodium concentrations and low intracellular potassium concentrations. These alterations are thought to alter myocyte membrane potentials and induce a transient myopathy that resolves with correction of the hypernatremia. Marked increases in serum sodium and osmolality in a cat with neck ventroflexion should suggest a diagnosis of hypernatremia induced polymyopathy. Creatine kinase (CPK) activity will also be increased.

**Idiopathic polymyositis** (uncommon)

Idiopathic polymyositis may present with generalized muscle weakness and ventroflexion of the neck. Fever is occasionally observed. The initial diagnosis is dependent on increased CPK activity, normal serum potassium, histologic evidence of myofiber necrosis and lymphocytic inflammation, and improvement following corticosteroid therapy. Electrophysiologic findings during electromyography (EMG) are generalized and identical to those seen in cats with hypokalemic polymyopathy. The underlying etiology is unknown but is presumed to be immune mediated. Polymyositis is an uncommon cause of neck ventroflexion. Treatment consists of immunosuppressive therapy. Prednisone (1 to 2 mg/lb BID-TID then
tapered) is the treatment of choice. Other immunosuppressive agents such as azathioprine or chlorambucil can be used with care.

**Polyneuropathy** (rare)

Polyneuropathies are poorly documented in the cat. The best characterized example is diabetic neuropathy, which presents as a distal neuropathy with clinical signs including plantigrade stance, depressed reflexes, and poor postural reactions rather than neck ventroflexion. However, polyneuropathy as a cause of ventroflexion of the neck has been observed. It is probable that other polyneuropathies will be reported with neck ventroflexion being a potential presenting complaint.

**Hyperthyroidism** (uncommon manifestation of a common disease)

Hyperthyroidism should be considered as a possible cause of neck ventroflexion is any adult cat, especially those over eight years old. Hyperthyroidism is the most common endocrinopathy affecting cats. Common clinical signs include weight loss, polyphagia, polydipsia, diarrhea, and nervousness. A small percentage (less than 20%) of hyperthyroid cats will be presented with primary signs of weakness and inappetence. A few of these cats will have marked ventroflexion of the neck. Three percent of the hyperthyroid cats in one large study presented with neck ventroflexion as one of the clinical signs. The ventroflexion is rarely of significant owner concern but is a striking finding on physical examination. The reason for the neck ventroflexion is not completely understood. One potential explanation is a concurrent thiamine deficiency due to anorexia, malabsorption, and/or polyuria. Because of this possibility, treatment with thiamine is warranted. Weakness and fatigue are frequent complaints of human patients with thyrotoxicosis. Often the weakness is most prominent in the proximal muscles. Thyrotoxic myopathy probably also occurs in some hyperthyroid cats and may contribute to ventroflexion of the neck when present. Diagnosis of hyperthyroidism can be made by demonstrating elevated resting T4 values. Treatment of hyperthyroid related neck ventroflexion should be geared toward treatment of the thyrotoxic state. Thiamine should also be given because of the possibility of concurrent thiamine deficiency. Response to thiamine does not rule out hyperthyroidism so a T4 should be checked on all adult cats that present for neck ventroflexion.

**Hereditary Neck Ventroflexion in Burmese and Devon Rex Cats** (rare in U.S.)

A heritable disease of Burmese cats manifested by episodic weakness and ventroflexion of the neck has been described in Australia. The signs were episodic and were apparently induced by stress. Less frequent signs included poor condition, muscle tremors, and limb stiffness. The age of onset varied from 4 to 10 months. Thiamine deficiency was thought to play a role in the observed clinical signs, but only equivocal improvement was reported following administration of thiamine. Since the report, there has been speculation that hypokalemia may have played a role in the pathogenesis of the disease syndrome. Serum and urinary electrolyte concentrations were not reported in any of the cats with congenital neck ventroflexion. However, one Burmese cat with hypokalemic myopathy has been reported. The diagnosis of hereditary neck ventroflexion is dependent on recognizing the typical clinical signs in a young cat.
Burmese cat and establishing a family history of the syndrome. There is no well accepted therapy, but thiamine and potassium supplementation should be considered. Breeding Burmese cats with this syndrome is not recommended.

A syndrome of muscle weakness manifesting as ventroflexion of the neck has been recognized in young Devon Rex cats in the UK and United States. It is an autosomal recessively inherited muscular dystrophy of congenital in origin. Typically the affected cats show marked cervical ventroflexion, a stiff gait, and dysphagia. Megaeosophagus is often part of the syndrome. Only the most severely affected cats show generalized muscle weakness. Serum chemistries are reportedly normal and effective treatment has not been demonstrated.

**Organophosphate Toxicity** (uncommon, usually due to exposure to yard insecticides)

A myasthenia-like syndrome can occur in cats exposed to acetylcholinesterase (AChE) inhibitors such as organophosphate (OP) compounds. Clinical manifestations may include generalized muscle weakness, tremors, and/or ventroflexion of the neck. Acetylcholine is the neurotransmitter at cholinergic nerve synapses and neuromuscular junctions. The neurotransmitter is normally inactivated by AChE within 5 msec after its release from presynaptic nerve terminals. OP insecticides act by binding to AChE, inactivating the enzyme and allowing the uninhibited buildup of acetylcholine. Continual stimulation of postsynaptic neuromuscular junctions leads to fatigue of the muscles and myasthenia-like signs.

The diagnosis of OP induced myasthenia-like disease is dependent on historical evidence of exposure to an OP in a cat showing consistent clinical signs. OP insecticide poisoning can be confirmed by demonstration of reduced cholinesterase activity in whole blood (EDTA or heparinized). A decrease in cholinesterase activity of at least 50% is considered significant inhibition with most cases of toxicity resulting in less than 25% activity. Cats with neck ventroflexion caused by myasthenia-like syndrome fail to respond to edrophonium. The weakness may even be more severe following edrophonium administration. Repetitive nerve stimulation will result in a decremental response similar to myasthenia gravis but the decremental response will not be abolished by administration of edrophonium (see discussion of myasthenia gravis).

Treatment with atropine will block the muscarinic and some central nervous system effects of OP but will not block the nicotinic receptor overstimulation that results in ventroflexion of the neck. Pralidoxime chloride (2-PAM) (20 mg/kg IM q 8-12 hr) also acts primarily at muscarinic sites but have been shown to be of benefit in treating cats with this form of toxicity. Diphenhydramine (Benadryl) (4 mg/kg of body weight PO every 8 hours) has been shown to block the nicotinic effects in man and dogs. Our clinical experience would suggest a similar efficacy in the cat. Diphenhydramine does not alter inhibition of cholinesterase but appears to act centrally to prevent the receptor paralysis.

**Myasthenia gravis**

Both congenital and acquired forms of myasthenia gravis have been reported in cats. In a review of eight cases, three presented with ventroflexion of the neck. Short strides, a choppy gait and weakness are other common signs. Palpebral reflexes are absent in most cats with myasthenia gravis. Voice change, regurgitation, and fine muscle tremors is less commonly seen.
Megaesophagus, a common abnormality associated with myasthenia gravis in the dog is less commonly seen in cats. Episodic weakness that worsens with exercise or activity is the typical presentation for myasthenia gravis in the dog but in our experience, clinical signs appear to be less episodic in cats. Approximately 50% of the cats that I have diagnosed as having myasthenia gravis presented with ventroflexion of the neck as the primary or only complaint. The ventroflexion worsened with activity in only one of these cats.

Diagnosis is dependent on pharmacologic, immunologic, and electrodiagnostic tests. Serum chemistry values, including CPK and electrolytes are consistently normal. Pharmacologically, a positive edrophonium test is suggestive of the diagnosis. Edrophonium chloride (Tensilon®), an ultrashort acting acetylcholinesterase inhibitor, is administered at a dosage of 0.25 - 0.5 mg IV. Alleviation of the weakness is considered a positive test result. Care must be taken in the interpretation of equivocal improvement as the weakness associated with other diffuse neuromuscular diseases will occasionally improve after the administration of edrophonium. Muscarinic signs of overdosage include salivation, lacrimation, urination, defecation, and bradycardia. These signs can be countered by the administration of atropine. Nicotinic signs of toxicity can be more serious and include exacerbation of weakness and respiratory paralysis. Animals with organophosphate toxicity are most likely to show these signs when given edrophonium. An endotracheal tube should be available during an edrophonium test so that intubation and ventilatory support can be performed should nicotinic signs of toxicity occur. Unequivocal confirmation of acquired myasthenia gravis can be immunologically documented by detection of acetylcholine receptor (AChR) antibodies. Cats with congenital myasthenia gravis will not have AChR antibodies. Electrophysiologically, a decrement of the evoked muscle action potential during repetitive nerve stimulation with normalization of the decremental response after administration of edrophonium is consistent with a diagnosis of myasthenia gravis.

Other potential causes
Hypocalcemia
Hepatoencephalopathy
Ammonium chloride toxicity
Chronic metabolic acidosis
A Case Based Approach to the Cat with Endocrine Disease

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Hypercalcemia is a common endocrine abnormality seen in small animal practice. It occurs secondary to aberrations in Calcium and Phosphorus metabolism, most often secondary to neoplastic diseases or renal failure. Idiopathic hypercalcemia is common in cats. Normally, calcium is absorbed from the intestinal tract via an active transport process. It is poorly absorbed with 80% of the daily calcium intake excreted in the feces and 20% excreted in the urine. A constant dietary source is therefore needed. Absorption is decreased by glucocorticoids and increased by vitamin D. Calcium is freely filtered at the glomerulus and reabsorbed from the tubules. Most is reabsorbed in the proximal tubule (70%) and ascending limb of Henle (20%). Renal control of reabsorption takes place at the distal tubule and collecting ducts and is under the control of parathyroid hormone (PTH). Most calcium in the body is stored in the bone with less than 1% being present in the serum. Of the calcium in the serum about 50% is ionized (the active component) and the rest is chelated to organic anions or protein bound (mostly to albumin). As it is ionized calcium that is important clinically but total serum calcium that is usually measure it is important to recognize those factors that can influence serum and ionized calcium. Reduced albumin available for binding will result in a decrease in the total serum calcium proportional to the decrease in albumin. The ionized calcium will not be affected by a decrease in albumin but the total serum calcium will be reduced. The formula:

\[
\text{Adjusted Ca (mg/dl)} = \text{Serum Ca (mg/dl)} - \text{Albumin (g/dl)} + 3.5
\]

is used to adjust for any decrease in albumin and gives one an estimate of whether a low calcium is low solely because of a decrease in albumin or is low partially because of a likely decrease in ionized calcium as well. This formula is useful in dogs but not as useful in cats. The concept holds for cats but the formula is not accurate. Changes in pH will cause shifts of Ca between protein bound/chelated and ionized. Therefore measured total serum calcium is not affected but relative concentrations of ionized calcium will be. Acidosis will increase the ionized calcium while alkalosis will decrease the ionized calcium. This can be important clinically when
evaluating clinical signs and when considering treatment.

Ionized serum calcium is the most accurate measure of calcium having a pathophysiologic effect. Ionized serum calcium is under very fine control from Parathyroid hormone (PTH), Calcitonin, and Vitamin D. PTH is produced by chief cells in the parathyroid gland and released when ionized calcium is low. High ionized calcium feeds back on the chief cells and inhibits PTH release. At bone, along with vitamin D, PTH increases the number and activity of osteoclasts, resulting in resorption of bone. This is the primary place where calcium is mobilized from in animals that become hypercalcemic. At the kidney PTH promotes activation of 25(OH)D3 to 1,25(OH)2D3, promotes distal tubular reabsorption of calcium (also Mg, H+, NH4+), and inhibits proximal tubular reabsorption of phosphorus (also K+, HCO3+, Na+, cAMP, amino acids). In the intestine it is primarily vitamin D that is responsible for increasing Ca absorption. PTH is only indirectly involved. Calcitonin is produced in parafollicular (C) cells of the thyroid gland and released when serum ionized calcium is high. It decreases osteoclastic activity and blocks renal reabsorption of calcium. Vitamin D [1,25(OH)2 D3 is the most active form] has its primary effects at the intestine (increase Ca absorption) and bone (promote resorption). It has minimal effect at the kidney.

**Clinical Signs of Hypercalcemia**

The clinical signs of hypercalcemia are fairly nondescript. They are best exemplified by those dogs diagnosed with primary hyperparathyroidism and include:

<table>
<thead>
<tr>
<th>Dogs</th>
<th>pu/pd 70%</th>
<th>anorexia 32%</th>
<th>vomiting 12%</th>
</tr>
</thead>
<tbody>
<tr>
<td>listless</td>
<td>45%</td>
<td>urinary signs 27%</td>
<td>stiff gait 10%</td>
</tr>
<tr>
<td>weakness</td>
<td>40%</td>
<td>shivering 17%</td>
<td>constipation 10%</td>
</tr>
</tbody>
</table>

Based on 72 dogs with primary hyperparathyroidism; Feldman and Nelson. 1996.

<table>
<thead>
<tr>
<th>Cats</th>
<th>urinary signs 47%</th>
<th>anorexia 27%</th>
<th>weakness 4%</th>
</tr>
</thead>
<tbody>
<tr>
<td>vomiting</td>
<td>31%</td>
<td>pu/pd 9%</td>
<td>diarrhea 4%</td>
</tr>
<tr>
<td>lethargy</td>
<td>31%</td>
<td>weight loss 7%</td>
<td>constipation 4%</td>
</tr>
</tbody>
</table>

Based on 45 cats with hypercalcemia of varying etiologies; Schenck, et al. 2006

Polyuria and polydipsia are the most often noted signs in dogs and can be quite dramatic. It is caused by inhibition of the effectiveness of ADH resulting in partial nephrogenic diabetes.
insipidus. Urinary tract signs including hematuria, dysuria, stranguria, pollakiuria, and inappropriate urination are noted most often in cats where the propensity of calcium crystal and stone formation is high in the hypercalcemic state. Other clinical signs are often seen in dogs and cats that are hypercalcemic but would be caused by the underlying disease that is resulting in the hypercalcemia.

**Differential Diagnosis** (from most to least common)

One should initially be certain that the patient is indeed hypercalcemic as spurious hypercalcemia due to sample error, lipemia, or an unrepeateable result is a reason to see a high calcium on a chemistry panel. It is best to repeat the calcium determination before imparting on an expensive work-up.

**Hypercalcemia of Malignancy (pseudohyperparathyroidism)** - This is the most common cause of hypercalcemia in dogs. It is also a common cause in cats but idiopathic hypercalcemia and hypercalcemia associated with renal disease are also common in cats. Malignancy may result in hypercalcemia by many factors that increase bone resorption including; direct bony lysis by tumor produced cytokines, production of parathyroid hormone related protein (PTH-rP) or less commonly by production of PTH, activation of vitamin D or production of a vitamin D like substances. The most common tumor to result in hypercalcemia is lymphosarcoma (LSA) with about a third of dogs with LSA and less than 10% of cats with LSA being hypercalcemic. Greater than 90% have enlarged lymph nodes or mediastinal involvement. Few have no obvious tumor, however. Another important tumor to consider is anal sac apocrine gland adenocarcinoma. This is the most common perineal tumor of female dogs and 90% will be hypercalcemic. Multiple myeloma is another important cause of hypercalcemia. About 15-20% of dogs with multiple myeloma will be hypercalcemic. When it is seen it is a poor prognostic factor. Squamous cell carcinoma is a common reason for hypercalcemia in cats. Hypercalcemia associated with squamous cell carcinoma is seen at about the same prevalence as hypercalcemia associated with lymphosarcoma in cats. In general animals with hypercalcemia of malignancy will have hypercalcemia but either hypophosphatemia or hyperphosphatemia may be seen.

**Renal Failure** - hypercalcemia is seen in approximately 10% of dogs with renal failure.
However, this is one of the most common causes of hypercalcemia in cats. It is more common in animals with congenital renal diseases (esp. Lhasa apso, Shih Tzu, and Doberman pinscher) but can occur in any breed, at any age. The mechanism can include autonomous parathyroid gland secretion (tertiary hyperparathyroidism), decreased renal calcium excretion, or increased responsiveness to vitamin D. Both hypercalcemia and hyperphosphatemia are generally seen. Ionized calcium is rarely high in patients with kidney disease; usually being normal or low.

**Idiopathic Hypercalcemia in Cats** - idiopathic hypercalcemia is one of the most common causes of hypercalcemia in cats (along with hypercalcemia of malignancy and renal failure). The etiology is not currently known. All cats will have increased ionized calcium and total calcium but as many as half will not show any clinical signs. Calcium concentrations may be mildly or severely increased. There does not appear to be an age or sex predilection but long-haired cats are over represented. PTH concentrations are usually low or low normal and PTHrP is not usually detected. Magnesium and vitamin D concentrations are typically normal. The role of diet has been debated but to date specific etiopathogenic factors have not been identified. A diagnosis of idiopathic hypercalcemia is made when other causes of hypercalcemia have been ruled out. Though idiopathic hypercalcemia is the most frequent diagnosis in cats with hypercalcemia, it is an exceedingly uncommon in dogs.

**Primary Hyperparathyroidism** - This is likely more common than is generally diagnosed because many animals will have mild increases in calcium and mild nondescript signs. The cause is usually parathyroid adenoma which is often a small, non-palpable tumor of a single parathyroid gland. Parathyroid carcinoma is rare. Familial hyperparathyroidism is a rarely reported cause of primary hyperparathyroidism in young dogs. There are few reports of primary hyperparathyroidism in cats. Most cats are middle aged to older with nondescript clinical signs (anorexia and lethargy most commonly; vomiting, polyuria, polydipsia and weight loss in more advanced cases). Calcium-containing urinary stones occur in some cats. Diagnosis is usually made by demonstrating high or normal PTH concentrations in the face of high ionized serum calcium. Parathyroid adenomas may be localized via ultrasound of the cervical region but the small size (usually less than 5 mm) make this technique of low sensitivity except in the hands of very experienced ultrasonographers. Rarely, parathyroid masses might be palpated; usually if
there are cystic changes associated with a small tumor or there is a larger parathyroid adenocarcinoma. Surgical exploratory of the cervical region and parathyroid biopsy may be considered as a means of definitively documenting this disease but it can be difficult to differentiate hyperplasia from neoplasia in some adenomas. Generally hypercalcemia (both total calcium and ionized calcium) and hypophosphatemia will be noted.

**Hypoadrenocorticism** - Mild hypercalcemia is seen in about a third of dogs with hypoadrenocorticism. It is usually the dogs with more severe disease and most are also hyperphosphatemic. Hypoadrenocorticism is very rare in cats but can cause hypercalcemia when present this this species as well. Azotemia, hyperkalemia, hyponatremia, and hypoglycemia should cause one to consider hypoadrenocorticism. It is important to think of this very treatable cause of hypercalcemia because the clinical and laboratory presentation would otherwise be easily confused with renal failure.

**Bone Disease** - hypercalcemia is uncommonly seen with diffuse osteomyelitis, primary or metastatic bone tumors such as osteosarcoma, and disuse osteoporosis.

**Granulomatous Diseases** - Hypercalcemia has been reported with Blastomycosis, Histoplasmosis, Coccidioidomycosis, Pythiosis, and Schistosomiasis. It is thought to be caused by mononuclear cell activation of vitamin D and/or cytokine release resulting in bone resorption. This is a rare cause of hypercalcemia unless one practices in an area where these infectious diseases are common. In Louisiana it is most commonly seen with Blastomycosis, where as many as 10% of infected dogs may be hypercalcemic.

**Hypervitaminosis D** - may be due to excessive supplementation of vitamin D, ingestion of vitamin D rodenticides, ingestion of vitamin D containing plants, or ingestion of vitamin D containing medications. Hypercalcemia and hyperphosphatemia are typically seen. In animals in which excessive supplementation is the cause of hypercalcemia the history is important. Large breed pups are most commonly oversupplemented with vitamin D by “well meaning” owners. Toxicity from Vitamin D containing plants (*Cestrum diurnum* {day-blooming jessamine}, *Solanum malacoxylon*, *Trisetum flavescens*) is uncommon in small animal medicine.
Toxicity from Vitamin D3 (cholecalciferol) rodenticides (QuintoxR, RampageR, Rat-Be-GoneR) is seen more commonly. Signs include hematemesis and bloody diarrhea which separates cholecalciferol rodenticide toxicity from other causes of hypercalcemia. Calcipotriene, a topical dermatological calcitriol analogue prescribed for the treatment of psoriasis in humans, has caused hypercalcemia from ingestion by licking the compound off of the owner’s skin.

**Diagnostic Approach** - The following is list of diagnostic tests that may be part of an approach to the patient with hypercalcemia.

Repeat Serum Calcium - an animal should not be considered hypercalcemic based on a single sample, especially if the sample is lipemic. Ionized calcium may help to differentiate hypercalcemia due to hyperparathyroidism and malignancy from hypercalcemia due to renal failure.

Go back to your Physical Examination - enlarged lymph nodes (R/O LSA), perianal mass (R/O apocrine gland adenocarcinoma of the anal sac)

**Serum Chemistry Panel and Urinalysis**

a. Hypoalbuminemia - correct calcium.

b. hypophosphatemia - prioritize hypercalcemia of malignancy or primary hyperparathyroidism.

c. azotemia - prioritize renal failure. However, the question that comes up is whether the renal failure is causing the high calcium or is caused by it. Additionally, the azotemia can be difficult to categorize into renal or prerenal causes because the high calcium itself will interfere with the ability to concentrate even if tubular function is still good.

d. hyperkalemia - prioritize hypoadrenocorticism or renal failure.
e. hypoglycemia - prioritize hypoadrenocorticism

CBC - helps rule out diseases that might cause inflammation

Thoracic and Abdominal Radiographs - R/O occult neoplasia, fungal disease. Radiographs of the thorax are especially important to rule out mediastinal lymphoma or fungal pneumonia.

Lymph Node Aspirate/Biopsy - R/O LSA

Bone Marrow - R/O LSA, multiple myeloma, and fungal disease.

PTH Concentrations - should be low when serum calcium is high. If high then prioritize primary hyperparathyroidism, renal failure, malignancy.

PTH-rP Concentrations - not done at very many labs but can be a marker of malignancy.

Measuring serum concentrations of 1,25-dihydroxycholecalciferol can be helpful in ruling out vitamin D toxicity.

Ultrasound of the neck - may visualize parathyroid adenoma.

Steroid Trial - useful after infectious disease has been ruled out. The calcium will usually drop if the hypercalcemia is due LSA but not if it is due to other malignancy. This is an inconsistent test, however.

Treatment of hypercalcemia

Hypercalcemia should be considered a medical Emergency if the calcium is greater than 18 mg/dl, the product of Ca x P is greater than 70 to 90, or the animal is azotemia and/or dehydrated. General principles of treatment include: 0.9% saline at a rate sufficient to replace deficits and twice maintenance. Saline infusion will increase GFR causing diuresis and
calciuresis. Sodium rich solutions decrease tubular sodium reabsorption and thus calcium reabsorption is decreased. Furosemide (Lasix®) - 2-4 mg/kg BID will inhibit reabsorption of calcium at the ascending limb. The animal must be rehydrated before diuresis will be effective. Glucocorticoids may result in tumor lysises (LSA) as a primary effect or may result in decreased gastrointestinal calcium absorption, interfere with vitamin D activation, increase renal calcium excretion, and inhibit osteoclast activating factor. It should be noted however that steroids should initially be avoided until infection can be ruled out and tests for hypoadrenocorticism and LSA can be performed. Prednisone can be used at 1-2 mg/kg. Calcitonin (Calcimar®) can be used in an emergency to decrease very high calcium concentrations quickly. Bone resorption and renal reabsorption of calcium and phosphorus is inhibited. The effect of calcitonin is rapid but short-lived. Bisphosphonates such as pamidronate disodium can be used in the treatment of hypercalcemia in dogs and cats (1.3 – 2.3 mg/kg; diluted in 150-250 mL of 0.9% sodium chloride and administered IV over 2-4 hours. It may be repeated every 21-28 days). Bisphosphonates act by inhibiting bone resorption via binding to hydroxyapatite crystals without inhibiting bone mineralization. They impede osteoclast activity, and induce osteoclast apoptosis. They are slower to effect than other forms of treatment but have a longer duration of effect. Care should be used in treating a patient with kidney disease. Alendronate is an orally administered bisphosphonate that has been used in cats and dogs. The dose in cats is initially 10 mg po per week. It should be given on an empty stomach to increase bioavailability. The drug can be very irritating to the esophagus so should be given with syringed water to minimize the time in the esophagus. There is less experience with the drug in dogs where 0.5-1 mg/kg daily has been suggested. Care should be used in patients with kidney disease. Compared to glucocorticoids, alendronate is more successful in lowering calcium concentration without the diabetogenic effects.
Feline Hyperthyroidism

Introduction

Definition = multisystemic disorder resulting from excessive circulating concentrations of the two thyroid hormones, thyroxine (T₄) and triiodothyronine (T₃). The disease was first described by Peterson in 1979. Increases in diagnosis have now made it the most common endocrinopathy of cats. The prevalence appears to differ from one region to another. It is postulated that circulating factors such as immunoglobulins, nutritional factors such as iodine, or environmental factors such as toxins or goitrogens may interact to cause thyroid disease in cats but the underlying cause of feline hyperthyroidism remains unknown. Increasing age, an indoor lifestyle, and eating canned cat foods all appear to be risk factors.

Etiology - most commonly caused by adenomatous hyperplasia of the thyroid gland(s). In 70% of cats both glands are involved and in 30% only one gland is involved. 1 to 2 % of the cases are caused by thyroid adenocarcinoma. It has been estimated to affect 10% of geriatric cats over their lifetime.

Signalment

Mean Age = 12.5 years old (range of reported cases is 8 months-22 years)

No breed or sex predilection.

Clinical Manifestations - the multisystemic nature of the disease and the broad range of clinical signs can make diagnosis confusing. Hyperthyroidism should be on your differential diagnosis for any older cat that presents with weight loss. Weight loss is the most consistent finding; being seen in approximately 88% of affected cats. Because, in most cats, the hyperthyroid state is slowly progressive and the cats usually maintain a good appetite and are active (or even hyperactive) the owner may not seek veterinary attention or realize there is a problem until later in the disease course. Many cats will be diagnosed through screening of older cats during yearly health checks.
### Frequency of Historical and Clinical Signs in 202 Cats with Feline Hyperthyroidism


<table>
<thead>
<tr>
<th>Findings</th>
<th>% of cats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td>88</td>
</tr>
<tr>
<td>Polyphagia</td>
<td>49</td>
</tr>
<tr>
<td>Vomiting</td>
<td>44</td>
</tr>
<tr>
<td>Pu/Pd</td>
<td>36</td>
</tr>
<tr>
<td>Hyperactivity/difficult to examine</td>
<td>31</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>16</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>15</td>
</tr>
<tr>
<td>Decreased activity</td>
<td>12</td>
</tr>
<tr>
<td>Weakness</td>
<td>12</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>10</td>
</tr>
<tr>
<td>Panting</td>
<td>9</td>
</tr>
<tr>
<td>Increased fecal volume</td>
<td>8</td>
</tr>
<tr>
<td>Complete anorexia</td>
<td>7</td>
</tr>
</tbody>
</table>

### Physical Examination Findings in 202 Cats with Feline Hyperthyroidism


<table>
<thead>
<tr>
<th>Findings</th>
<th>% of cats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpable thyroid mass</td>
<td>83</td>
</tr>
<tr>
<td>Thin</td>
<td>65</td>
</tr>
<tr>
<td>Heart murmur</td>
<td>54</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>42</td>
</tr>
<tr>
<td>Gallop rhythm</td>
<td>15</td>
</tr>
<tr>
<td>Hyperkinesis</td>
<td>15</td>
</tr>
<tr>
<td>Aggressive</td>
<td>10</td>
</tr>
<tr>
<td>Unkempt</td>
<td>9</td>
</tr>
<tr>
<td>Increased nail growth</td>
<td>6</td>
</tr>
<tr>
<td>Alopecia</td>
<td>3</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>2</td>
</tr>
<tr>
<td>Ventral neck flexion</td>
<td>1</td>
</tr>
</tbody>
</table>
**General Appearance and Behavior** - Affected cats are often thin, may have an unkempt hair coat, and are sometimes restless or difficult to handle. They are at times intolerant of stress and may become dyspneic and weak on manipulation. In general, the number of clinical and physical exam abnormalities have decreased as veterinarians have become more aware of the disease and are diagnosing it sooner. Many of the cats that we presently diagnose as hyperthyroid may appear quite normal to the owner or may only present for mild weight loss.

**Enlarged Thyroid Gland** - In approximately 90% of cats with hyperthyroidism physical exam will reveal enlargement of one or both thyroid glands. Thyroid palpation is an important part of the physical exam in any cat!!!! Normally, the thyroids are not palpable.

**Nervous System** - thyroid hormone directly stimulates the nervous system which may result in hyperactivity, restlessness, pacing, and irritability.

**Gastrointestinal System** - About half of affected cats will be polyphagic, yet still lose weight. About 1 in 5 may show decreased appetite or even complete anorexia, however. Chronic intermittent vomiting, and less often diarrhea, are important clinical signs to recognize.

**Renal System** - Both polydipsia and polyuria are induced by excessive thyroid hormone. Profound pu/pd is seen in about a third of cats with hyperthyroidism due reduced ADH release, nephrogenic diabetes insipidus, or primary polydipsia. Excessive thyroid hormone does not appear to directly cause renal failure but chronic renal failure is common in old cats and the two diseases often occur concurrently. The hyperthyroid state may actually improve renal function by increasing GFR and may improve the appetite of azotemic cats.

**Respiratory System** - Increased CO₂ production and respiratory muscle weakness can result in tachypnea, panting, or dyspnea, especially after stress.

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**Cardiovascular System** - cardiovascular abnormalities may be seen in cats with hyperthyroidism. They are usually very late findings and are not seen often when hyperthyroidism is diagnosed early. **Tachycardia, systolic murmur, gallop rhythm, arrhythmias, and evidence of congestive heart failure** may be noted. Thyrotoxic heart disease is the underlying problem and is characterized by **hypertrophic** changes, hyperdynamic contractility, and inefficient diastolic function. Congestive heart failure, when present, is a form of high output failure. The high output state causes volume overload which in turn leads to dilatation and hypertrophy. The hypertrophy can eventually result in inefficient diastolic filling. In most cases the changes are reversible if the hyperthyroid state is adequately treated. Rarely a dilated cardiomyopathy may be seen.

**Electrocardiography - abnormalities from most to least likely**

- **Sinus tachycardia** - most common finding
- Increased R wave amplitude in lead II
- Right bundle branch block
- Left anterior fascicular block
- Atrial arrhythmia (APC, atrial fibrillation)
- AV block
- Ventricular arrhythmias are very rare.

**Radiography** - most cases will not have radiographic abnormalities

- Cardiomegaly - is the most commonly recognized abnormality.
- Pleural effusion or pulmonary edema is less common.

**Echocardiography** - changes on echocardiography will be seen earlier than on thoracic radiographs.

**Left ventricular hypertrophy**

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Left atrial enlargement
Interventricular septal hypertrophy
Left ventricular dilatation
Hyperdynamic wall motion

Hypertension - reported prevalence between 20% and 80% in hyperthyroid cats. More significant problem in cats with concurrent renal failure. Blood pressure should be monitored as part of the minimum database in cats with hyperthyroidism.

Muscular System - Profound weakness is seen in a small percentage of hyperthyroid cats. It most commonly presents as ventroflexion of the neck similar to that seen in hypokalemic polymyopathy.

Rule Out List for non-painful Neck Ventroflexion
Hypokalemic polymyopathy
Thiamine responsive disease
Hyperthyroidism
Congenital neck ventroflexion of Burmese or Devon Rex cats
Polymyositis
Organophosphate intoxication
Polyneuropathy
Myasthenia gravis
Hypernatremia
Hepatic encephalopathy
Hypocalcemia

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Apathetic Hyperthyroidism - about 5% of hyperthyroid cats will present weak, lethargic, depressed, and anorectic. This is almost opposite of what you would expect. Weight loss is still usually present. Many of these cats will have significant thyrotoxic heart disease.

Conclusion - just about any sign that might be seen in a sick, old cat can be caused by hyperthyroidism. Add to that the fact that hyperthyroidism is common and *common things occur commonly* and the conclusion that you draw is that you should routinely screen for hyperthyroidism in any old cat that presents sick. If you’re not diagnosing this disease, you’re missing it!

Laboratory Tests

CBC
Stress leukogram is noted in about a third of affected cats [(leukocytosis (21%), neutrophilia, eosinopenia (34%), lymphopenia (40%)].

RBC count and PCV may be high-normal to slightly increased in about half of affected cats. This is due to increased erythropoietin and direct stimulation of the bone marrow by thyroid hormones. The MCV is also increased in about a third of affected cats.

Serum Chemistry Tests

Liver enzyme activities (SALT, SAST, SAP) are significantly increased in 50-75% of hyperthyroid cats.

BUN and Creatinine - azotemia is seen in 20-40% of hyperthyroid cats. It is not thought to due to the hyperthyroid state, but to concurrent chronic renal failure.

Hyperglycemia is seen in about 20% of hyperthyroid cats.

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Hyperphosphatemia is seen in about 10% of hyperthyroid cats many of whom are not azotemic. Hyperbilirubinemia is seen in about 4% of affected cats. Other electrolytes and serum chemistry tests are usually normal.

Urinalysis

SG - variable, cats that are polyuric may have an isosthenuric specific gravity.

Sediment - usually normal.

Thyroid Testing - definitive diagnosis

Resting serum T₄ and T₃ (T₃ is not useful as a screening test)

T₄ values will be increased in most hyperthyroid cats. Daily fluctuation are evident in some hyperthyroid cats causing T₄ values to dip into the normal range at times. Multiple samples at different times thus may be required in some cats to diagnose the hyperthyroid state.

T₃ values will also be increased in most cats. The T₃ is more variable than the T₄ and offers no advantages over T₄. It is thus not useful as a screening test.

TSH concentrations will be decreased but the low end of the sensitivity of TSH assays in cats is close to the normal concentrations for TSH making it difficult to show that TSH is actually low.

Free T₄ - Total T₄ can be reduced by illness (euthyroid sick syndrome). This can bring the total T₄ in as many as 20% of hyperthyroid cats into the high-normal range. Free T₄ is not affected as dramatically by non-thyroidal illness as total T₄ is. Studies would suggest that free T₄ is likely to be increased in hyperthyroid cats even when total T₄ is
normal. Therefore, free T4 should be evaluated in cats where the clinical signs support hyperthyroidism but the total T4 is normal. Note that some sick cats that are not hyperthyroid will have low or low-normal total T4 but have a high free T4 [the reason for this is not known] so total T4 and free T4 should always be evaluated together when trying to diagnose hyperthyroidism in a cat with a normal T4. T4 can be used by itself but Free T4 should not be used by itself!

**Results**

**Normal cat:** Normal T4 with a normal free T4 → rule out hyperthyroidism

- Low or low normal T4 with a high free T4 → equivocal result
  - (probably not hyperthyroid)

**Hyperthyroid cat:** High T4 → hyperthyroidism (you don’t need a free T4)

- Normal or high normal T4 with a high free T4 → hyperthyroidism

**Triiodothyronine (T₃) Suppression Test**

**Use** - to diagnose early cases where the T₄ is high normal or normal and free T4 is not available or is equivocal. The T₃ suppression test more definitively rules in or out hyperthyroidism than the free T4.

**Theory** - in the normal cat exogenous thyroid hormone will feedback on the hypothalamic-pituitary axis and decrease TSH secretion. The result will be decreased thyroidal production of endogenous thyroid hormone. The hyperthyroid cat should already have low TSH due to feedback inhibition from high endogenous thyroid hormone concentrations, therefore giving exogenous thyroid hormone will have no further effect on thyroid hormone production.

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**Test Protocol** - Serum T₃ and T₄ values are determined prior to T₃ administration. The following morning 25 μg of T₃ is given orally and repeated every 8 hours for seven doses; the final dose being given on the morning of the third day. Approximately 4 hours after the last dose serum is drawn for a second T₃ and T₄.

**Results**

**Normal Cat** - suppression of T₄ concentration by 50% or greater when compared to pretreatment value. High T₃ concentration confirms that the owner gave the T₃. If T₃ is normal than you need to be concerned about the cat not having gotten the T₃ medication.

**Hyperthyroid Cat** - little or no suppression of T₄ concentration is seen.

**Thyrotropin-Releasing Hormone (TRH) Stimulation Test** - The TRH stimulation test has the advantages of being shorter and easier to perform. It does not depend on administration of an oral medication and can be done in 4 hours. The test is performed by collecting blood for serum T₄ before and 4 hours after intravenous administration of 0.1 mg/kg of TRH. Normal cats and cats with non-thyroidal disease should show an increase in serum T₄ of greater than 50% while hyperthyroid cats will not. The big disadvantage of the test is that most cats will salivate, vomit, defecate, or become tachypneic after being given TRH.

**Thyroid Radioiodine Uptake** (Radioiodine Uptake Test) - hyperthyroid cats have increased uptake of the radionuclides radioiodine and technicium. Measurement of radioiodine uptake is a sensitive means of documenting hyperthyroidism. The actual uptake is dependent on dietary iodine levels and other sources of iodine, however.

**Thyroid Imaging (Radionucleotide Scanning)**

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Use - sensitive means of diagnosis of hyperthyroidism and localization of hyperactive thyroidal tissue. It can determine if one or both glands are hyperactive or if the hyperthyroid state is due to ectopic thyroidal tissue elsewhere in the body (the mediastinum is most often ectopic site). Functional metastatic tissue can also be visualized. This information is important to the surgeon considering thyroidectomy.

Isotopes - $^{131}$I, $^{123}$I, or $^{99m}$Tc can all be used. $^{99m}$Tc (technetium 99) is preferred for safety and ease of administration.

Therapy

Antithyroid Drugs - methimazole (Felimazole®, Tapazole®) is the drug of choice and will be discussed here. Carbimazole is an antithyroid drug that is metabolized to methimazole. It has fewer side effects than methimazole but is also less effective. Propylthiouracil (PTU) is effective but has a much higher incidence of side effects and is not recommended when methimazole or carbimazole are available.

Mechanism of action - block iodination steps in the formation of T₃ and T₄.

Indications: Long term control in animals that are not surgical candidates or candidates for radioiodine therapy. Short term control prior to surgery or radioiodine therapy. Initial Treatment (first 3 months or until surgery)

Goal - maintain the T₄ in the low or low normal range.

Dose - 5 mg BID PO or transdermal - most cats will be euthyroid in 1-3 weeks. The dose will need to be adjusted up or down based on T₄ determinations. Transdermal delivery results in slower normalization of serum T₄.
Follow-up - the cat should be rechecked at 2-3 week intervals. Serum T4, CBC, platelet count, and serum chemistry panel should ideally be performed at each recheck. After the first 3 months follow-up can be performed less frequently.

Side effects (oral treatment) - about 15% of cats will have mild side effects (anorexia [11%], vomiting [11%], lethargy[9%], and behavioral changes) associated with methimazole use. They usually resolve after lowering the dose. Severe side effects include hepatopathy [1%], agranulocytosis [1%], and thrombocytopenia with bleeding [2%]. Excoriation of the head due to methimazole induced pruritus is seen in about 2% of treated cats. If these less common signs are seen the drug should be discontinued and alternative therapy (low iodine diet, surgery, or radioiodine) should be considered. Side effects are less frequent with transdermal administration.

| TABLE 95-5. CLINICAL SIDE EFFECTS AND HEMATOLOGIC AND IMMUNOLOGIC ABNORMALITIES ASSOCIATED WITH METHIMAZOLE TREATMENT IN 282 CATS WITH HYPERTHYROIDISM |
|-------------------------------------------------|-----------------|-------------------|
| Sign                                           | No. of Cats (%) | Time When Signs Developed |
|                                                | Range   | Median |
| Anorexia                                       | 29 (11.1) | 1-78   | 18.4 |
| Vomiting                                       | 28 (10.7) | 7-60   | 15.4 |
| Lethargy                                       | 23 (8.8)  | 1-60   | 21.0 |
| Excoriations                                   | 6 (2.3)  | 6-40   | 19.0 |
| Bleeding                                       | 6 (2.3)  | 15-50  | 22.5 |
| Hepatopathy                                    | 4 (1.5)  | 15-60  | 41.0 |
| Thrombocytopenia                               | 7 (2.7)  | 14-90  | 24.0 |
| Agranulocytosis                                | 4 (1.5)  | 26-95  | 62.5 |
| Leukopenia                                     | 12 (4.7) | 10-41  | 23.0 |
| Eosinopenia                                    | 30 (11.3) | 12-490 | 21.0 |
| Lymphocytosis                                  | 19 (7.2) | 14-90  | 18.5 |
| Antinuclear antibodies*                        | 52 (21.8) | 10-870 | 46.0 |
| Positive Coombs’ Test*                         | 3 (1.9)  | 45-60  | 50.0 |

*Antinuclear antibodies determined in 239 cats and direct antiglobulin (Coombs') tests performed in 160 cats


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Treatment of systemic hypertension

Amlodipine (calcium channel blocker) (0.625-1.25 mg/cat sid-bid)  
ACE inhibitor (such as enalapril or benazepril) may need to be added

**Long-Term Treatment** - the lowest dose of methimazole that maintains low normal T₄ concentration should be used. Some cats will do fine on once a day methimazole, most will need twice a day, and some will require three times a day dosing. Long term follow-up should include a T₄ every 3 to 6 months to help with dosage adjustments. The hematologic and hepatic side effects rarely occur after the first 3 months of treatment, so routine CBC and chemistry panels are probably not needed after that time unless other problems develop. Owner compliance may tend to wane as time goes on. It should be stressed that cats can become thyrotoxic if even one day of medication is missed. Cats not receiving medications for as few as 2-3 days may have thyroid hormone concentrations rebound to very high levels and these cats can die due to the "thyroid storm" that develops during the thyrotoxic events.

**Treating hyperthyroidism and chronic kidney disease** - hyperthyroidism and chronic kidney disease are both common in older cats. The hyperthyroid state has been shown to increase GFR and decrease some of the signs associated with chronic kidney disease. Increase in GFR has both prerenal reasons (increased cardiac output due to increased sympathetic tone and decreased peripheral resistance) and renal reasons (stimulation of the renin-angiotensin-aldosterone system which dilates the afferent arteriole while constricting the efferent arteriole at the glomerulus. This increases filtering pressure which can increase GFR but also damage the glomerulus resulting in proteinuria and eventual tubular damage. However, as the hyperthyroid state worsens the thyrotoxic heart disease and hypertension can worsen the renal disease. Some
hyperthyroid cats will develop anorexia and have a worsening of their renal disease after treating their hyperthyroid state. After treating cats for hyperthyroidism, iatrogenic hypothyroidism may decrease GRF and worsen underlying kidney disease. Maintaining T4 in the mid to high normal range is important and may require thyroid hormone supplementation in some cases. Azotemic cats that are treated for hyperthyroidism should have T4, free T4, and cTSH monitored to prevent iatrogenic hypothyroidism.

**Low iodine containing diet** - diets very low in iodine have been shown to reduce thyroid hormone synthesis in hyperthyroid cats. Hill’s y/d is a low iodine containing prescription diet that can be used to treat hyperthyroidism as long as there are no other foods or treats eaten. It has been shown to take about 3 weeks for T4 concentrations to normalize in newly diagnosed hyperthyroid cats fed Hill’s y/d. The diet became available in fall of 2011 and gives another option in the management of hyperthyroid cats.

**Surgery** - thyroidectomy is a highly effective means of treating hyperthyroidism but can be associated with significant morbidity.

**Preoperative Preparation** - a euthyroid state should be achieved (methimazole or low iodine diet [see above]); a beta-blocker (atenolol) should be administered if significant tachycardia or thyrotoxic heart disease is present. 2-4 weeks is usually a sufficient period of time for medical treatment prior to surgery. More time will be necessary in cats with severe heart disease. The last dose of methimazole should be given the morning of surgery.

**Surgical Considerations**

**Unilateral disease** - hemithyroidectomy should be performed. It is rare for the hyperthyroid state to recur if the cat truly has unilateral disease. If bilateral disease was present but not recognized the hyperthyroid state will usually recur within the first 9-12 months following surgery.
Bilateral disease - bilateral thyroidectomy should be performed with care taken to preserve the parathyroid gland integrity and blood supply. Inadvertent parathyroidectomy or devascularization due to less than ideal tissue manipulation will result in postoperative hypocalcemia.

Postoperative complications

Iatrogenic hypoparathyroidism - Signs of hypocalcemia include muscle tremors, tetany, and convulsions. Serum calcium should be monitored daily until it is normal. Mild hypocalcemia (6.5-7.5 mg/dl) does not need to be treated unless accompanied by clinical signs. More severe hypocalcemia may need to be treated with calcium and vitamin D.

Hypothyroidism - rarely permanent but may require transient thyroid hormone supplementation if radioiodine has been used at higher doses or bilateral thyroidectomy has been performed. This is probably a significant contributor to kidney disease after treating hyperthyroidism.

Horner's syndrome
Laryngeal paralysis
Radioactive Iodine Therapy - treatment of choice

Theory - radioactive iodine (\(^{131}\)I) is concentrated in the thyroid gland where it emits β and γ radiation which destroy the hyperfunctioning thyroid tissue. Atrophied normal thyroid tissue will not be affected if appropriate radiiodine dosages are used because the β and γ particles only travel a short distance (≤ 2 mm). The "ideal" dose can be calculated based on thyroid kinetics or an empiric dose of 2 to 6 mCi can be given. Higher doses (10 to 30 mCi) have proven effective in treating cats with thyroid carcinomas. Hypothyroidism is more likely when higher doses are used.

Precautions - after treatment the cat will need to be quarantined for 1 to 4 weeks to allow time for the radioactivity to decrease. All material removed from the cage must be handled as radioactive waste.

Expense - this is currently the most expensive approach to treatment at most referral centers. (est. cost, LSU; approx. $ 2,500-$3,000). It may be the ideal approach for many cases, however.
A Case-based Approach to the Icteric Cat: Hepatic Lipidosis (Part 1) and Inflammatory Liver Disease (Part 2)

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Most of the noninvasive techniques used in evaluating the feline patient with suspected hepatobiliary disease, such as hepatic enzymology, liver function tests, and hepatobiliary imaging are useful in localizing disease to the liver or biliary system, however, they can rarely be used to establish a definitive diagnosis or an accurate prognosis. Invasive techniques are usually required for this purpose. Invasive (laparotomy, laparoscopic, ultrasound guided percutaneous, or blind percutaneous) techniques are necessary to obtain liver tissue for cytologic or histopathologic evaluation. Techniques for biopsy of the liver may require anesthesia, special equipment, and carry the risk of complications. Fine needle aspiration (FNA) can be utilized to obtain liver tissue for cytology. FNA of the liver is a relatively safe procedure that is simple to perform while requiring no special equipment and minimal patient sedation. Together with the rest of the diagnostic evaluation, FNA can be a useful tool in establishing a diagnosis and prognosis in selected patients with hepatobiliary disease. Additionally, it is a non-invasive technique that can be useful in deciding which subset of patients may require biopsy.

Hepatic Ultrasonography and Ultrasound Guided Biopsy

Ultrasonography is becoming more and more routine in the evaluation of the patient with hepatobiliary disease, especially in the referral setting. Indeed, the availability of ultrasound is often used by the primary care practitioner when making the decision whether or not to refer a patient. Hepatobiliary ultrasonography is readily available and often considered the non-invasive procedure of choice for trying to differentiate between primary hepatic and post-hepatic causes of cholestasis, for identifying portosystemic vascular anomalies, and for identifying focal or multifocal hepatobiliary abnormalities. Recent work has tried to correlate hepatic ultrasonographic images with histopathologic findings. Hepatic lipidosis in cats and hepatocutaneous syndrome (superficial necrolytic dermatitis, necrolytic migratory erythema) in dogs are examples of diseases where findings on hepatic ultrasonography are helpful in making a diagnosis. Care must be taken not to over-interpret results, however, because unfortunately, there can be tremendous variability in the echogenic pattern produced by a given disease. It is usually difficult, if not impossible, to predict the histopathologic infiltrate from the echogenic pattern observed.

One of the advantages of ultrasonographic evaluation of the liver is that ultrasound may be used to guide placement of needles for biopsy or FNA. This technique is especially useful when investigating focal or multifocal disease that might be missed by blind techniques. Biopsy guides are available for most transducers to facilitate ultrasound-guided biopsy. Visualization of the needle and biopsy site during the procedure may improve accuracy of biopsy and detection of complications. Ultrasound guided biopsy is widely considered safer than other biopsy techniques but studies supporting or refuting this contention are lacking. The small gauge needle used for biopsy in many of the percutaneous ultrasound guided techniques can be a limiting factor when trying to interpret hepatic biopsies obtained.

Numerous liver biopsy techniques have been described. Blind percutaneous techniques are the simplest and most cost effective in many situations. There is a perception, however, that they are less accurate than other techniques and carry a higher risk of complication. Few studies have looked at the relative risk and diagnostic accuracy of percutaneous biopsy in the dog and cat. A 0% to 8.4% risk of complication has been reported in the few small studies reported. There was positive correlation between biopsy and necropsy findings in 80% of the cases in one study. In man, larger studies (189,085 people biopsied) have identified a complication rate of 0.28% and a mortality rate of 0.03%. Anemia and cancer would appear to be factors positively correlating with an increased risk of complication. Type of needle used, operator experience, biopsy technique (transabdominal vs. transthoracic), and platelet count are not.

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Hepatic Fine Needle Aspirate (FNA)

Fine needle aspirate of the liver is simple and requires no special equipment. It can be performed with a 6- or 12-cc syringe and a 22-gauge, 1.5- to 3.5-inch disposable hypodermic or spinal needle. The 22-gauge spinal needle is useful in larger animals because of the longer sizes available but is rarely necessary when being used in cats. The needle is inserted into the liver via a percutaneous transabdominal (in cats and most dogs) or transthoracic approach (in large deep chested dogs) and gentle suction (3-5 ml) is applied. While maintaining suction, the needle is gently but quickly thrust into the liver parenchyma and then brought back to the original position without exiting the liver. The suction is then released and the needle is withdrawn. If the technique is properly performed, blood will rarely be noted in the syringe or needle hub as the entire specimen should remain in the needle. To transfer the specimen to a clean glass slide detach the needle, draw a few milliliters of air into the syringe, reattach the needle, and gently expel the liver sample onto the slide. Do not forcibly "blow" the specimen onto the slide as this may damage the cells and result in preparation artifacts. Squash prep smears or blood film techniques may be used to smear hepatic samples.

The transabdominal technique can be performed either in dorsal or right lateral recumbency with the pelvis of the animal positioned slightly lower than the head. I prefer lateral recumbency because patient restraint is generally easier. With the animal in lateral recumbency the needle is inserted at the point where the left costal arch begins its dorsal ascent. It is angled at about 45° to the body wall. The left caudal thoracic mammary gland is usually just ventral and slightly caudal to the point where the needle is to be inserted. Once the peritoneal cavity has been entered the needle is brought parallel to the body wall and slowly advanced while gently feeling down for the liver with the tip of the needle. Once the liver is felt the needle is again angled at 45°, the needle tip is placed into the liver parenchyma, and the aspirate is performed.

FNA is most useful in evaluating patients with hepatomegaly but it often gives valuable information in patients with normal sized livers as well. Diffuse infiltrative, inflammatory, and neoplastic diseases lend themselves best to an FNA diagnosis. FNA is less applicable to focal or multifocal diseases or diseases in which cells do not exfoliate easily, such as fibrosis or sarcoma. Kristensen, et al. recently described a classification scheme for interpretation of hepatic cytology: their categories include normal, hyperplastic, inflammatory, degenerative, necrotic, cholestatic, neoplastic, mixed reactions, other reactions, and non-diagnostic.

Hepatic Cytology

The predominant cell type in a normal hepatic FNA is the hepatocyte, often found in cohesive clusters or regular sheets. Hepatocytes are large polyhedral to rounded cells with abundant gray to basophilic cytoplasm. They have a single (occasionally two) eccentric nucleus with uniformly course chromatin and a small, distinct nucleolus. The cytoplasm is usually granular with a small amount of green bile pigment occasionally present. Small columnar epithelial cells of biliary origin may also be observed. Low numbers of macrophages (Kupffer's cells) with or without intracellular hemosiderin are sometimes seen. Because of the highly vascular nature of the hepatic sinusoidal milieu a background of erythrocytes and blood-borne leukocytes is invariably present.

Degenerative diseases are characterized by cytoplasmic vacuolar changes. The differential diagnosis for hepatic vacuoles includes fat, glycogen, hydropic degeneration, and storage diseases. Feline hepatic lipidosis is the characteristic example of diseases of this type. In the dog, glycogen deposition associated with steroid hepatopathy or hydropic degeneration associated with an ischemic or toxic insult is more likely. Extracellular deposition of amorphous material is seen in hepatic amyloidosis. It is not uncommon to see mild hepatocellular vaculization in cats with a large variety of chronic diseases so care must be taken in interpreting the finding vacuolar hepatopathy in this species. Inflammatory specimens are characterized by increased numbers of inflammatory cells interspersed between normal and/or reactive hepatocytes. The predominant inflammatory cell type characterizes the inflammation present. A definitive diagnosis can be made in some protozoal or systemic fungal diseases based on the
presence of identifiable organisms. Histoplasmosis is the systemic fungal disease most likely to be diagnosed via hepatic FNA. One of the most useful applications of hepatic FNA is the diagnosis of hepatic neoplasia. Lymphosarcoma, biliary carcinoma, or metastatic neoplasias are the most likely hepatic tumors to be diagnosed.

Because FNA is usually a blind tissue sampling technique it is most applicable when the clinical evaluation suggests diffuse parenchymal disease. Focal diseases are less likely to be diagnosed by blind aspirate techniques. The accuracy of hepatic FNA can be improved by obtaining multiple aspirates so at least 3 aspirates taken from slightly different angles should be routinely obtained.

Complications of hepatic FNA are extremely rare. Bleeding is rarely a clinically significant problem even in animals with coagulation abnormalities. Using a blind technique to aspirate cells from the liver will occasionally result in inadvertent gall bladder aspiration. Aspiration of the gall bladder rarely causes serious problems for the patient. In fact, with ultrasound guidance the technique is routinely used to sample bile in cases of suspected cholangitis or liver fluke infestation. It should be noted that while FNA is a quick and easy technique, the sample does not always accurately reflect the underlying histopathologic diagnosis. Few studies have looked at correlation between FNA cytology and histopathology in the dog and cat. There was a 66% correlation in one study. The fact that correlation is not 100% stresses the point that care should be taken when interpreting results that do not seem to fit the presenting clinical picture. Liver biopsy is still often needed for definitive diagnosis.

Feline Hepatic Lipidosis

Feline hepatic lipidosis is the most common feline liver disease in many studies. It is characterized by massive hepatocellular accumulation of triglycerides accompanying a disruption in hepatic lipid metabolism that often results in severe liver dysfunction. Most cases are idiopathic but diabetes mellitus, prolonged starvation, over-nutrition, hyperthyroidism, and hyperparathyroidism are possible initiating causes. Female cats are affected almost twice as frequently as males. Chronic vomiting is the most common presenting sign. Anorexia, weight loss, icterus, and hypersalivation are also seen. Many affected cats are (or were) obese yet show significant muscle wasting at the time of diagnosis. Not all cats with hepatic lipidosis are obese. Total bilirubin, SAP, SALT, SAST, and GGT are usually increased (>2-5 times normal about 75% of the time). About half of affected cats will be hyperglycemic (glucose > 200 mg/dl). Abdominal radiographs may reveal mild hepatomegaly and ultrasound may reveal increased hepatic echogenicity. Diagnosis is dependent on demonstration of heavily vacuolated hepatocytes on fine needle aspirate or liver biopsy. Aggressive treatment is important. If an underlying disease process is evident it should be treated. General therapy should include treating dehydration, hypoglycemia (if present), hypokalemia, hypophosphatemia, and hepatencephalopathy (lactulose 1-3 ml/cat adjust to maintain soft stool and metronidazole 7-10 mg/kg PO bid-tid). Vitamin K1 (0.5 to 1.5 mg/kg SQ) can be administered if cholestasis has resulted in a bleeding tendency. PIVKA will be increased if vitamin K1 is needed. Nutritional support is the most important aspect of therapy. Total caloric intake should be 80-100 Kcal/kg/day. Protein supplementation is important. Diets based solely on carbohydrates may worsen the disease so moderate or even high protein diets such as Hills Prescription Diet® p/d™ or a/d™, Eukanuba Veterinary Diets® Nutritional Recovery Formula™/Canine & Feline, or Abbott Animal Health™ Clinicare® Canine/Feline Liquid Diet or Clinicare® RF should be used. Switch to a lower protein diet if signs of hepatencephalopathy ensue. Dietary supplements that have been recommended but not critically evaluated in cats with hepatic lipidosis include l-carnitine (250-500 mg/day), taurine (250-500 mg/day), B-complex, zinc (7-10 mg/kg elemental Zn/day), and vitamin E (20-100 mg/day). Force feeding or enteral feeding is invariably necessary to maintain appropriate caloric intake. Appetite stimulants may assist the owner who wishes to force feed their cat but will rarely result in enough of an increase in appetite to meet the nutritional needs appropriate to treatment goals. Cyproheptadine [Periactin®] 2 mg/cat, mirtazapine [Remeron®] 1/8 to ¼ of a 15 mg tablet per cat, and oxazepam [SeraX®] 1 mg/kg sid-bid may be used. Diazepam (0.1 ml IV) and Midazolam (2-5 mcg/kg IV) can also result in appetite stimulation. The effect of diazepam is usually short lived and causes significant sedation. Midazolam may cause a more lasting stimulation and less sedation. Care must be taken if benzodiazepines such as oxazepam or diazepam are used because they may worsen
hepatoencephalopathy. Oral diazepam has been noted to occasionally be hepatotoxic. Enteral feeding will probably be needed in most cats with hepatic lipidosis. Esophagostomy, gastrostomy, or nasoesophageal feeding may all be used successfully. Gastrostomy and esophagostomy feeding is tolerated well by most cats. The tubes can be placed surgically or percutaneously via endoscopy or blind techniques. Enteral feeding may need to be continued for months in some cases. With aggressive nutritional support 75-95% of cats have a good prognosis while without aggressive nutritional support less than 10% of cats will do well. Pancreatitis as a concurrent disease process should be considered in cats not responding to therapy. Refeeding induced hypophosphatemia is a rare complication that can cause hemolysis or neurologic signs that may mimic hepatoencephalopathy.

Feline Inflammatory Liver Disease

Cholangitis and cholangiohepatitis is a complex of related inflammatory hepatobiliary disorders. They accounted for approximately 26% of the liver diseases reported in cats in one large retrospective study (Gagne, et al. JAVMA, 1999; 214:513). This was second to hepatic lipidosis which accounted for approximately 50% of the cases. Inflammatory liver diseases are characterized by the predominant inflammatory cell infiltrate seen histopathologically. The inflammation is usually seen in the portal areas; and can be characterized as suppurative (neutrophilic), non-suppurative (lymphocytic/plasmacytic); sclerosing lymphocytic cholangitis, or biliary cirrhosis (fibrosis). There have been many terms used in the veterinary literature to describe inflammatory liver diseases prompting the World Small Animal Veterinary Association (WSAVA) Liver Standardization Group to suggest standardized criteria for diagnosis of liver diseases of dogs and cats. The standards define three main forms of cholangitis which are recognized to occur in feline patients: neutrophilic cholangitis, lymphocytic cholangitis, and chronic cholangitis associated with liver fluke infestation. Cholangitis is often associated with periportal necrosis. Neutrophilic cholangitis can be further subdivided into acute (also termed suppurative by some authors) in which neutrophils are seen and chronic in which a mixture of neutrophils and lymphocytes/plasma cells are seen. Lymphocytic cholangitis (formerly lymphocytic portal hepatitis) is the term that has become accepted to describe the histologic classification in which lymphocytes and/or plasma cells are noted to infiltrate the portal areas. This replaces the older term, "lymphocytic/plasmacytic cholangiohepatitis." Lymphocytic cholangitis was more common than neutrophilic cholangitis; being seen in 61% of the cats with inflammatory liver disease in the study by Gagne, et al. Although other studies have noted that chronic neutrophilic cholangitis may be more common. Whether these classifications represent different stages in the progression of one disease or are separate etiologic entities is not known. Nor is the underlying etiology of inflammatory liver disease in cats. Bacterial, allergic, and immune mechanisms have all been speculated to be involved. Bacterial cholangitis may either initiate the inflammatory process or perpetuate it early in the disease course. Immune mechanisms probably also play a role especially in chronic neutrophilic cholangitis and lymphocytic cholangitis. Cats with inflammatory hepatobiliary disease, especially those with suppurative disease, may also have pancreatitis and inflammatory bowel disease. The relationship between these three inflammatory conditions is not well worked out but it has been speculated that the underlying initiator of the inflammatory process may affect the liver, the pancreas, and the small intestine concurrently. The term, “triaditis” has been coined to describe those situations in which inflammation of the liver, pancreas, and small intestine are seen to occur concurrently. While not a very accurate description, the term seems to have stuck.

The clinical findings seen in cats with inflammatory liver disease are similar to those seen with hepatic lipidosis and other liver diseases. Vomiting, anorexia, lethargy, and weight loss are typical. Fever is occasionally seen. Diarrhea while not usual is more common than in cats with hepatic lipidosis and may represent the subset of cats with concurrent inflammatory bowel disease. Affected cats are rarely obese. Cats with neutrophilic cholangitis tend to be younger and are more likely to be severely systemically ill when compared to those cats with lymphocytic cholangitis. Any age cat can be affected. Males predominate in populations of cats with neutrophilic cholangitis as compared to those with lymphocytic cholangitis. Suppurative disease often has an acute course while disease characterized by lymphocytic/plasmacytic inflammation may be more chronic. In evaluating liver enzymes, alkaline phosphatase tends not to be as elevated as in cats with hepatic lipidosis and transaminase activities tend to be higher. It is important to note that liver enzymes can be normal, even in cats with significant...
hepatobiliary inflammation. Neutrophil counts, transaminase activities, and total bilirubin concentrations tend to be higher in cats with neutrophilic cholangitis when compared to cats with lymphocytic cholangitis. All liver enzymes may be normal early in the course of disease, however. Diagnosis is usually dependent on biopsy as FNA is often normal or reveals non-specific changes. Biopsy for both histopathology and culture should be performed if inflammatory liver disease is suspected. The advent of readily available ultrasonography has resulted in Tru-cut needle biopsy becoming the most popular method of obtaining tissue for histopathology. The diagnostic accuracy of Tru-cut obtained biopsies has been questioned (Cole, et al. JAVMA, 2002; 220:1483-90). In the study by Cole, et al. liver biopsies obtained from dogs and cats by tru-cut techniques were compared to wedge biopsies. Paired 18 g Tru-cut needle biopsies commonly yielded a different diagnosis than wedge biopsy. If it is assumed that the wedge biopsy is the “gold standard” then the 18 g Tru-cut biopsies were highly inaccurate. Larger samples obtained with a 14 g needle may be more accurate. Laparoscopically obtained samples should be considered when feasible. Prior to biopsy, coagulation parameters should be evaluated. PIVKA may be the most sensitive indicator of potential bleeding tendencies. Vitamin K1 (0.5-1.5 mg/kg SQ given within 24 hours of biopsy may decrease the risk of bleeding.

In addition to the supportive and nutritional support used to manage cats with hepatic lipidosis, antibiotics should be used when treating cats with inflammatory liver disease. For patients with suspected loss of hepatic function, it is ideal to select drugs that rely on the kidneys for elimination rather than hepatic biotransformation. In the case of antibiotic therapy, the β-lactam antibiotics (penicillin, ampicillin, cephalosporins) are the best choice. (Hepatic reactions observed in people caused by amoxicillin-clavulanate were associated with a specific leukocyte antigen and have not been reported in animals.) The fluoroquinolones (enrofloxacin, marbofloxacin, orbifloxacin, difloxacin) have had a good safety record and increased risk of toxicity in animals with hepatic disease has not been documented. Although some of these drugs are metabolized, the clearance is low and probably not affected unless there is substantial loss of hepatic function. These drugs are also cleared by the kidneys. Fluoroquinolones have been known to cause central nervous system (CNS) problems in susceptible individuals. This is most likely caused by penetration across the blood-brain-barrier (BBB) and inhibition of the action of the GABA neurotransmitter. Problems observed have been seizures, excitement, and disorientation. Animals with seizure disorders caused by hepatic encephalopathy may be more prone to CNS problems caused by fluoroquinolones. If a complication is observed after prescribing a fluoroquinolone drug, a switch to a safer drug is appropriate. Macrolides (erythromycin, azithromycin, and similar drugs) are sometimes used for infections in animals with hepatic disease. There are no specific problems identified in patients with hepatic disease, but these antibiotics are often associated with gastrointestinal problems in animals (diarrhea and vomiting). Therefore, when prescribing these drugs, veterinarians should be careful not to mistake a drug-related problem for an underlying disease, or complicate an already-existing problem. Metronidazole and related drugs (tinidazole, ronidazole) are sometimes used in patients with hepatic disease because of the anaerobic spectrum. They have been safe drugs when prescribed according to standard dose recommendations, but when doses have been exceeded, problems may arise. The most serious problem caused by metronidazole has been attributed to CNS toxicity and include seizures, ataxia, nystagmus, tremors, and rigidity. These signs have been attributed to inferring with the inhibitory neurotransmitter GABA. Because animals with hepatic disease also may be prone to CNS disorders that also share these clinical signs, veterinarians should understand the risks of metronidazole, and become familiar with the signs associated with toxicity. When using other antimicrobials, veterinarians should be aware of the common adverse effects that may occur if a drug accumulates because of a deficiency in metabolism. Drugs to avoid, if possible, include: trimethoprim-sulfonamides, tetracyclines, rifampin, nitrofurantoin, and chloramphenicol.

Immunosuppressive agents should be added to the treatment regime in cats with lymphocytic disease and in cats with neutrophilic disease that fail to respond to antibiotics alone or antibiotics and nutraceuticals. Prednisolone (2-4 mg/kg/day initially then slowly tapered to 1 mg/kg QOD) is used most commonly. Other immunosuppressives that may be used in cats responding poorly to glucocorticoids include chlorambucil (1.5 to 4 mg/M² twice a week to every other day; approximately 1 mg < 7 lb cat, 2 mg > 7 lb cat) [probably a safer alternative to azathioprine in the cat], azathioprine (0.3 mg/kg q24-72 hrs) [Note that cats are much more sensitive to the myelosuppressive effects of azathioprine than dogs].
methotrexate (0.4 mg divided into 3 doses and given over 24 hours and repeated every 7-10 days has been advocated as a pulse therapy but has not been extensively studied). Ursodeoxycholic acid (Actigall® 10-15 mg/kg PO SID is a safe treatment alternative that can be used in cats with either suppurative or non-suppurative disease. The drug appears to have multiple actions including shifting the bile acid pool to a less toxic hydrophilic population, a choleretic effect, reducing expression of Class 2 major histocompatibility complex, and an antinflammatory effect. Vitamin E (aqueous alpha tocopherol, 10-100 IU/kg/day) has been advocated for its antioxidant effects. SAMe (90-180 mg PO SID; Denosyl® NutraMax) is a precursor of glutathione. Glutathione is an important antioxidant that has been shown to be reduced in dogs and cats with liver disease. The nutriceutical SAMe may help replace glutathione. It also may have hepatoprotective effects in preventing programed cell death (apoptosis) that occurs during inflammatory liver disease. Milk thistle (silymarin) is a nutriceutical that is widely used for its hepatoprotective effects. It may be of benefit as an antioxidant, as an antifibrotic agent, or as an aid in hepatic regeneration. Many studies have evaluated its use in people and show mixed results. Studies in dogs and cats are lacking. Anecdotal evidence would suggest it may be useful at a dose of 50-200 mg/kg PO SID. A combination of silybin and SAMe is available as the nutriceutical Denamarin Advanced® for cats by Nutramax. The small tablet size together with the ability to crush the tablets and mix with a small amount of food without substantially decreasing bioavailability makes this formulation much easier to use than previous formulations for cats. Silybin is one of the active ingredients in milk thistle. It is complexed with phosphatidylcholine to increase the bioavailability.

Pancreatitis

Pancreatitis is a common inflammatory disease that has historically probably been over diagnosed in dogs and under diagnosed in cats. It can be acute, recurring, or chronic. Acute necrotizing pancreatitis is most common in dogs. It is a pathophysiologic process in which intrapancreatic enzymes are activated resulting in increases in capillary permeability, initiating of vasoactive amines, and direct tissue damage. Vascular injury and tissue necrosis within the pancreas often extends locally to the stomach, duodenum, colon, and liver. Systemic inflammatory response syndrome (SIRS) is a common sequel. Acute necrotizing pancreatitis is seen less commonly than chronic pancreatitis in cats. Chronic pancreatitis is associated with inflammation and fibrosis. Pancreatic stellate cells appear to be important in the pathophysiology of chronic pancreatitis. Stimulated by oxidative stress and cytokines involved in the inflammatory process, activated stellate cells migrate to the periacinar areas to deposit collagen and fibronectin. The fibrosis contributes to obstruction of pancreatic ductules which in turn contributes to inflammation. Fibrosis appears to be important to the pathophysiology of disease in cats. The pathologic characteristics of feline pancreatitis appear to be similar to those in people; especially when compared to that of dogs.

Signalment: Any age or breed of cat or dog may develop pancreatitis. In the dog middle-aged, obese females are overrepresented. In cats most cases are domestic short-haired cats but Siamese and Persian cats may be overrepresented.

Clinical signs: The typical presentation in dogs includes sudden onset of vomiting, anorexia, depression, and abdominal pain. There is often a history of recent ingestion of a fatty meal or dietary indiscretion. Presenting clinical signs in cats include anorexia, lethargy, dehydration, hypothermia, and weight loss. Vomiting and abdominal pain are noted less frequently in cats than in dogs with pancreatitis. Diarrhea is occasionally noted. Dogs and cats with severe pancreatitis may develop ascites and dyspnea associated with pleural effusion. Icterus is a variable finding. An abdominal mass may be noted and was noted in as many as a third of cats in some studies. This is probably representative of only those cats with very severe pancreatitis. Hypotension and shock are severe complications seen commonly in acute necrotizing pancreatitis. While usually idiopathic, pancreatitis has been associated with hyperlipoproteinemia and hypertriglyceridemia, cholinesterase inhibitors such as organophosphates, trauma resulting in hypoperfusion, and drugs such as thiazide diuretics, furosemide, estrogens, azathioprine, L-asparaginase, sulfonamides, tetracycline, metronidazole, H2-receptor blockers, acetaminophen, procainamide, and nitrofurantoin in dogs. In cats toxoplasmosis, FIP, hepatic lipidosis, liver and pancreatic flukes, lymphosarcoma, trauma, fenthion toxicity, idiopathic chylomicronemia, and
diabetes mellitus have all been implicated. Potential risk factors for pancreatitis in dogs, such as obesity, dietary indiscretion, a high fat meal, high fat diets, and pre-existing endocrine diseases do not appear to be risk factors in cats.

**Diagnosis:** Hematology and serum biochemistry findings are generally non-specific. A mild normocytic, normochromic non-regenerative anemia and leukogram findings consistent with a stress or mild inflammatory leukogram are typical in cats. In dogs a more significant inflammatory leukogram and hemoconcentration would be more likely. A severe neutrophilia with a left shift is usually only seen in severe acute necrotizing pancreatitis. Thrombocytopenia may be noted and is usually mild. Increased ALT, AST, GGT, and alkaline phosphatase activities are typically noted. Bilirubin may be mildly increased but this is not a consistent finding. Dogs are often azotemic but cats are less likely to be azotemic than dogs with pancreatitis. Hyperglycemia is common and may be associated with stress or with the development of diabetes mellitus. The relationship between pancreatitis and diabetes mellitus is well documented in dogs but not well described in cats. However, cats with diabetes mellitus caused by chronic pancreatic inflammation appear to be very sensitive to insulin administration. Anorexia may result in hypokalemia. Hypocalcemia is common but it is rarely severe enough to cause clinical signs. Hypocalcemia may indicate a poor prognosis in cats with pancreatitis. Occasionally hypercalcemia may be noted. Hypoalbuminemia may be noted, especially in dogs and cats with severe disease or concurrent liver disease. Serum cobalamin is low in a high percentage of cats with pancreatitis.

A lack of sensitive and specific markers of pancreatitis may make antemortem diagnosis of pancreatitis difficult, especially in cats. Serum amylase and lipase have long been used as screening tests for pancreatitis in dogs but are of little use in the diagnosis of pancreatitis in cats. Serum lipase is thought to be the better of the two enzymes for diagnosing pancreatitis in dogs because it is less likely to be increased in renal or other intraabdominal disease. That said, it is neither sensitive nor specific. Feline trypsin-like immunoreactivity (fTLI) has been used as a test for pancreatitis in cats but has not proven sensitive. Feline TLI appears to increase acutely but returns to normal very early in the disease course in most cats making it less than ideal as a diagnostic test. It has been suggested that serum concentration of fTLI > 100 µg/L is approximately 80-90% specific and 30-60% sensitive for feline pancreatitis. An abnormal result is therefore usually, but not always, associated with pancreatitis. Azotemia may increase fTLI and increases have been noted in cats with severe inflammatory bowel disease. An immunoassay for measuring pancreatic lipase [pancreatic lipase immunoreactivity (PLI)] has been developed by the Texas A&M Gastrointestinal Diagnostic Laboratory and licensed to Idexx Laboratories. It is now considered to be the most sensitive and specific test for diagnosing pancreatitis in dogs and cats. Studies in cats with experimental pancreatitis would indicate that fPL increases rapidly after the development of pancreatitis and stays increased for much longer than fTLI. In one published study (Forman et al., J Vet Inten Med 2004;18:807-815), fPL was found to be 80% sensitive for feline pancreatitis, but there was not a significant difference between cats with pancreatitis and healthy cats. The use of fPL is recommended in combination with abdominal ultrasound (see below). Commercial assays for measurement of cPLI (Spec CPL™) and fPL (Spec fPL™) are based on the original cPLI and fPLI technology. The Spec fPL™ has become available through IDEXX Laboratories.

**Diagnostic Imaging:** Radiographs are usually non-specific. Decreased serosal detail may be noted if ascites is present. Decreased detail in the upper right quadrant on the ventrodorsal view may be noted but is seen less commonly in cats than in dogs with pancreatitis. A mass effect may be noted in severe cases. Pleural effusion may be noted on thoracic radiographs. Ultrasound of the pancreas in pancreatitis may reveal a mixed or hypoechoic pattern, cavitary lesions, dilation of the pancreatic ducts, or evidence of peripancreatic edema and effusion. The pancreas may appear normal on ultrasound in many cats with pancreatitis, but a recent study (Forman et al.) found 80% sensitivity and 88% specificity for ultrasound in diagnosing feline pancreatitis. Because of the similar sensitivity and higher specificity of abdominal ultrasound vs. fPLI found in this study, ultrasound could be considered the more useful diagnostic test. Further study is needed before firm recommendations can be made. Abdominal computed tomography (CT) has not been shown to be useful in diagnosing pancreatitis in cats.
Biopsy: The gold standard in diagnosis of pancreatitis is histopathology. Findings in cases of acute pancreatitis include peri-pancreatic fat necrosis, and focal to multifocal pancreatic acinar cell necrosis and inflammation. The inflammation can be quite variable making evaluation of multiple biopsies from different sites critical. Chronic pancreatitis is more common in cats and is usually characterized by variable degrees of fibrosis and lymphocytic inflammation. Fibrosis appears to be more important than inflammation in chronic pancreatitis in cats. The pancreas may appear grossly normal so biopsy is warranted even in cases where the pancreas appears normal at laparotomy or laparoscopy. In a recent study the prevalence of pancreatitis based on histopathology was 67% in cases with GI and other disease and 45% in apparently healthy cats.

Treatment (Canine): Depending on the severity of the pancreatitis, treatment of dogs can at times be both difficult and frustrating. In most cases of canine pancreatitis a specific underlying etiology cannot be determined but if it is, specific treatment for that cause should be initiated. Treating shock, rehydration and maintenance of normovolemia are the initial goals of therapy. Fluids such as 0.9% NaCl or lactated Ringers should initially be given. Potassium should be added to the fluids to maintain normal potassium, and glucose should be added if hypoglycemia is noted. Maintaining pancreatic microcirculation may be enhanced by plasma (20ml/kg IV) or colloid (10-20ml/kg/day IV) administration. Plasma transfusion is widely recommended in veterinary medicine but has not been critically evaluated in dogs and cats with pancreatitis. Studies in human patients with pancreatitis have not shown an advantage of plasma therapy. Dextran 70 and hetastarch may have antithrombotic effects that help maintain the microcirculation in addition to their colloidal effects. An external source of heat may be necessary to treat hypothermia, especially in smaller dogs with a larger surface area to weight ratio. Antibiotics should be directed against a bacterial infection if one is suspected. Even if a primary bacterial infection is not suspected, a broad spectrum antibiotic should be given to minimize the effects of bacterial translocation. Abdominal pain is common so analgesics should be used as needed to keep the patient comfortable. When pain is present, parenteral administration of opioid agonists such as hydromorphone, morphine, and fentanyl provide relief to most patients with severe pain. A fentanyl patch can be applied as an effective means of delivering analgesia in a dog that is likely vomiting. An epidural catheter can be placed for epidural delivery of analgesic medications or local anesthetic can be administered into the caudal thoracic space or cranial peritoneal cavity. Corticosteroids are indicated in acute pancreatitis only if shock is present. There is some controversy as to whether steroids may have negative effects on patients with pancreatitis but there is little convincing evidence that steroids are either helpful or detrimental except in situations such as shock. Immune-mediated pancreatitis, especially in association with systemic lupus erythematosus, is increasingly recognized as an important cause of pancreatitis in people, and steroid therapy has been shown to reduce mortality significantly in these patients. Primary immune-mediated pancreatitis has not been described in dogs and cats, but it should be considered that a definitive cause is not found in most dogs and cats with pancreatitis. Conventional therapeutic approach to patients with pancreatitis would indicate that the patient should be fasted to allow the pancreas to “rest.” Fasting should result in a physiologic state in which less pancreatic enzyme is being produced and released which may result in reduced pancreatic damage during periods of pancreatic inflammation. The conventional approach is to fast the patient until the clinical signs associated with the pancreatitis have stopped. In some cases the clinical signs may linger for quite some time and nutritional support may become indicated. Dogs are metabolically suited for long fasts and one should not be too quick to start feeding in canine patients with pancreatitis. If nutritional support is deemed necessary, however, ideally, jejunostomy tube feeding or TPN should be considered to reduce pancreatic activity. It should be noted that even when jejunostomy feeding or TPN is used pancreatic activity will be increased over the basal fasted state.

The common practice of fasting dogs with pancreatitis is somewhat questionable. The underlying mechanism of pancreatic damage involves abnormally high levels of cholecystokinin, resulting in activation of digestive enzymes within the pancreatic parenchyma and suppression of pancreatic secretion. One could argue that feeding to restore more normal pancreatic secretion might be advantageous. In fact, large-scale studies in human pancreatitis have shown decreased morbidity and mortality when patients are not fasted. Some veterinary internists recommend feeding of dogs with...
pancreatitis unless vomiting prevents it, and the practice of fasting these patients should probably be reconsidered.

Treatment (Feline): Therapy for cats with pancreatitis is not well described or agreed upon. If a specific underlying etiology is noted it should be treated. Cats with acute necrotizing pancreatitis should be treated with fluids such as 0.9% NaCl or Lactated Ringers. Potassium should be added to the fluids to maintain normal potassium and glucose should be added if hypoglycemia is noted. Treating shock, dehydration and maintenance of normovolemia are the goals. Maintaining pancreatic microcirculation may be enhanced by plasma (20ml/kg IV) or colloid (10-20ml/kg/day IV) administration. Dextran 70 and hetastarch may have antithrombotic effects that help maintain the microcirculation. An external source of heat may be necessary to treat hypothermia. Antibiotics are indicated if bacterial infection or toxoplasmosis is suspected but are not necessary to prevent the bacterial translocation that appears to be more common in dogs. Abdominal pain is not common so analgesics are not indicated in most cases. When pain is present, butorphanol (0.2–0.5 mg/kg every 4–6 hours) can be given. Buprenorphine (0.005-0.01mg/kg SQ q6-12hrs) or oxymorphone (0.05-0.1mg/kg cats IM, SQ q1-3hrs can also be used but may have a negative effect on respiration. Non-steroidal antiinflammatory agents should probably not be used. Corticosteroids are indicated in acute pancreatitis only if shock is present. Corticosteroids may be indicated in cats with chronic pancreatitis and should be used if concurrent inflammatory bowel disease or liver disease is present. Because cobalamin deficiency is common, supplemental parenteral cobalamin should be considered. Injectable cobalamin can be administered at a dose of 250 ug subcutaneously once a week for 6 weeks, then every 2 weeks for 6 doses, then monthly. Most generic cobalamin preparations contain 1 mg/ml (1000 ug/ml). Most multi-vitamin and B-complex injectable formulations contain significantly lower concentrations of cobalamin. This practice of fasting the patient to "rest" the pancreas is more controversial in the cat because hepatic lipidosis can be a concurrent problem or a sequela to fasting. Ideally, jejunostomy tube feeding or TPN should be considered but if the patient is not vomiting gastrostomy tube, esophagostomy tube, or nasoesophageal tube feeding are probably appropriately used. Some authors would suggest that treatment indications include use of antioxidants such as vitamin E, SAMe, or Silybin. Supportive studies are lacking but the possible association with inflammatory liver disease and the mechanisms of actions of such nutraceuticals make their use logical.

Concurrent pancreatitis, inflammatory bowel disease, and liver disease in cats: Clinicians have noted an apparent relationship between inflammatory bowel disease, pancreatitis, and liver disease in cats. Damage to intestinal mucosal epithelial integrity occurs during inflammation such as that seen in IBD which may permit inflammatory mediators, endotoxins, and microbial components access to the portal circulation. The concentration of these inflammatory mediators may exceed the capacity of hepatic macrophages to remove and degrade them resulting in deposition of immune complexes in the liver, complement system activation, and eventually hepatocellular inflammation and necrosis. The anatomic association between the common bile duct and the pancreatic duct may allow for ascending bacterial infections to affect both organs. While this association is often referred to, there is little objective evidence in the literature that documents it well. The relationship was confirmed in a study designed to determine whether cats with inflammatory hepatic disease had concurrent IBD, pancreatitis and interstitial nephritis. [Weiss DJ, et al. JAVMA 209:1114; 1996] In Weiss’s study, the prevalence of IBD (83%) and pancreatitis (50%) was significantly greater for cats with cholangiohepatitis (suppurative cholangitis) compared to cats without inflammatory liver disease. However, the relationship was not apparent in cats with lymphocytic portal hepatitis (lymphocytic cholangitis). In studies of cats with pancreatitis, an association between hepatobiliary disease and pancreatitis has been observed. [Akol KG, et al. JVIM 15:327; 2001], [Hill RC, et al. JVIM 7:25; 1993], [Clark JEC, et al. JFMS 13:570; 2011] There appears to be a detrimental effect on prognosis for cats with both pancreatitis and hepatic lipidosis and pancreatitis and inflammatory liver disease. An association with inflammatory bowel disease was implied in Clark’s study. In a study evaluating cats with subnormal serum concentrations of cobalamin, 22 of 49 cats had simultaneous presence of inflammatory disease of the intestines, pancreas, or hepatobiliary system. [Simpson KW, et al. JVIM 15:26; 2001] While none of these studies conclusively makes an association, the evidence is compelling that inflammatory disease can at times affect multiple gastrointestinal organs. Based on the limited data available it would appear that cats with pancreatitis that die are more likely to have multiple organ systems affected.
Treatment of cats with concurrent inflammatory bowel disease and pancreatitis is generally based on management of the inflammatory bowel disease (or inflammatory liver disease). The effect of corticosteroids on cats with pancreatitis is not known but there is no evidence that steroids would have a detrimental effect in cases that are not of primary bacterial origin. In chronic pancreatitis, the anti-inflammatory effect of the corticosteroids may be of benefit for similar reason to the benefit achieved when treating inflammatory bowel disease or inflammatory liver disease. Steroids have long been considered a cause of pancreatitis in dogs, but a clear cause and effect relationship has not been established. It’s possible that steroid-induced pancreatitis has been over-diagnosed in the past. Studies have shown that steroids are associated with increases in serum amylase and lipase independent of any detectable pancreatic pathology. Nutritional support probably plays a more important role in the management of cats with concurrent inflammatory bowel disease and pancreatitis because of the potential association with hepatic lipidosis. Fasting cats with concurrent disease is not recommended.
Cytauxzoonosis

I. Introduction

A. Etiologic agent – *Cytauxzoon felis*, a tickborne blood protozoal disease of domestic and exotic cats.

B. Distribution – lower midwest, south central, and southeastern U.S.

C. Primary Tick Vector - *Amblyomma americanum*, (lone star tick).

1. Transmission – occurs after an infected tick has fed on a cat, inoculating sporozoites. Incubation period is 5-20 days so disease is most often seen in the spring and summer months when ticks are active.

D. Pathogenesis – Schizonts develop in macrophages which then occlude small vessels causing vasculitis and thrombosis of multiple organ systems, especially the lungs. Severe illness is the result of mechanical obstruction to blood flow and multiorgan failure. Late in the disease course merozoites will be released that infect red blood cells and have a signet ring appearance similar to *Babesia canis*. A hemolytic crisis with shock-like state and DIC is often the terminal event. Occasionally merozoites will be noted in red blood cells as an incidental finding. The North American bobcat is thought to be the primary reservoir host but serologic prevalence is high in the Florida panther and the Texas cougar as well.

II. Clinical Findings – Cats usually develop fever and rapid course of illness; lasting between 2 and 12 days. Fever, dyspnea, lethargy, anorexia, icterus, and dark urine may be noted with progression to hypothermia, recumbency, coma, and death; many cats dieing within 24 hours of presentation to a veterinary clinic. Death is seen in about 90% of infected cats. Early in the disease course clinical disease may be confused with hemotrophic mycoplasmosis. Some cats will survive and probably become chronically infected with merozoites noted in red blood cells incidentally. A less virulent strain with survival more likely appears to be seen in northern Arkansas, southern Missouri, and Oklahoma. Chronic disease has not been characterized but up to 28% of healthy feral cats in regions of Arkansas and Georgia have been reported to be subclinical carriers.

III. Diagnostic Findings

A. CBC – anemia, leukopenia, and thrombocytopenia are typical.

1. Normocytic, normochromic non-regenerative anemia

2. Thrombocytopenia

3. Leukopenia
4. Plasma is usually icteric
5. Blood smears – reveal signet ring shaped merozoites in red blood cells. Early in the disease course merozoites may not be evident but can increase in number rapidly. If suspected, repeated blood smears should be examined. Fine needle aspirate of liver, spleen, or lung may reveal organisms before merozoites are seen in red blood cells.

B. Chemistry panel – non-specific findings depending on organ systems involved; hepatic involvement results in increased bilirubin and transaminase activities. Hyperglycemia (stress) is common.

C. Urinalysis – bilirubinuria usually seen

D. Thoracic Radiographs – severe bronchointerstitial pattern is typical

E. Diagnosis

1. Evaluation of blood smears – Signet ring shaped merozoites noted in red blood cells. Erythroparasitemia is generally persistent in surviving cats.
2. PCR testing – is available but is not usually needed

IV. Treatment – Supportive treatment is important. Blood transfusion may be needed. Atovaquone (15 mg/kg, PO, tid) and Azithromycin (10 mg/kg, PO, q24h) given in combination for 10 days has been reported to result in the highest survival rates (60% in one study compared to 23% for imidocarb). Imidocarb dipropionate (3.5-5 mg/kg IM once, repeat in 7-14 days) is an additional treatment for C. felis infection. Treatment with tetracyclines is not effective but high dose enrofloxacin (5 mg/kg po bid) has been recommended to give while acquiring atovaquone or imidocarb. Note that high doses of enrofloxacin may cause retinal toxicity and it is not likely to be effective against C. felis by itself. Azithromycin may also be started before atovaquone is obtained. Parasympatholytic drugs (atropine or glycopyrrolate) should be given with imidocarb to reduce parasympathetic side effects which are common in cats given imidocarb. NSAIDs should not be used as they seem to be associated with a worsened prognosis.
References

Cytauxzoonosis

Hemotrophic Mycoplasmosis or Hemoplasmosis (formerly Hemobartonellosis)

I. Introduction

A. Etiologic agent – Mycoplasma hemofelis (H. felis), Mycoplasma hemominutum, and Mycoplasma turicensis are the causative agents of hemotrophic mycoplasmosis in cats. Mycoplasma hemocanis (H. canis) is the etiologic agent in dogs. They are gram negative, bacteria infecting epicellular portion of erythrocytes. The disease is common in cats but rare in dogs.

B. Primary Vector – Fleas are thought to be the primary vector although Rhipicephalus sanguineous, the brown dog tick has been implicated as well.

1. Transmission – is thought to occur when fleas take a blood meal but transplacental and translactational transmission can occur to kittens. Tick transmission is thought to occur in dogs but the importance of the tick is unknown in the cat.

C. Pathogenesis –

1. In cats - 1-3 weeks after transmission of Mycoplasma hemofelis cats develop erythroparasitemia. The PCV drops rapidly during bacteremic episodes due to hemolysis and sequestration of RBC’s in the spleen. The PCV rises rapidly at the end of each episode due to release of sequestered RBC’s. Episodes will be cyclical and repeated parasitic episodes appear to cause progressive erythrocyte damage and shorten erythrocyte lifespan. Resultant immune-mediated damage to erythrocytes over time causes more severe disease. Without treatment about a third of infected cats will die from progressive anemia. Cats that develop an effective immune response to the infection will recover but remain chronically infected for months to years.
Mycoplasma hemominutum and Mycoplasma turicensis are less likely to cause disease unless the cat is immunosuppressed by FeLV or other causes.

2. In dogs - bacteremia rarely results in anemia or clinical signs unless the dog has been splenectomized.

V. Clinical Findings – Any age cat may be affected. Adult male cats may have a higher prevalence. Clinical signs are attributed to the anemia. Acute hemolytic anemia may result in pale mucous membranes, depression, anorexia, weakness and tachypnea. Fever is seen in about half of acute infections. Icterus may occur but is not a consistent finding. Splenomegaly may be evident on physical examination. Weight loss may be evident in cats with more chronic infection. Dogs generally show no clinical signs unless splenectomy has been performed in which case they may show clinical signs associated with intravascular hemolytic anemia.

VI. Diagnostic Findings
A. CBC – acute, regenerative anemia and thrombocytopenia are the most consistent finding.

1. Anemia is typical. It is usually characterized as a macrocytic, hypochromic regenerative anemia but occasionally a non-regenerative anemia more consistent with anemia of chronic disease is seen.

2. Blood smears may reveal red blood cell parasitemia. Organisms may be obvious on RBC but may disappear completely in as little as two hours in experimentally infected cats so negative smears do not rule out infection and repeated smears are indicated in suspected cases.

3. WBC - normal to high
4. Platelets - usually normal
5. Plasma may be icteric

B. Chemistry panel – non-specific findings. Anemia will often result in increased ALT and AST activities if severe.

C. Urinalysis – usually normal, bilirubinuria or hemoglobinuria may be seen

D. Diagnosis
1. Evaluation of blood smears – Blood smear evidence is typically used for diagnosis. The parasitemia (bacteremia) waxes and wanes sometimes making it difficult to make a diagnosis from smears. It can sometimes be
difficult to distinguish organisms and differentiate them from stain precipitate and nuclear remnants. Parasitemia is sometimes described as having ring, rod, and chain forms depending on how the organisms present themselves in the erythrocytes.

2. IFA staining techniques – can be done to increase the likelihood of finding organisms.

3. PCR techniques – have become the diagnostic test of choice if organisms are not apparent on blood smears. Screening cross-sectional surveys of healthy cats in the U.S. have reported up to a 14% prevalence. PCR testing should be done in cats to be used as blood donors.

4. Coombs’ test is usually positive

VII. Treatment – Supportive treatment is important. Blood transfusion may be needed. Supportive care should include fluids and potassium as needed.

A. Antimicrobial therapy – Doxycycline and enrofloxacin are considered the treatments of choice.
   1. Enrofloxacin (5 mg/kg PO sid x 14 d) ***
   2. Doxycycline (5 mg/kg PO bid x 21 d) ***
   3. Marbofloxacin (2 mg/kg, PO sid x 14 days)
   4. Tetracycline (20 mg/kg PO tid x 21 d)
   5. Chloramphenicol - less effective

B. Immunosuppressive therapy - in severely affected cats where immune mediated hemolysis is likely a significant part of the pathogenesis immunosuppressive therapy with prednisolone (2-4 mg/kg) is warranted.

VIII. Prevention - Flea control is the most important aspect of prevention.

References
VETERINARY TECHNICIAN PROGRAM

PROCEEDINGS

February 1, 2020
The Cat & The Kidney
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Introduction
Kidney failure is one of the most common diseases that affects feline patients. With the advances of treatment options and the understanding of kidney disease, feline patients are living longer and more productive lives after being diagnosed with kidney disease. Due to the allowed length of the proceedings notes, treatment of kidney disease for both the dog and cat will be discussed in the proceeding notes titled “The Dog and the Kidney”.

Physiology
The kidneys filter approximately 20% of the body’s blood. The kidneys are responsible for a myriad of tasks including: regulation of water and electrolyte balances, excretion of metabolic waste products and foreign chemicals, regulation of arterial pressure, regulation of acid-base balance, regulation of calcium excretion, metabolism of certain minerals, production of the active form of vitamin D, glucose synthesis and erythropoietin production. In a normal pet, the kidneys account for almost all the erythropoietin that is secreted into circulation. Erythropoietin stimulates the production of red blood cells.

Each bean-shaped kidney contain millions of functional units called nephrons, which filter blood through the glomerular filtration (GF) process and produce urine. Each nephron is a long tubule which consists of five main parts: glomerular capsule, proximal convoluted tubule, loop of Henle, distal convoluted tubule and collecting duct. As blood enters into the glomerular capsule, high pressures force fluid and small molecules out while larger particles (blood cells, plasma and protein molecules) are retained in the blood and continue through.

The proximal convoluted tubule reabsorbs 65% of the filtered sodium, chloride, potassium and bicarbonate. It also filters almost all of the glucose and amino acids. The proximal convoluted tubule concentrates nitrogenous waste which helps to create urea. Certain drugs and toxins are secreted into the filtrate and carried into the bladder via urine. This is why certain drugs, like penicillins, work well for treating bladder infections.

The loop of Henle helps to regulate the concentration and volume of the urine by removing excessive amounts of water. It reabsorbs considerable amount of calcium, bicarbonate and magnesium into the ascending loop of Henle. It maintains a balance with the body’s extracellular fluid (ECF) so if an animal is dehydrated less water will be absorbed and if it is overhydrated more water will be absorbed.

The distal convoluted tubule is responsible for making the some of the final adjustments to the fluid by reabsorbing even more sodium, secreting potassium and regulating the acid/base balance. Lastly, the collecting duct is responsible for collecting the fluid and making the very final adjustments so that it maintains a complete balance with the ECF. This is where the concentrated urine is collected.

Renal Failure
Renal failure is divided into two forms: acute or chronic forms. Either form may be due to a large number of medical problems. Both are hallmarked by an elevated serum creatinine
and blood urea nitrogen (BUN), known as azotemia. When the kidneys malfunction, they cannot filter properly which leads to abnormal fluid levels in the body, deranged acid/base levels, hematuria, anemia, isosthenuria (urine specific gravity of 1.008 - 1.012), and abnormal levels of potassium, calcium and phosphate.

Uremia is a term used to describe most of the clinical signs and biochemical findings that occur with renal failure. The most common uremic complication is the appearance of gastrointestinal (GI) symptoms (nausea, anorexia, vomiting, diarrhea). Gastrointestinal signs can escalate to include hemorrhage of the GI tract, ulcers in the mouth and necrosis of the tongue due to the increase of gastric acid juice because up to 40% of gastrin is metabolized within the kidneys. Other signs of uremia include polyuria, polydipsia (due to impaired urine concentrating ability), hypertension and anemia.

The goal with any kidney disease is to decrease the level of azotemia, therefore decreasing the uremic signs. During treatment, kidney values should be monitored and treatment should continue so long as improvement is seen or a plateau is reached. An average hospital stay is between 3 to 6 days.

**Acute Kidney Injury**

Acute kidney injury (AKI) results from a dramatic decrease in GF rate because of either prerenal, intrinsic renal or postrenal causes. Many causes of AKI are reversible pending diagnosis and treatment is made early.

Prerenal azotemia is not caused by primary kidney disease, but rather by a decrease in cardiac output resulting in inadequate blood supply to the kidneys. When mean arterial pressure (MAP) starts to fall below 60 mmHg, perfusion to the kidneys becomes compromised. Prerenal kidney azotemia is reversible because it is not associated with morphologic damage to the kidneys. It is marked by mild azotemia with BUN levels less than 80 mg/dl and serum creatinine levels less than 4 mg/dl. Any patient with renal failure, including prerenal azotemia, should not be administered nonsteroidal anti-inflammatory drugs (NSAIDS) or angiotensin-convertin enzymes (ACE) inhibitors because they can cause a worsening of the azotemia by further decompensating GF.

Intrinsic damage to the kidneys occurs from damage to the renal parenchyma, specifically to the vasculature, glomeruli, tubular epithelium and interstitium of the kidney. In cats, the most common causes occur from toxins, infectious diseases and ischemic causes (such as heat stoke, pancreatitis and disseminated intravascular coagulation). The kidney is particular vulnerable to toxins because of its high rate of blood filtration.

Some of the most common nephrotoxic drugs/chemicals include ethylene glycol, gentamicin (and other antimicrobials), cholecalciferol (vitamin D) and lilies. While not as common as in the dog, ethylene glycol toxicity it is widely talked about because of its common availability in such products as antifreeze, cleaners, cosmetics and flavoring extracts. In cats, the lethal dose of 95% ethylene glycol is 1.4 to 4 ml/kg. Ethylene glycol causes a toxic effect by forming oxalate which binds to plasma calcium and forms calcium oxalate crystals in the renal tubules. The calcium oxalate crystals clog the tubules leading to AKI.

Lilies are a common toxicity in cats and while the principle toxic factor is still unknown, it is known that all parts of the plant are toxic including pollen. After initial ingestion of the plant, cats may exhibit gastrointestinal signs such as nausea and vomiting. Signs develop within 12 hours, but the plant may still have effects on the body for 2 to 5 days after ingestion. Though the exact amount needed to produce a toxic effect is unknown, it is known that even a single bite
can cause symptoms, which is why any cat exposed to a lily plant should be treated as if it were going to suffer nephrotoxic effects.

One of the most common diseases that causes AKI in cats is pyelonephritis. Pyelonephritis (inflammation of the kidneys) most commonly occurs secondary from a lower urinary tract infection. Clinical signs may include fever, vomiting, anorexia and abdominal pain (generally when palpating the kidneys). Most commonly, Escherichia coli (E. coli) is the organism that is isolated. Antibiotics that are specific to the organism isolated should be administered as a treatment along with treating the AKI symptoms.

**Postrenal** causes occur from obstruction or rupture of the urinary tract system. Urethral obstruction is most commonly seen in young to middle-aged male cats. Cats that have had feline interstitial (idiopathic) cystitis (FIC) have an increased risk to becoming obstructed. In cats that have been obstructed for a long period of time, AKI can occur. When a cat becomes obstructed, pressure within the urethra and urinary bladder will be transmitted up the ureters to the nephrons. Eventually the pressure starts to alter the GF pressure until the rate is zero. Early detection and treatment is imperative in order to correct the azotemia. Approximately 25% of cats that obstruct have a complete resolve of their azotemia in 2 to 5 days. Another 40% retain mild azotemia and are successfully managed with medical treatment.

Obstruction may also occur because of bilateral or unilateral obstruction of a kidney from nephroliths or ureteroliths (most commonly calcium oxalate). Cats with unilateral ureteral obstruction may be asymptomatic and symptoms may occur only when the kidney becomes enlarged due to hydronephrosis. Bilateral ureteral obstruction will result in more symptoms including azotemia, vomiting and anorexia. Hematuria may occur.

**Chronic Kidney Disease (CKD)**

Cats, unlike dogs, generally can live many years with CKD. Roughly 30% of felines over 15 years will experience CKD. The causes of CKD are numerous and can be congenital, familial or acquired. Congenital causes are often suspected based on the age of the cat, breed and family history. Polycystic kidney disease (PKD) is more common in Persians and is inherited as a autosomal dominant trait. PKD is characterized by the presence of multiple fluid-filled cysts (hence "polycystic") which can result in the enlargement of the kidneys. The cysts generally develop at an early age (as early as 7 weeks), but signs of renal failure may not occur until the cat is middle aged (between 7-8 years). It’s important to note that not all cats with PKD will develop kidney failure. For breeders of at-risk breeds, genetic testing is available for cats older than 8 weeks old (Veterinary Genetics Laboratory, University of California-Davis: www.vgl.ucdavis.edu). Treatment is limited to dealing with the symptoms of renal disease.

Amyloidosis is a common familial disease found in Abyssinians, Oriental Shorthairs and Siameses. Amyloidosis occurs when protein is lost from an increase permeability of the glomerular membrane due to the abnormal deposit of the amyloid protein. Amyloidosis can occur rapidly causing renal failure to develop within one year of diagnosis. In other cases the effects on the kidneys is mild and cats may live without the disease ever being detected. Symptoms include poor hair coat, weight loss, polydipsia, polyuria, and anorexia. Proteinuria is a variable finding and may not reflect the severity of the disease. In order to diagnosis amyloidosis a renal biopsy must be obtained. Treatment is limited to dealing with the symptoms of renal disease.
Acquired CKD can result from any disease process that injures the kidneys to a point where the nephrons can no longer function appropriately. Some common diseases that lead to CKD include: feline infectious peritonitis, neoplasia (renal lymphosarcoma), hyperthyroidism, glomerulonephritis and chronic tubulointerstitial nephritis.

Feline infectious peritonitis (FIP) affects the kidneys, liver, mesenteric lymph nodes, central nervous system, and eyes. Besides renal failure symptoms, fever, lethargy, anorexia and weight loss may be present. In order to diagnosis FIP, a fine needle aspiration or biopsy of the enlarged kidney must be obtained.

If left untreated, hyperthyroidism may cause renal failure. Thyroid hormones help support GF rate by increasing renal blood flow. Hyperthyroidism generally results in systemic hypertension which could be transmitted to the glomeruli, causing glomerular hypertension and glomerular hyperfiltration. Unfortunately, when treating the thyroid disease, the hypertension will dramatically decrease causing a decrease in renal blood flow and GF rate. Studies have reported that 14% of hyperthyroid cats have pre-existing renal disease, while approximately 30% of hyperthyroid cats become azotemic after therapy of hyperthyroidism.

Lymphosarcoma (LSA) is the most common renal neoplasm of the cat. It usually affects both kidneys. Approximately 50% of cats with renal LSA are feline leukemia positive. Treatment is aimed at dealing with the kidney disease and using conventional chemotherapy. Unfortunately, prognosis is poor.

Glomerulonephritis appears less common in the cat than in the dog and it is generally classified as idiopathic. There are generally two types of glomerulonephritis: classical nephrotic syndrome and chronic renal failure. With classic nephrotic syndrome edema, ascites, proteinuria, and hypoalbuminemia are often present. Azotemia may or may not be present. Laboratory findings usually include proteinuria, hypoalbuminemia, hypercholesterolemia, and nonregenerative anemia. A biopsy must be performed in order to make a diagnosis. Cats that have edema and ascites without azotemia can be treated with loop diuretics (furosemide) and prednisolone. Enalapril is not only used to treat the hypertension, but also has been found to have additional beneficial effects such as reducing the proteinuria and slowing the rate of disease progression.

Chronic tubulointerstitial nephritis (CTIN) is the number one finding in CKD cats (approximately 70%). Chronic tubulointerstitial nephritis occurs gradually over years and results in renal tubules atrophy and interstitial fibrosis which results in decreased renal function. The causes of CTIN are numerous and, despite a thorough work up, no cause may be determined. Failure to identify the cause is likely due to the numerous diseases that cause similar changes to the kidneys. In 2012 researchers from Hong Kong isolated a paramyxovirus known as feline morbillivirus from domestic cats. Approximately 12.3% of the cats tested using PCR methods were positive for morbillivirus. They then looked at what other common diseases these same cats were associated with. Ultimately they were able to isolate out the virus from the kidneys. In conclusion approximately 7 out of 12 cats that had the morbillivirus also had tubulointerstitial nephritis.

Conclusion
Because causes can be numerous, it is important cats with kidney failure receive a complete diagnostic work up in order to diagnose the underlying cause. Kidney failure is not a death sentence for cats. With advances in treatments many cats live long and productive lives with both AKI and CKD.

References Available From The Author
Introduction: Though not as common as in the feline, dogs can certainly experience kidney failure for a variety of reasons. Due to the length permitted for the notes, physiology of the kidneys and renal failure in general is discussed in “The Cat & The Kidney”

Acute Kidney Injury

Acute kidney injury (AKI) results from a dramatic decrease in GF rate because of either prerenal, intrinsic renal or postrenal causes. Many causes of AKI are reversible pending diagnosis and treatment is made early.

Prerenal azotemia is not caused by primary kidney disease, but rather by a decrease in cardiac output resulting in inadequate blood supply to the kidneys. When mean arterial pressure (MAP) starts to fall below 60 mmHg, perfusion to the kidneys becomes compromised. Prerenal kidney azotemia is reversible because it is not associated with morphologic damage to the kidneys.

Intrinsic damage causes include from toxins, infectious diseases and ischemic causes. In the dog ethylene glycol toxicity is the most common nephrotoxic drug likely because of its wide availability. Ethylene glycol causes a toxic effect by forming oxalate which binds to plasma calcium and forms calcium oxalate crystals in the renal tubules. The calcium oxalate crystals clog the tubules leading to AKI. Mortality rates are between 50-70%. Besides treating the AKI, dogs are usually given fomepizole (Antizol-Vet®), a synthetic alcohol dehydrogenase which helps to absorb the ethylene glycol.

Vitamin D (cholecalciferol) toxicity is more common in the dog than in the cat. Cholecalciferol can be found in some rodent poisons, vitamin supplements and psoriasis creams. AKI occurs because cholecalciferol is metabolized to calcitriol which, in turn, increases intestinal, bone and renal absorption/resorption of calcium. The toxic effects are due to the hypercalcemia and hyperphosphatemia. Initial detoxification should occur followed by treatment for AKI, hypercalcemia and hyperphosphatemia.

Raisin and grape toxicity in dogs has been well documented since 1999. The exact toxic substance in the grape is still unknown. The amount of ingested raisins and grapes needed to produce nephrotoxic effect varies from 3 to 57 g/kg. Within 12 to 24 hours of ingestion dogs develop vomiting, anorexia, diarrhea, abdominal pain and AKI.

Leptospirosis is a zoonotic disease that infects dogs. Transmission occurs through contact with urine, bite wounds or ingestion of infected tissues and has a 1 week incubation period. There are two forms: acute or chronic. Symptoms with the acute form include lethargy, anorexia, shivering, and vomiting. If it progresses, uremic symptoms become present. Approximately 70% to 85% of dogs survive with treatment. For those that do survive chronic renal and liver dysfunction are common. Treatment is aimed at treating the AKI signs and antibiotics (doxycycline).

Lyme disease is caused by the spirochete bacterium Borrelia burgdorferi and is transmitted by the Ixodes tick (deer tick). Many dogs carry lyme disease without ever being
symptomatic. Those that become sick often present with signs that include lameness (shifting leg), fever, lethargy and anorexia. In dogs that have chronic ongoing lyme disease lyme nephritis/nephropathy can occur. Prognosis is guarded to poor for dogs that develop AKI. Besides treating the AKI symptoms, doxycycline is the preferred antibiotic used.

**Chronic Kidney Disease**

The average age of dogs that develop chronic kidney disease (CKD) is around 7 years. The causes of CKD are numerous and can be congenital, familial or acquired.

Congenital causes are often suspected based on the age of the dog, breed and family history. Polycystic kidney disease (PKD) is more common in cats, but West Highland White Terriers, Bull Terriers and Cairn Terriers can carry a recessive trait to developing PKD. PKD is characterized by the presence of multiple fluid-filled cysts which can result in the enlargement of the kidneys. Treatment is limited to dealing with the symptoms of renal disease.

Amyloidosis is an uncommon familial disease found mainly in Shar-peis (Shar-pei Fever) and is the most common cause of CKD in the breed. Amyloidosis occurs when protein is lost from an increase permeability of the glomerular membrane due to the abnormal deposit of amyloid protein. Amyloidosis can occur rapidly causing renal failure to develop within one year of diagnosis. Symptoms include poor hair coat, weight loss and anorexia. In the case of Shar-pei Fever signs may include an intermittent fever lasting 24 to 36 hours and, as the disease progresses, signs of renal and liver failure may occur. In order to diagnosis amyloidosis a renal biopsy must be obtained. Treatment is limited to dealing with the symptoms of renal disease.

Fanconi syndrome is a disease that is inherited in the Basenji, but can also be acquired. Acquired causes include heavy metal intoxication (lead, copper, mercury), amyloidosis, neoplasia (multiple myeloma), hyperparathyroidism and vitamin D deficiency. Fanconi syndrome is a disease where the proximal tubule function of the kidney is affected, which results in decreased reabsorption of electrolytes and nutrients. Glucose will “spill” into the urine while the body’s blood glucose is normal. Fanconi syndrome dogs are resistant to ADH which causes them to develop nephrogenic diabetes insipidus.

Glomerulonephritis occurs in roughly 27% of dogs diagnosed with CKD and it is generally classified as idiopathic. There are generally two types of glomerulonephritis: classical nephrotic syndrome and chronic renal failure. A biopsy must be performed in order to make a diagnosis.

Chronic tubulointerstitial nephritis (CTIN) is the number one finding in CKD dogs (over 50%). Chronic tubulointerstitial nephritis occurs gradually over years and results in renal tubules atrophy and interstitial fibrosis resulting in decreased renal function. Often the causes are numerous and, despite a thorough work up, no cause may be determined. Failure to identify the cause is likely due to the numerous diseases that cause similar changes to the kidneys.

**Treatment of Kidney Disease**

In general all kidney disease is treated the same, with the exception of a few additional therapies depending on the disease. Fluid therapy, monitoring acid-base and electrolytes, ensuring appropriate nutrition and monitoring for anemia and hypertension is important in every kidney failure patient.

**Fluid Therapy**
The gold standard is diuresis. It’s important to account for any body water deficits as well as any ongoing losses such as vomiting and diarrhea. Initial solutions are generally isotonic crystalloids. If a patient has cardiac disease or hypernatremia, low sodium fluids should be used (such as 0.45% NaCl). Once a patient is rehydrated, they should produce 1 to 2 ml/kg/hr of urine. Ideally urine output should be monitored to ensure that fluid therapy is adequate. The most accurate way of monitoring urine production is by placing an indwelling urinary catheter. In the case of oliguria additional fluids or treatment may be required. Furosemide, dopamine and other osmotic diuretics (mannitol) can be used to increase urine production.

**Acid-Base/Electrolytes**

Acid-base status and electrolytes must be constantly monitored. Metabolic acidosis and hyperkalemia are common in oliguric AKI patients and is commonly seen in feline urethral obstruction patients. In severely hyperkalemic patients bradycardia, peaked T waves, loss of P waves and life threatening cardiac arrhythmias can be seen. In such severe cases, several treatments can be initiated to help deal with the hyperkalemia.

Chronic renal disease feline patients are more likely to suffer hypokalemic effects because the potassium is closely regulated by the kidneys. Dogs rarely experience hypokalemia, but more commonly, they experience metabolic acidosis and hyperkalemia during AKI. Signs of hypokalemia typically include anorexia, polyuria, vomiting and weakness. In serum potassium levels less than 2.5 mEq/L neuromuscular signs can occur which include a reluctance to move, a stiff gait, ventroflexion of the neck, and tremors. Intravenously administration of potassium, at a constant rate infusion, can be used to correct initial hypokalemia. Once hydration is adequate, cats rarely require oral supplements at home.

Hyperphosphatemia is commonly observed in CKD patients because the kidney plays an important role in excreting phosphorus. Typically hyperphosphatemia does not produce clinic signs, but it can lead to the progression of secondary hyperparathyroidism which can lead to death. Secondary hyperparathyroidism can lead to muscle weakness and central nervous system disturbances. Typically calcitriol (the most active metabolite of vitamin D) is used to treat secondary hyperthyroidism because it inhibits parathyroidism gland growth (which is a task vitamin D receptor does in the parathyroid gland).

Another common finding in chronic renal disease patients is hypocalcemia. Roughly 26% of CKD cats suffer this electrolyte disturbance. Intravenous calcium gluconate may initially be administered to help correct any serious hypocalcemia and then oral calcium supplements may be used after. There are many oral calcium based products that can be administered for the added phosphorus-binding effects. Serum calcium and phosphorus levels should be monitored every 2 weeks initially and then as needed.

**Hypertension**

Kidneys that are suffering from acute or chronic disease are more at risk because they lose the ability for autoregulate renal blood flow and glomerular filtration rate. These changes are transmitted directly to the glomerular capsule which results in glomerular hypertension. Ultimately all patients with hypertension should receive a antihypertensive drug to help prevent further damage to the kidney and other organs. The choice of which drug(s) to use is dependent on the degree of hypertension, the presence of target organ damage, the available routes of administration and the underlying disease.
Anemia

Often times, patients with CKD suffer from moderate to severe anemia. There are a myriad of reasons for patients to suffer anemia. Red blood cell transfusion is rarely recommended because of the decreased life span of red blood cells with uremic patients. As the patient’s kidney values decrease, the anemia starts to resolve. Red blood cell transfusion is only recommended for patients undergoing surgery. Recombinant Human Erythropoietin and darbepoetin are both commercially available and is used to treat CKD anemic patients. Depending on the dose, it can take 2 to 8 weeks for the hematocrit to rise to low normal.

Early Detection of Renal Disease

IDEXX created a test in 2014 that detects renal changes earlier than other testing methods. It worked by testing SDMA (a methylated form of the amino acid arginine). SDMA releases in to circulation when protein is broken down. It resides in almost every cell in the body. It is eliminated only by the kidneys. Therefore if the kidneys have any disease the filtering of SDMA does not occur as well and the biomarker increases. IDEXX reports SDMA can be used to detect CKD an average of 9 months earlier in dogs and 17 months sooner in cats.

What does this mean? Because treatment in pets with renal disease is limited to nutrition, SQ fluids and treatment of GI symptoms, treatment is unlikely to be altered with such an early diagnosis. Many times the pets with increases in SDMA are not exhibiting GI symptoms. No studies have been published on if earlier intervention with SQ fluids and nutrition increases life expectancy longer than average. In both dogs and cats increases in SDMA should prompt veterinarians to determine the cause of the increase.

Renal Transplant/Intermittent Hemodialysis

More than 90% of cats survive past one year and most survive to three years. The success rate of canine renal transplants is not as great as in cats. The University of California at Davis only has about a 40% success rate while other universities have discontinued the program due to the poor prognosis. Clients who wish to pursue this treatment option must be prepared to pay over $13,000 and adopt the dog/cat who donates the kidney. The actual renal transplant is long, roughly 4 hours, and complications include bleeding, hypertension, embolism, infection and, ultimately, rejection of the new kidney. Lifelong medication and monitoring is required. If kidney failure is manageable, transplant surgery is not recommended.

Intermittent hemodialysis has been a successful treatment in managing renal failure in cats and dogs. Its purpose is to correct the effects associated with uremia by filtering the blood across an artificial “kidney” membrane outside the patient's body. Due to its expensive price tag, complications, and limited facilities performing the treatment, it is commonly reserved for pets suffering from AKI. Complications include neurologic (caused by disequilibrium from shifting osmotic gradients), gastrointestinal (vomiting, nausea) and hypotension during the treatment. In 2000 it was reported that 60% of cats with AKI undergoing intermittent hemodialysis survived. It is unknown how many would have died without treatment.

Continuous Renal Replacement Therapy (CRRT)

As the name implies CRRT relies on continuous gradual blood purification. The patient’s blood is filtered until the kidney function returns to normal. CRRT is almost always used for acute kidney injury, but can be used for a toxin ingestion as well to help diuresis the body. The patient's blood is passed through a filtration circuit tubing in a machine to a
semipermeable membrane where waste products and water are removed. Replacement fluid is added to the blood and is returned to the patient.

In human nursing literature for CRRT it states that the benefits are: the ease of systems used to treat AKI patients; enables higher doses of therapy to be delivered consistent with current clinical literature; allows for 24 hour therapy; allows for better hemodynamic stability; allows for volume reduction allowing for fluids & nutrition; and allows for cytokine removal. While complications are less than that of intermittent hemodialysis the technician staff must constantly monitor these patients. Coagulation disorders can occur so clotting times need to be constantly monitored. Hypotension can be a problem as well likely due to the large amount of blood needed for the CRRT unit (50-84mls) as well as the reduction of blood volume. Patients weighing as little as 2.4kg have been successfully treated with CRRT leaving one to believe there may be no size restriction. Certainly more research must be done in veterinary medicine, but the limited research available has shown CRRT to be very effective and safer than intermittent hemodialysis.

References Available From The Author
PROCEDURES FOR THE NEONATE/PEDIATRIC PATIENT
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Introduction
The neonatal and pediatric patient can prove challenging when performing certain nursing techniques. The sheer size and lack of developmental anatomy result in challenges that are unique to this age group of canines and felines. Being prepared ahead of time with the understanding of what challenges one may face before the procedure will hopefully help make the technique successful. With any nursing procedure in a neonatal or pediatric it is possible that even the skilled veterinary personnel may not succeed. Generally, the larger and healthier the pediatric or neonate, the better chance of successful procedure taking place.

Venipuncture & Catheterization

Venipuncture
Venipuncture can prove difficult in a neonate or pediatric patient. The largest concern is that multiple blood draws or a large blood draw can result in an anemic patient very quickly. It is imperative that pressure bandages are utilized to minimize hematomas. Even a hematoma under the skin can lead to additional blood loss.

This author found it very difficult to find a conclusive number with how much blood can be drawn from a dog or cat let alone a neonate/pediatric. There were several references from laboratory animal science suggesting that between 1 to 2% of the total animal’s body weight in kilograms could be removed safely per day. The amount removed would be referenced in liters. For example, an animal that weighed 25 kg could have 250 mL removed a day. On the veterinary information network there were a few internal medicine diplomats that stated, “10% of blood volume should be removed within a twenty-four hour period. Neonatal blood volume is approximately 68 ml/kg.” Finding more concrete references proved challenging.

There were several human pediatric and neonate references but the author did not feel it appropriate to list them as references for another species likely do not apply to canines and felines. With that said many of the references were similar to the references found for canine and feline laboratory animals. Under those guidelines a 2.2 kg pediatric would only be allowed to have about 2.5 mL of blood removed during a day.

The conclusion is that it is imperative that neonates and pediatric patients do not have excessive venipuncture performed. While obtaining blood for a packed cell volume/total solids is small, if this occurs multiple times throughout the day it may result in more than three milliliters of blood loss because of hematomas. Doctors and nurses should ensure that the amount of blood that is drawn from a neonate/pediatric is the most minimal amount necessary while also ensuring that the total amount is obtained on the first attempt to avoid a second attempt. Most of these patients will require some type of intravenous fluid. Intravenous fluids help to support blood volume. This should be taken into consideration if the patient is not on intravenous fluids and a significant amount of blood was removed from the patient. Intravenous fluids should be considered in such patients.
Location

In order to obtain enough blood from a neonate/pediatric patient you may need to get creative. These same veins can be used for a catheter placement. Anything that is blue is a vein and is free game when it comes to taking blood from it. The largest vessels, the jugular and femoral, should be considered if you need to obtain a large amount of blood (> 2.0mls). They should not be considered if the patient is coagulopathic or has a low platelet count. Do not use the jugular or femoral veins if the patient is icteric unless previous bloodwork has shown the patient's ability to clot. If only a drop of blood is needed, as in the case of obtaining a drop of blood for a blood glucose or lactate level, veterinary personnel should attempt ear prick, lip prick, or even a tale prick. It is impractical to try to gain venous access for a drop of blood in these patients. Veins should be preserved for larger blood draw amounts only.

Intravenous/Intraosseous Catheter Placement

One of the most challenging nursing techniques that may need to take place on a neonate or pediatric is that of an intravenous (IV) catheter placement. Because of the size of the patient many times catheterizing the jugular vein is easiest. In the case of an emergency catheterization of the jugular vein is preferred because it offers the quickest route for drugs and fluids to the central circulation system. Often times nurses and veterinarians are not comfortable placing a catheter into the jugular vein.

The American Heart Association (AHA) recommends intraosseous (IO) as the second route of choice if venous access cannot be obtained. Studies have shown that IO is as effective as central venous access. In veterinary medicine IO is typically reserved for neonates, puppies or kittens. While it may be just as effective as obtaining venous access via the jugular vein, it generally takes slightly longer to obtain IO access as opposed to venous access of a peripheral vein.

Most of the time IV catheter placement will be attempted. If such attempts fail, an IO attempt may be attempted. Peripheral catheters come in a variety of sizes and types. The most commonly used is the over-the-needle catheter. The type and gauge of catheter should be selected based on patient size, catheter location, volume and rate of fluid to be infused, and health of veins. In some larger pediatric dog breeds larger gauge catheters may be able to be placed (18g, 20g). Small gauge catheters such as 22g and 24g should be reserved for neonates under 2.2 kg (5 lbs). A larger catheter may not be possible due to vasoconstriction, anemia, trauma or other damage to the cardiovascular system which may result in a decrease in vessel integrity. Shorter over-the-needle catheters are preferred because they allow for faster fluid flow.

Since it is important to obtain catheterization on the first attempt to avoid blood loss, shaving the patient’s leg all the way around, preparing all supplies and having adequate restraint are all important to the success of the attempt. It is important to remember that the veins of neonates and pediatrics are a thinner. Because they do not have limited muscle or fat most of the times the vein is very superficial. It is easy to go through it and cause a hematoma. Often times if the first attempt fails it is very difficult to be successful on the same limb. Using slow methodical movements and ensuring there is adequate lighting and good restraint will also help with successful IV catheterization.

While it can be a little nerve-racking to attempt an intraosseous catheter in a neonate or pediatric patient, sometimes this is the fastest way to obtain access in a patient that is critical.
Intravenous fluids, drugs, blood, plasma, dextrose can all be administered into an IO catheter. The absorption time is the same as if not faster than venous access.

There are commercially made IO catheters, but bone marrow or spinal needles can also be used. In a newborn or young neonate using a regular over-the-needle catheter can also be done. The most common sites are the trochanteric fossa of the femur (right next to the ball/socket joint), the greater tubercle of the humerus, (right next to the ball/socket joint), the wing of the ilium and crest of the tibia.

Depending on how critical the patient is a local anesthetic, lidocaine, may be needed in order to facilitate the procedure. In many patients that are very critical, they do not seem to react to the placements of the catheter. The skin can be nicked with a scalpel blade or, in very young neonates the needle can be advanced without the need to make a small skin incision.

Once the bone is felt the pressure should be increased and the catheter should be rotated in a clockwise or counterclockwise position similar to a drill that is drilling into something. Once a catheter is in the cortex you will no longer feel any resistance. If you move the limb that is associated with the catheter the needle will move along with it. Aspiration into a syringe will bring bone marrow up and also confirm placement. Initially when flushing the catheter may have mild resistance, but once it has been flushed there should be little to no resistance. Human patients who have had this procedure done state that the most painful part of the procedure is when the bone marrow is flushed.

IO catheters are usually only used for emergency situations for no greater than 24 hours. While the risk of complications is minimal and identical to that of venous IV catheterization, it is uncomfortable for the patient to have a catheter protruding out of a bone. It makes sitting and laying on the affected limb difficult. Once the patient is stable generally venous catheterization can be obtained.

The EZ-IO gun is currently marketed by Arrow®. This small handheld precision drill has the ability to place I/O catheters in under three seconds in veterinary patients. Initially when this product launched they recommended that patients needed to be greater than 4.5kg. Since that time the EZ-IO gun has been used in patients at the author’s hospital weighing as little as 2.2kg. The company who designed the product produced a video in which they drilled over 50 holes into a regular size egg. The egg never cracked and remained egg shaped the entire time. While there is no data on how little of a patient this product can be used on, it is likely that any patient requiring an IO catheter can have it placed with the EZ-IO gun.

**Feeding Methods**

Regardless of the disease or injury one of the most important components to ensuring the survival of the neonate/pediatric patient is nutrition. Because they do not have the adipose and glycogen reserves of an adult, when they decrease their caloric intake they can become hypoglycemic very quickly. The safest and most effective way is to have the neonates/pediatric patient eat orally.

Since the mother will not be hospitalized with the patient this oral feeding generally must take place with a nipple bottle. The hole in the nipple bottle should be of sufficient size so that when the neonate/pediatric patient cycles it, formula is readily available. If it is not large enough a whole can be made larger by using an 18 gauge needle. Commercially prepared formula is best when working with diseased or injured neonate/pediatric patients. Warming the formula using
warm water is best. Warming the formula in a microwave can cause part of the formula to be very hot while the rest is not. This can result in burning of the patient. When feeding neonates/pediatrics they should be lying down on their stomachs. The bottle should be angled in a manner that is similar if they were nursing with their mother. You can help facilitate this by rolling a small towel and resting them on top of it so they need to lean up to get to the nipple bottle. This is a natural nursing posture for the patient.

Depending on the disease or injury, it may not be appropriate for the patient to feed orally. While it is certainly fast, the disease or injury may impede the patient’s natural ability to feed appropriately. Even though the neonate/pediatric patient is feeding off of a bottle it is important that the calories are calculated out to ensure they are getting enough nutrition. Often times it may look like they are feeding, but without actually calculating out how much they took in as well as the number of calories they took in, it will be impossible to just gauge it based on eyesight.

If the patient is too sick to nurse, then bottle feeding should be avoided. Aspiration pneumonia can occur because a sick patient is forced to nurse when they have a week or absent suckling reflex. Feeding with an eyedropper, bulb syringe, or other syringe should always be avoided because of the high risk of aspiration pneumonia. If you have to squeeze the plastic nipple bottle to force the formula out, then likely the patient is not suckling appropriately or the hole is too small. The patient should have the ability to suckle the formula out of the nipple bottle themselves. Squeezing the bottle will result in a high chance of aspiration pneumonia. If oral feeding is not appropriate for the patient, then a feeding tube should be placed.

**Nasogastric/Nasoesophageal Tube**

Nasoesophageal (NE) tubes (a feeding tube that ends in the esophagus) can be used for short term nutritional support. It is contraindicated in patients that are still vomiting. Mild sedation is rarely needed, but may be required in order to place the NE tube. Tilt the animals head up and place several drops of lidocaine or proparacaine into the nostril. The smallest tube available is a 3.5 fr.. They come available as either red rubber or clear argyle catheters. In a larger breed pediatric patient, it may be possible to place a 5fr. Because of the small size of the feeding tube one can expect that any material being pushed through the two must be very dilute and will go through slowly.

Measure the feeding tube from the tip of the nose to the fifth intercostal space and mark it with a marker. Grasp the patient’s head and keep their head in a normal position while briskly inserting the feeding tube. Once the tube is passed to the level of the mark, secure it with suture to the nostril.

There are many different techniques on how to fasten a NE tube, but no matter what the technique, the important part is to make sure it is secure (so it cannot slip out) and the patient is as comfortable as possible (so the tube is not lying over their eyes). Tube position can be checked by taking a lateral radiograph or inserting a small amount of water 0.5-2mls (2mls for larger pediatric puppies and 0.5mls for smaller neonates) through the tube and observing for a cough reflex. Negative pressure with a 5-10 ml syringe can also be observed if it is in the esophagus, while air will be obtained if it is in the trachea.

Nasogastric (NG) tubes (a feeding tube that ends in the stomach) are placed in a similar fashion as a NE tube except that the tube is measured to the 13th rib. Some veterinarians prefer a NG over an NE tube because you are able to aspirate stomach contents out (like excessive stomach acid). However, others worry it can cause an increase in gastric reflux because it
interferes with the gastric sphincter. Studies have not proved a benefit of an NG over an NE tube. After placement of a nasogastric tube it is ideal to also check the tube position by taking a lateral radiograph. Because it does not take a lot of fluid to cause life-threatening pneumonia in such a small patient, it is best to always take a post placement radiograph to verify that it is in fact in the correct position and not in the trachea or airway.

Most commonly a commercially prepared liquid diet is given through a NG or NO tube. The liquid diet is usually given at a constant rate infusion to allow for continuous nutrition until the pet is ready to intake food orally. Because the tube size is so small using a gruel or viscous liquid is unfeasible. The tube may also have a tendency to clog if it is not constantly running with a slow drip for it is not flushed appropriately after syringe feedings.

If the patient is not on a constant infusion of a liquid diet, then syringe feedings will occur. Depending on the caloric requirements of the neonate/pediatric patient they may occur every 2-3 hours or more. It is imperative that the patient does not vomit to avoid aspiration pneumonia. If the patient has a forceful vomit it can actually vomit up the feeding tube. When syringe feeding such small patients it is best to only push 0.1-0.3mls at a time. If the patient seems agitated, starts salivating, burps, or has excessive lip-smacking the amount should be decreased or the patient should be given a break. The patient will be able to feel the food going into the stomach. If the patient is excessively nauseous it may produce a vomiting response. Watching for the previous listed signs is important to be able to stop the feeding before the patient vomits.

When the feeding tube is not in use it should be flushed with a little water to ensure that it does not clog. It is important to remember the size of your patient when flushing tubes. Two to three milliliters of water is a significant amount in an animal that only weighs less than a kilogram. If the tube clogs it is imperative to check to make sure there is not a kink in the line first. If there is no kink and the clog is most likely a result of food that has become lodged, then you can try to push warm (not hot) water into the line. You can also try to aspirate back on the line to see if adding a “suctioning” pressure may help to free up the clog. Lastly, you can squeeze any visible line with your fingers in an effort to “crush” and break up the clog. Unfortunately, if the clog is significant the tube may need to be pulled and replaced. While it seems unlikely that such a small patient can remove a nasal tube, it is advisable to consider a small Elizabethan collar to prevent forceful removal by the patient. Size and activity level should be considered when considering in Elizabethan collar.

**Orogastric Tube Feeding**

Orogastric tube feeding is also an appropriate way to feed a neonate or pediatric patient. In some patients placing a nasoesophageal or nasogastric tube may not be physically possible. Getting a 3.5 fr feeding tube into the nose of a patient that weighs less than a kilogram may not happen. In these cases, a 5 fr red rubber or clear argyle tube can be placed down the esophagus and fed directly into the stomach to deliver food. The tube is measured from the front of the mouth to the last rib. Similar to the placement of a NE or NG tube grasp the patient’s head and keep their head in a normal position. You should pass the tube along the roof of the mouth and stop when it has reached the mark you placed on the tube. The neonate’s head should be flexed forward as the tube is advanced along the roof of the mouth to the predetermined length. Tube position should be checked inserting a small amount of water 0.5-2mls (2mls for larger pediatric puppies and 0.5mls for smaller neonates) through the tube and observing for a cough reflex. It is not practical to take a radiograph because the tube is removed after the feeding. Since feedings
would occur multiple times throughout the day this would result in a cost that is prohibitive for most clients. Because there is a risk of aspiration pneumonia when performing this procedure regardless of whether the tube is incorrect position or not, the veterinary staff must auscult the lungs, look for coughing, and observe respiration rate and effort throughout the entire day.

While feeding a patient with an orogastric tube the same early signs of vomiting should be looked for such as agitation, coughing, burping, or excessive salivation. When the tube is removed it should be pinched off to avoid any remaining formula trickling out and down into the lungs as the tube is removed. One of the most common problems that occur is overfeeding. It is important that daily caloric intake is calculated out to avoid overfeeding using an orogastric tube.

Cardiopulmonary Resuscitation

Please note: The first set of veterinary specific CPR guidelines were published in June of 2012 by the RECOVER campaign in the Journal of Veterinary Emergency and Critical Care. (Special Issue: Reassessment Campaign on Veterinary Resuscitation: Evidence and Knowledge Gap Analysis on Veterinary CPR, June 2012, Volume 22, Issue s1, Pages i–i, S1–S131)

If a neonatal/pediatric patient goes into cardiopulmonary arrest it often times does not have a good outcome. This is because what caused them to arrest in the first place is likely life-threatening disease or injury. Because they are not fully developed when their heart or lungs stop functioning it most often results in death. Clients may want veterinary personnel to attempt cardiopulmonary resuscitation. It is strongly advised that any veterinary personnel who may have to performed CPR on any veterinary patient, which is anybody who works with animals, review the above listed guidelines that were published in 2012.

Oxygen Therapy

Neonatal/pediatric patients may need oxygen therapy for a variety of reasons. Unlike an adult canine or feline patient, it may be impossible to fully assess lung function in the smaller patients. This is because it is unlikely that veterinary personnel can obtain an arterial blood gas or even a reliable pulse oximetry reading. Assessment of lung function in the respiratory system generally can only take place through auscultation using a stethoscope and thoracic radiographs. When in doubt, administer oxygen if you feel that the patient is compromised and may not be ventilating appropriately.

Conclusion

Neonatal/pediatric patients require common veterinary procedures in order for them to successfully recover from their disease or injury. The largest issue with performing these veterinary procedures on them is their size. It is difficult to be successful with some of these procedures in less one has had experience performing them in such small animals. This comes with time and experience. Being patient and understanding the
THE ICK IN TICK
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CANINE TICK PATHOGENS

Canines are significantly over-represented in the small animal population. Currently canines may be affected with Ehrlichiosis, Anaplasmosis, Borrelia (lyme), Rocky Mountain Spotted Fever (RMSF), Babesiosis, Cytaxzoosmosis, American Hepatozoonosis, Bartonellosis and tick paralysis. A study of 1,764 DNA feline blood were taken from all areas of Japan. Of those only 2 came up positive for Ehrlichia or Anaplasma based off PCR testing. All were negative for RMSF infection. While tick borne illness can occur in cats, it is exceptionally rare compared to that of the dog.

There are several families of tick borne diseases; Anaplasmataceae (Ehrlichia, Anaplasmosis), Rickettsiaceae (RMSF), Lyme borreliosis, Apicomplexan parasites (Babesiosis, American Hepatozoonosis).

Ehrlichiosis

Ehrlichiosis is transmitted by the Lone Star and brown dog tick by introducing an intracellular, gram-negative, bacteria called Ehrlichia canis, E. ewingii, and/or E. chaffeensis. It is most common that dogs are infected with and suffer symptoms from E. canis. The long star tick is found up the Atlantic coast all the way up to Maine. It resides in Canada primarily in areas bordering Maine and in eastern Canada. Dog ticks can be found worldwide. Ticks become affected with the organism by feeding on already infected dogs, coyotes and foxes. Transmission from the tick to the dog occurs about 24-48 hours after attachment of the tick.

Approximately 8-20 days after infection dogs will develop symptoms. There are acute and chronic stages of Ehrlichia though it is difficult to distinguish between the stages. Acute signs may last 1-3 weeks and are generally resolved after 4 weeks. Initial signs may be subtle, i.e. lethargy, anorexia and fever. More commonly the acute symptoms are hallmarked by inflammation and thrombocytopenia. As a result of the thrombocytopenia epistaxis, melena, petechial and ecchymotic hemorrhage, retinal hemorrhage, anemia and hematuria may be seen. It is possible for the dog to resolve signs/symptoms without treatment. The organism may replicate in the reticuloendothelial tissues (macrophage areas) which may result in enlarged lymph nodes, edema and splenomegaly. Rarely the dog may experience eye disease and CNS symptoms such as ataxia, nystagmus or seizures.

Chronic stage signs range from mild to severe. The signs are the similar to the acute form, but exaggerated as they have been suffering with the disease for an extended time. Now they are stiff, some are unable to move, bleeding is more common, edema may be worse.

Testing for E. canis occurs though indirect fluorescent antibody (IFA) testing, enzyme-linked immunosorbent assay (ELISA) technology, polymerase chain reaction (PCR), or Western blotting. Most hospitals utilize either ELISA (SNAP 4Dx, IDEXX) testing in-house or IFA to an outside lab. With IFA antibodies can be detected between 7 and 28 days after initial infection. Therefore if the infection is chronic or signs started before 7 days it may offer a false negative. ELISA testing offers high sensitivity. A recent study showed that it accurately detected 96.2% of positive cases and 100% of negative dogs. This means roughly 4% of those tested will have a false negative. PCR testing is the most sensitive test of E. canis and therefore should be considered if the dog is showing signs and IFA testing was negative. PCR testing should occur if E. chaffeensis and E. ewingii are suspected. Though neither are as common as E. canis (E. chaffeensis is extremely rare) testing should be considered if the dog is symptomatic. E. ewingii is most commonly seen in the south-central and southeastern part of the United States.

Treatment of asymptomatic dogs is controversial as there is the fear it may lead to antimicrobial resistance or adverse side effects of drug therapy. This is well proven in both human and veterinary medicine. That being said the ACVIM Infectious Disease Study Group states that dogs should be treated for 28 days with doxycycline at 10mg/kg PO SID. Most dogs improve dramatically after 24-48 hours of treatment. Other drugs have been tried, but nothing has been as effective as doxycycline. Any symptoms (dehydration, bleeding, pain) should be treated accordingly until they resolve (fluids, transfusion, analgesia). As long as this disease is caught early the pet generally does well. It’s important to explain to the owner that they will not suffer lifelong affects from this disease after they are treated.

Anaplasmosis

It is transmitted by the Ixodes family of ticks including the black-legged tick (deer tick), western black-legged tick, tiaga tick and castor bean tick which transmit the bacteria Anaplasma phagocytophilum or A. platys. One or more
of the ticks can be seen across the entire North America, Europe and Asia. It is rare to have a dog infected with symptoms from *A. platys*.

Approximately 1-2 weeks after initial infection dogs will experience symptoms which often start as nondescript signs (anorexia, lethargy, fever). Similarly to Ehrlichiosis the pet will experience stiffness, lameness with rare vomiting/diarrhea and CNS signs. Sometimes a nonproductive cough may develop. Most pets will present with a polyarthritis, which is similar to those infected with Lyme disease making it difficult to distinguish between the two. In more than 80% of the cases a mild to severe thrombocytopenia occurs, although the pet may not show clinical signs.

Diagnosis can be obtained by looking at a blood smear under a microscope and finding morulae within the neutrophils. This takes a trained eye and is not often done because of the high potential of missing the morulae. More commonly indirect IFA testing, ELISA or PCR will be run. False negatives can occur with IFA and ELISA testing during the early stages of Anaplasmosis. PCR is the most sensitive.

Treatment is through the use of doxycycline at 5 mg/kg PO BID for 2 weeks. Like Ehrlichiosis it is important to treat any other symptoms as they present themselves.

**Borrelia (Lyme Disease)**

This tick transmitted disease is perhaps the most common and be found in most parts of the world. The *Borrelia burgdorferi* spirochete is transmitted by any of the *Ixodes* ticks. Most commonly it's transmitted by *I. scapularis* (deer tick) or *I. pacificus* (western black-legged tick). While it is primarily a canine disease, natural infection has been documented in cats, but poorly so. Pet owners frequently ask if their cat can get Lyme Disease. Approximately 13% of cats in the United States and 4% in the UK tested positive with antibodies to the *Borrelia* spirochete. That being said there have been no known cases where cats actually became symptomatic. They appear to be only carriers. When cats were injected with the spirochete experimentally they did develop signs with arthritis and meningitis being the two most common signs. So while Lyme disease and cats is something that is not currently worried about, it may be something in the future that we see as a symptomatic disease in felines.

Approximately 24-48 hours after the transmission the spirochete is transmitted through the saliva of the tick into the animal. It is well known that dogs can be infected, but never become symptomatic. It is unknown as to why some dogs will become symptomatic and even develop life threatening condition from it. Currently, predictions state that roughly 5-10% of infected dogs will develop the disease symptoms 2-5 months after infection.

Signs may start out fairly nondescript with lethargy, anorexia and a fever. Most of the time they quickly progress to lameness (shifting leg), polyarthritis and lymphadenopathy. Arthritis, and consequently lameness, begins in the joint closest to the tick bite though often signs progress so quickly that owners are unaware which leg was affected first. Owners often describe "fine this morning" or "limping a little this morning" to "now won't move at all" or "limping everywhere" and often describe it quickly getting worse in less than 24 hours.

While most symptomatic dogs present in a similar manner there are some rarer life threatening syndromes that may occur. Lyme nephritis (protein-losing glomerular disease), myocarditis and neurologic disease can occur as a result of infection from the *burgdorferi* spirochete. It is not known if dogs experience chronic reoccurring symptoms like people do, but at this time it is not thought that they do.

In 1997, a large study was done out of University of Pennsylvania which termed the disease known as "Lyme nephritis". The study showed that 18 out of 18 dogs that developed protein-losing renal disease also were positive for Lyme. Consequent studies have been few and far between. It is now known that the *Borrelia* organisms in fact do not invade the kidney at all. It is now thought that perhaps the nephritis is a result of the body's immune compromised state brought on by the infection and as such some literature is terming it "Lyme-specific immune-complex". Unfortunately, there are no tests to identify which dogs are at the highest risk. Golden and Labrador retrievers that are between 5-6 years of age appear to be predisposed. While only 1-2% of dogs will develop nephritis, all positive dogs should be screened and monitored for proteinuria and renal disease. Nephritis signs often mimic those of leptospirosis so dual testing should be performed in these dogs.

Samples of skin tissue can be submitted out for diagnoses along with the actual tick, but it is rarely performed and inaccuracies can occur. More commonly indirect IFA testing, ELISA or a C6 will be run. ELISA laboratory testing offers very accurate results but does not differentiate between an active infection versus exposure. Very few false negatives occur with ELISA testing. The ELISA test is most accurate 4-6 weeks after exposure. The C6 test is the most accurate test and can test for infection as early as 3 weeks post exposure. It is also not affected by the vaccine. Both the IDEXX SNAP 3Dx or SNAP 4Dx tests utilize the C6 technology. The laboratory out-of-clinic C6 test offers more detail and titer levels are given. This is useful for monitoring therapy as the titer will often decrease with therapy. This may also be a useful test in helping to determining how high the titer is and whether to treat or not. Lastly, a
western blot test can be performed, but it is significantly more expensive and is not as accurate. However, veterinarians who are monitoring titers of vaccines may utilize the western blot for this purpose.

Treatment of Lyme disease relies heavily on treatment of the symptoms. Initially, the animal may need to be hospitalized to manage its pain and hydration with the use of analgesics, anti-inflammatory and IV fluids. Antibiotics are the treatment of choice for the actual Lyme disease itself. Tetracyclines, ampicillin, amoxicillin, IV third generation cephalosporins, and erythromycin have been all used to treat Lyme disease. Doxycycline given at 5 mg/kg PO BID or 10 mg/kg PO SID for 30 days is the treatment of choice. Within 24-48 hours dogs make an amazing turn around and signs often disappear completely within that time frame. Intravenous doxycycline may need to be started in severe cases where the dog will not take oral medications or experiences nausea. Owners often wonder if their dog will have lifelong issues like some humans do that contract the disease. Almost all dogs go on to a full recovery without any signs/symptoms.

**Rocky Mountain Spotted Fever (RMSF)**

This life threatening disease is caused by *Rickettsia rickettsii* and most commonly occurs in the south-central and southeastern states. The American dog tick (*Dermacentor variabilis*) is primarily responsible to for transmission in the southeastern states while the Rocky Mountain wood tick (*Dermacentor andersoni*) is known to transmit the disease in the central states and Canada. There was a report of an outbreak in Arizona where RMSF was transmitted by the brown dog tick (*Rhipicephalus sanguineus*). The tick only needs 4-24 hours of attachment to transmit the *Rickettsia* and then approximately 4-14 days later the dog will become symptomatic.

German shepherds appear predisposed to developing some of the most severe signs. Like most tick borne illnesses nonspecific signs start including lethargy, anorexia, vomiting, abdominal pain and enlarged lymph nodes. Sometimes edema of the limbs will occur. The dog typically becomes stiff and lame. Ocular issues can start including mucopurulent discharge, scleral injection and uveitis. Thrombocytopenia occurs in 85% of dogs. As a result peteciae and/or ecchymoses may develop. In more than 80% of dogs neurologic signs have been reported including ataxia, stupor, vestibular signs, hyperesthesia and seizures. As the disease progresses the dog may develop myocarditis, liver and renal failure. Death ultimately occurs from organ, heart or central nervous system failure.

Unfortunately, RMSF has a high cross reactivity and current tests do not yield accurate results until 7-10 days after infection. ELISA testing is available, but IFA testing is considered the gold standard in both human and veterinary medicine. PCR testing is relatively new in veterinary medicine and offers a cheaper alternative to IFA testing.

Treatment is with the use of tetracyclines, chloramphenicol and fluoroquinolones. Doxycycline continues to be the preferred treatment choice at a dose of 5 mg/kg PO BID or 10 mg/kg PO SID for 14 days. As always it is important to treat any other symptoms that may occur as a result of the disease. This may include blood transfusions, IV fluid therapy, pain medications, anticonvulsants and cardiac medications.

**Babesiosis**

The *Babesia* protozoal organisms is transmitted by ticks and usually affects those in warmer regions of the United States. Both dogs (*B. canis* or *B. gibsoni*) and cats (*B. felis*) are affected. The brown dog tick (*Rhipicephalus sanguineus*) and ornate dog tick (*Dermacentor reticulatus*) passes along the protozoan approximately 24-48 hours after attachment. Because dogs travel and are imported in to Canada, ticks that carry the *Babesia* protozoa are now found in Canada. In 2013, a child in Manitoba was diagnosed with the first ever locally acquired *Babesia* protozoa from a tick.

Initially the animal may present with signs of anorexia, lethargy, fever and depression. In both the dog and cat it is common for them to have thrombocytopenia. As such the animal will often present anemic and have petechiae and/or ecchymoses on their body or mucous membranes. In dogs more serious signs can develop which include CNS disturbances, renal failure, liver failure, pancreatitis and coagulopathies. In cats these signs are less common.

The diagnosis is made by finding the organisms within red blood cells utilizing a Wright's stain on a microscopic blood smear. PCR testing is available, but blood smears offer a faster result. Treatment can then take place.

Current recommended treatment is with imidocarb dipropionate (6.6 mg/kg IM, repeated in two weeks). In dogs that have tested positive through PCR to *B. gibsoni*, the combination of atovaquone (13.5 mg/kg PO TID with a fatty meal) and azithromycin 10 mg/kg PO SID for 10 days may reduce and possibly eliminate the protozoa. In cats, primaquine phosphate (an antimalarial drug) can be given 1 mg per cat orally every 36 hours for four treatments. It is then reduced to just 1 mg every 7 days for four more treatments.

**Cytaxzoanosis**
**Cytauxzoon felis** protozoan is transmitted by the American dog tick (*Dermacentor variabilis*) and usually only affects cats in the south-central and southeastern states. Cats are usually asymptomatic, but if symptoms start cats usually die in 2-5 days.

More than 90% of all cases will be diagnosed between April and September. The protozoan specifically attacks the vascular system of the kidneys, brain, lungs, liver and spleen. Usually, owners will notice that their cats are depressed, not eating, and have pale mucous membranes. Thrombocytopenia is one of the most common findings in cats. Cats typically present anemic, icteric and severely ill. Within 5-6 days after infection, you will likely see a decrease in the packed red blood cell volume. There is a >90% mortality rate associated with this disease. (pic 4)

Rapid diagnosis is key to any chance of survival. The protozoan can be identified using a Wright's stain on a microscopic blood smear. A classic signet ring is easily identified most times. PCR testing is available, but takes about 2-3 business day for results.

Supportive care and anticoagulants (heparin) are the standard of care for treating *Cytauxzoon*. A newer treatment using atovaquone-azithromycin has been shown to offer a 60% survival rate in one study. Atovaquone (10 mg/kg PO Q24) and azithromycin (15 mg/kg PO TID) should be used for 10 days with aggressive supportive care. Imidocarb dipropionate (2 mg/kg IM once every two weeks) can also be given, but does not yield as high of a survival rate.

**Bartonellosis** (cat scratch fever)

While *Bartonella* is primarily transmitted to the dog or cat by fleas, increasing evidence has shown that it can be transmitted by ticks as it is a highly adaptive bacteria. Dogs may carry *Bartonella henselae* and *Bartonella vinsonii* while 41% of cats will carry *Bartonella henselae*, but may also carry *Bartonella clarridgeiae*. As it learns to adapt we may find ourselves diagnosing it more. Primarily known as a cat disease, dogs that are infected are more likely to become ill from the bacteria.

Dogs will present with symptoms of fever, endocarditis, hepatitis and myocarditis and epistaxis. In cats signs may be more life-limiting such as a fever that lasts 48-72 hours. Rarely in cats it can progress to vomiting and lymph nodes enlargement. Typically in cats the symptoms appear during periods of stress.

Blood smears have not been effective in locating the bacteria. Blood cultures can be submitted to the lab. PCR testing is available though IFA as the preferred test because it yields the most accurate results. Enrofloxacin (5.4-7.6 mg/kg PO BID) for 14 or 28 days is the current treatment of choice.

**Tick Paralysis**

This tick borne disease occurs mainly in the spring and summer months. Infection occurs through the *Dermacentor* or *Ixodes* tick transmitting holocyclotoxin, a presynaptic neurotoxin into the blood stream. Approximately 5-9 days post-transmission flaccid tetraparalysis occurs to the dog. Initially it may present with just pelvic limb weakness and in 48-72 hours the dog will become recumbent. In severely affected dogs, megaesophagus and consequently aspiration pneumonia can occur. Some dogs may require ventilatory support as all muscles have a potential to be affected. Spontaneous recovery usually occurs about 3 days post removal of the tick. Ticks must be removed in order for the dog to recover so often the dog will need to be shaved down completely. Spraying the dog with fipronil sprays or organophosphates will help to ensure all ticks are removed from the dog.

**CONCLUSION**

There's no escaping tick borne diseases because ticks are everywhere. Understanding each disease and how it affect the patient will allow you to better treat the pet and offer excellent communication to the owner. Tick prevention and education for owners is the best defense against tick diseases.
INTRODUCTION
Providing excellent nursing care for the critical patient may be the difference between the patient's survival or demise. Being able to monitor your patient for trends, recognize when there are changes in your patient's status and knowing how to react is important to helping the pet recover. Critical pets also require some unique nursing care solutions.

TRENDS, TRENDS, TRENDS
Being a veterinary technician means you are the advocate for the patient. You are the one who will spend the most time with the pet. You must advocate for your patient's needs. If your patient has soiled itself you are the person that patient relies on to help them. It is imperative that you really monitor the critical patient closely. Identifying trends is the most important aspect to critical care nursing.

For example, if your feline patient has had a heart rate readings of: 180bpm, 190bpm, 184bpm, 190bpm and now the heart rate is 212 bpm you must investigate what is causing an elevated heart rate in this pet. A heart rate of 212bpm is still within physical exam parameters, but is likely not normal for this patient. Something caused that heart rate to increase. Was it pain? A large bladder? Perhaps the patient is more alert after a procedure and the 212 will be the new normal. It's important to monitor for trends and not just put all your patient's values and numbers in a box.

FORWARD THINKING SKILLS
You cannot be the best technician for your patient if you do not:

- Interpret: Understand & Explain the meaning of information or an event
- Analyze: Investigate a course of action that is based on data
- Evaluate: Assess the information you receive and determine if a reaction is needed

WHEN DO YOU FAIL?
- You yield to tradition
  It’s always been done this way
  Creative approaches are not tried
- You become biased
  You dislike the owners so you don’t provide best care
- You are right. All else is wrong.
  You close the door to suggestions
  You stop looking

TO SUCCEED:
- Pay Attention
Come in to work clear minded!
- Communicate What Your Patient Needs
- Own Your Patient
It’s a team approach at ALL times
It’s not the doctor’s patient
You don’t just follow orders
NURSING SKILLS

Basic Nursing Care

Critical patients should minimally have a full physical exam performed every 4 hours. In some instances a patient may require a nurse to stay with them continuously and vitals be checked every 5-15 minutes. A full physical exam should include a heart rate, respiratory rate and effort, mucous membrane color, capillary refill time, rectal temperature and neurological status. A veterinary technician must own or have use of a good quality stethoscope if they are going to be caring for critical patients. It is important to remember that you get what you pay for and while some stethoscopes are cute to look at, if you can't adequate hear a low grade heart murmur or arrhythmia then your money was wasted on a decorative piece that hangs around your neck. If there is any change from normal or the previous parameters, the veterinarian should be notified.

Critical patients are often at risk for disseminated intravascular coagulopathy (DIC). It is important to look for signs, which includes excessive bleeding after venipuncture sticks and/or petechiae on the gums, pinna or abdomen of the pet. When performing a mucous membrane check it is important to look at the gums for petechiae.

Monitoring the patient's fluid therapy is important. Patients should be weighed at the beginning of being hospitalized and then at least two times a day to determine fluid losses and gains. Rapid changes in body weight are usually a result of fluid gains or losses. Critical patients can often experience large fluctuations in weight due to fluid shifting, retention or loss of fluids through vomiting and/or diarrhea. A 0.5 kg weight gain is equivalent to a 0.5 liter fluid gain.

Urine output should be monitored and recorded. Quantifying urine output is key in monitoring fluid therapy and also to look for signs of renal injury in critical patients. Since critical patients may experience multiple organ dysfunctions (MODs), kidney failure may occur in these patients. The total volume you are giving into the patient should ideally be urinated out. Therefore if you have a patient who is on 50ml/hr, after 4 hours they should urinate 200mls. You can place non-absorbent litter in cages with cats and you can catch the urine of canine patients in a bowl for quantification. Critical patients most often benefit from urinary catheter particularly if they are non ambulatory.

Patient should be kept on clean, dry and padded bedding at all times. If the patient is recumbent than purchasing orthopedic foam beds is key to helping older animals in particular be able to walk sooner after recovery. Placing critical pets on thin towels or one small blanket is not sufficient. This will cause pets to develop bed sores, ulcers and stiffness in the muscles and joints. If an orthopedic bed is used it should likely be covered over with plastic (like a trash bag) to prevent soiling through the foam. Large orthopedic beds usually cannot be put through a standard washing machine rendering them unusable if they become soiled. Typically in the author's hospital orthopedic beds are covered in multiple trash bags and then blankets are put on top of the plastic to allow for more comfort.

If a patient soils itself it is imperative the nursing staff act quickly to completely bathe the patient. Wiping the pet down is usually not enough. Urine and feces will cause severe scalding if it is not completely removed from the fur/skin. Besides severe discomfort to the pet, owners are often very unhappy with the care provided if they pick up their pet to find their rectal are violently red and shaved and their pet forced to wear an Elizabethan collar for several days until it heals. If scalding occurs applying specialized creams (SSD, Desitin (Zinc Oxide) will help to reduce inflammation.

Advanced Nursing Skills

Since critical patients often require frequent blood draws a central line should be placed. This will allow for faster and pain-free blood collection from the patient. Without a central line often times veins become overused and obtaining blood can be a real, if not impossible, challenge. A central line may not be possible if the patient is in DIC, experiencing a coagulation disorder or head trauma. If a patient is admitted and is critical it is up to the technician staff sometimes to advocate for a central line as this will benefit the patient in the long run. Drawing blood, monitoring central venous pressure, administering higher dextrose concentrations (≥ 7.5%) and parental nutrition can all be done with the placement of a central line. Central lines should be maintained by flushing saline every 4-6 hours in
unused ports. The use of heparinized saline is no longer indicated. Unwrapping all IV catheters at least every 24 hours down to the site of injection is important to monitor for signs of redness, inflammation, infection or irritation. The catheter should be flushed and if the animal reacts painful phlebitis should be suspected and the catheter should be removed after a new one is placed.

An arterial line should be considered in patients experiencing respiratory problems or blood pressure issues. This will allow for measurement of PaO₂ (partial pressure of oxygen in arterial blood), which is the gold standard when measuring overall oxygenation ability. It also allows for the gold standard of measuring blood pressure through invasive blood pressure monitoring. Arterial lines should be labeled properly. Drugs and certain types of fluids should never be administered into an artery. Arterial lines should have all lines leading up to them with luer lock adaptors. If a patient disconnects a line leading into an arterial line they can suffer massive blood loss. Arterial catheter should be carefully unwrapped every 24 hours to look at the injection site and ensure it is free of infection and inflammation. If it is not constantly being used (as in the case of invasive blood pressure monitoring) then it should be flushed every 1-4 hours. The literature is not very clear if heparinized saline is indicated for flushing arterial lines or if plain saline is just as effective. In this author’s experience it is up to the veterinarian. The author has worked with boarded criticalists who ask for hep-saline and those that just ask for plain saline. The times for flushing vary from every hour to every 4 hours depending on the literature.

Besides a stethoscope and thermometer to monitor vitals there are generally a couple other tools necessary for appropriately monitoring the critical patient: blood pressure, blood glucose, lactate and central venous pressure (CVP).

It is important that critical patients have their blood pressure monitored minimally every 4-6 hours. Critical patients are at risk of developing hypotension. If the mean arterial pressure (MAP) falls below 60 mmHg, the kidneys and other organs are not appropriately perfused putting them at risk for organ failure. Arterial hypotension is defined by a MAP (diastolic + 1/3(systolic-diastolic)) less than 60 mmHg or by a doppler ultrasonic blood pressure with a systolic reading less than 80 mmHg. Normalization of blood pressure, defined by a MAP of 80-120 mmHg or systolic between 110-160 mmHg, is the goal in any patient.

Blood pressure can be monitored either directly or indirectly. Direct (invasive) arterial pressure monitoring is gold standard. It requires the placement of an arterial catheter, which can also be used to obtain arterial blood gas samples from to monitor PaO₂. An electronic transducer is then placed at the end of the arterial catheter and measured continuously. If an electronic transducer is not available then the blood pressure can be measured using a central venous pressure manometer. Special lines must be used that are manufactured for that particular unit otherwise the machine will not work or give incorrect readings. Indirect methods include oscillometric devices or doppler ultrasound flow detectors. Indirect readings are less accurate, but require less skill and are noninvasive.

Central venous pressure (CVP) is generally used when a patient is prone to changes in blood pressure or when aggressive fluid therapy is being utilized, which is the case with septic patients. CVP is considered a measurement of cardiac pumping ability, circulating blood flow, vascular tone and intrathoracic pressures. A central line is placed into the jugular vein and is fed down until it rests on the right atrium. The pressure in the right atrium indicates how the heart handles the volume of fluid presented to it. The measurement helps to determine how much fluid can be administered to a patient without causing fluid overload or dehydration. Depending on the literature normal CVP measurements vary, but most will agree it is somewhere between 1-10 cm H₂O. Certain multiparameter machines have the ability to perform digital CVP readings. This eliminates the subjectivity to the procedure. The most accurate machines pass a transducer into the central line and allow for CVP readings to be taken right off the heart electronically.

Lactate accumulates in the tissues and blood as a result of inadequate oxygen availability which is generally caused by tissue hypoperfusion. In some cases increases in lactate may be the only indication that hypoperfusion still exists. Increases in lactate are commonly seen in critical patients that are not perfusing well. A value of under 2.5 mmol/L is normal. In human medicine monitoring lactate trends are common. Studies in human medicine have shown that lactate values that remained above 4 mmol/l are a
predictor of poor outcome with mortalities of greater than 40% in some critical patients. Lactate can be measured using a simple hand-held device similar to a blood glucose machine. It is important to normalize lactate concentrations through fluid therapy and blood pressure normalization.

Urinary catheters should be placed in any recumbent critical patient. Urinary catheters should be placed aseptically. Depending on the literature the rate of dogs or cats obtaining a urinary tract infection (UTI) as a result of an indwelling urinary catheter ranges from about 10% in cats to about 50% in dogs. Placing a temporary catheter and removing it immediately causes a UTI in about 20% of females and almost none in male dogs or any sexed cat. A study in 2012 showed a decrease in UTI if the catheter, ports and lines were all wiped down with a chlorhexidine based solution every 6 hours decreased the rate of UTI in dogs to about 12%. While this was only one study it certainly is not contraindicated to practice such a technique. Bags and lines should not be allowed to touch or drag on the ground. People touching lines should wear gloves or, more importantly, wash right before handling the line. The use of prophylactic antibiotics has been showed to increase, decrease or not cause any change in the rate of UTI in patients.

Critical patients may have chest tubes, drains, feeding tubes or nasal lines. Any patient who is alert that has a nasal line for either oxygen support or nutritional support should have an Elizabethan collar on them. Nasal lines are very irritating and failure to put an E-collar on the patient can result in them creating trauma to their nares. Drains and chest tubes in critical patients should be handled with gloves on. Both drains and chest tubes require you to remove air or fluid from the patient which may be contaminated with bacteria. It is good practice to protect yourself as well as the patient. Patients with chest tubes should be monitored closely as disconnection from a suction machine or having a cap fall off may result in a fatal open pneumothorax. Chest tubes should always have a 3-way stopcock on them which is moved into the off position as added security. At least once a day the insertion site of the drain or tube should be monitored for signs of swelling or localized infection. The prophylactic use of antibiotics is not recommended. If the chest tube is not being continuously suctioned then it should be manually evacuated every 4-6 hours to avoid clotting of the line. As aspiration is occurring the line should be checked for kinks. Checking for kinks is important in patients that have drains or nasal lines as well.

**Nutritional Support**

Nutritional support must be considered in critical patients that are hospitalized more than 48 hours. Disease and injuries causes an increase in resting energy expenditure and an increased protein consumption. Providing nutritional support to these patients early is essential in order to minimize weight loss and to provide adequate energy for metabolic support. In both human and veterinary patients a better outcome is seen in those that receive nutritional support earlier. Enteral feeding is the best. Many times these patients will not eat on their own, so placement of a feeding tube should be considered. Certainly if the patient continues to vomit or enteral feeding is not appropriate, parenteral feedings should occur.

**Pain Management**

Most critical patients are in some level of pain. This is particularly true for any post-operative patients. As the patient’s nurse it is imperative that you watch for signs of pain. In dogs this may include vocalizing, shaking, aggression and panting. In cats, more commonly, they will become aggressive or hide. If a pet is painful it should receive pain medication. Opioids are the choice of drugs for critical patients. They offer excellent analgesia with limited effects on the hemodynamic system. Multimodal and continuous rate infusion analgesia should be considered in these patients.

**CONCLUSION**

Most veterinary technicians will encounter a patient that is critical at some point in their career. It is important to understand the unique nursing care your patient will require. Providing excellent nursing care will mean the difference between life and death to the critical pet.
TURN THE NEGATIVITY AROUND: HOW TO CONVERT A TEAM'S THINKING
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Introduction
Working in veterinary medicine can be difficult because it involves working in a team. So many went into the industry thinking that they enjoyed animals more than people only to find out that they work with people the same amount, if not more. In hospital settings it is a matter of life and death on a daily basis for patients. In order to perform even the simplest task, like drawing blood, team members must work side-by-side with each other. This is unlike human medicine were often times the registered nurse performs phlebotomy solo. The stress of day-to-day experiences, coupled with having to work so very closely if not on top of each other, can result in a stressful work environment. Being a great team member not only allows for better experience for everyone else but yourself as well.

The Team Members
People leave managers, not jobs. That saying is mostly true, but it can be argued that people also leave bad teams with bad morale. Usually the teams that have bad morale and high turnover are the direct result of also bad managements. Rarely, but sometimes, a team member may leave a job simply because they want a challenge outside of what the company can offer. That said I personally worked in a veterinary hospital where the management was terrible, but my team was amazing. I stayed because of the amazing team members that I had working alongside me.

A team is made up of many individuals all with different personalities. There are many personality testing software’s and theories out there that attempt to classify one’s personality. There is no exact or perfect testing method, but certainly having a good understanding of the different types of personalities out there allows any team member to interact with their coworker in a more productive manner.

One of the more popular method is the Myers-Briggs personality test which categorizes people into 16 different personality types. It is based on the conceptual theory that was proposed by Carl Jung and created by Katharine Cook Briggs in the early 1900s. It is such a popular personality classification system that numerous websites, including www.16personalities.com, offer tests to classify you into one of the 16 different personality types. There are four main groupings of personalities with two choices in each group.

- People tend to be either extroverted or introverted.
  - Extroverts tend to drawl energy from action. They like crowds and they react first and think later. Solitude is stressful to them and take more energy than interacting with people. Being with people recharges them.
  - Introverts tend to drawl energy from inaction. They are thinkers first and react second. Crowds are stressful to them and take more energy than being alone. Being alone recharges them.

- People tend to be either sensing or intuition
  - Sensors tend to focus on real senses they can see, touch and feel. They trust the information that a tangible and that they can see.
- Intuition individuals tend to focus on possibilities. They learn from larger experiences and can apply it to what could be in the future.
- People are either thinkers or feelers
  - The thinkers tend to be over analytical and they do not use feelings to place judgment on a decision
  - Feelers tend to look at the impact it would have on those around them and take into consideration others’ feelings
- People are either judging or perceiving
  - Judging individuals like to live in a very organized manner. They feel satisfied when a plan comes to a closure. They like planning and organization
  - Perceiving individuals like to keep options open. They are spontaneous and adaptable.

While there are plenty of ways to categorize human behavior, the Myers-Briggs method is certainly one that many people enjoy and can relate to. There are certainly people who are very extroverted and people that are very much thinkers. There are also people who fall in the middle. Having the team take a Myers-Briggs test or other personality test will allow the members to understand how best to interact with each other.

The 10 Key Traits to Being a Great Team Member
- Start the day off on a good foot.
- Be Kind, Respectful & Polite to each other
- You all Love Animals. Remember That.
- Be a cheerleader or at least offer applause
- Be Observant & Take Initiative
- Be Engaged
- Don’t Gossip & Assume Good Intention
- Remember it’s ONE team, not a department or a group
- Create moments of laughter & fun
- Ending the day with a unicorn flying by

Starting the Day
In veterinary medicine all team members perform shiftwork. It might be an overnight shift or day shift, but team members are expected to arrive and end the shift at a certain time. In order to start the day off on a good foot (or perhaps it’s the night you are starting) you must arrive on time. This doesn’t mean just in the nick of time. You must arrive before your shift, put away your belongings, check your cell phone one last time, and be ready to work at the start of the shift.

Say hello to your team members. Say something nice. The first words out of your mouth should not complaining. Starting the day off with the complaint sets the tone for the rest of the day. No one wants to hear about how you’re tired and you didn’t want to come into work. Probably several other team members feel the same way. Complaining just breeds negativity. Don’t let it be the very first thing that exits your mouth when you walk into work. Instead, put in
a few positive sentences before maybe adding in about how you are tired and would rather sleep in.

Be Kind, Respectful & Polite To Each Other

This seems to go without saying, but it is difficult to remember this when there is a patient who is not doing well or a client yelling at you. If the exam room appointment start getting backed up and a technician is taking longer than usual to read a blood smear or a fecal things get said that are not kind. One of the largest issues in veterinary medicine is that people forget to be polite, kind and respectful to each other.

No one should be permitted to yell at each other. It simply should not be tolerated. Throwing of items or slamming things on tasks should be immediate reasons that an employee is written up. While at times it seems like a casual place of employment, it is a working hospital performing medicine. It is a professional environment that many times employees forget to be professional in.

If there is a heated exchange of words or actions it should be immediately corrected once the individuals have had time to reflect on the inappropriate behavior. They need to apologize in order to mend the relationship they have as team members. And while they may not agree with each other, they need to agree that they are working towards the same common goal and will treat each other in a more respectful manner moving forward.

Team members should not be permitted should not be permitted to curse frequently. There may be a rare instance where cursing happens. The team member who said the bad word, should apologize and make it known that it was inappropriate behavior but that they were reacting to the situation. Cursing directly at a team member is grounds for immediate action from a manager.

Above all else it is important to remember that every team member works in a professional environment. Maintaining professionalism and being polite and respectful is important to good team health.

You Love Animals

All team members love animals. A good team environment is one where the members remember to treat all animals as if they were their own. In human medicine when a doctor or nurse does not like a particular patient a don’t announce their grievance to the patient. They don’t say nasty things to the patient or take pictures to make fun of them or yell at them to try to get them to behave. It is unfortunate that these things happen frequently in veterinary medicine.

If a dog is barking loudly do not yell at the dog. This adds to the stress of the team. No one likes the dog barking. Don’t be the team member to yell back at it. It only reinforces fear and even resentment in that dog as to why they were barking in the first place. Instead investigate why the barking is happening. Maybe they have to go outside to eliminate, maybe they are in pain, maybe they are lonely or hungry.

It’s okay if you don’t get along with every single patient. Ask a coworker to work with a particular patient that is causing you stress rather than take your stress out on the entire team. There’s probably someone on the team that can connect with that animal better or at least handle the stress better. If you find yourself stressed out about your patience more often than not, you may be suffering from burnout. It is important to recognize this and seek the help that you need so you can remember that you love animals.
Be a Cheerleader

Not every team member is going to be vocal and cheering on every buddy all the time. That’s okay. However, whether you’re an introvert or extrovert it’s important to give praise to your team members when they did a good job. Be genuine about your applause to the person. “Good job getting that catheter in” or “Thanks for cleaning up the vomit” are important to maintaining the best team.

Even if the day was terrible and not much seemed to go right, it’s important to acknowledge that the team worked hard in some way despite the failure. Leaving the day without a single complement, praise, or pat on the back often makes employees wonder “why am I even working here?” Our animal patients do not provide praise. They rarely provide affection. If we are not kind to each other that it becomes a very long and stressful day.

Doing simplistic things like putting a smiley face on a piece of paper next to someone’s stethoscope is the difference between that person having a good day or a bad day. If you know what lunch bag they bring in, put a note on it that says something nice like “thanks for always stocking the drawers” and let them find it at lunch. If you know what car they drive put a note on the car or just print out a big smiley face emoji with the words “thanks” and put it on their car for them to see.

Be Observant & Take Initiative

If you do not notice how your team members are doing then you are not a good team member. It may take some work if it’s not your normal personality type to be a feeler or be perceptive. That’s okay. But even non-feelers and those that lack perception, can sense when someone is sad or having a bad day. May be the non-feelers may only respond to those they see crying in the corner or those that are vocalizing their distaste for a situation, but being a good teammate requires you to step up to the plate for your team member when it’s necessary.

If you see somebody always grumbling about having to take care of the dog with the bloody diarrhea or they talk about how they don’t want to handle the cat that is growling and hissing, ask if you can help. Take initiative to help that team member out because at some point you will need help yourself.

If you think someone is suffering from compassion fatigue or burnout, talk to their practice manager or them. It’s certainly not your job as a teammate to coach them through a difficult time, but it is your job to ask them if they are okay. If that teammate is an introvert and if they want to seek help, going to their friend or their manager out of concern is important. Losing a team member because they are burnt out or suffering from compassion fatigue adds stress to the whole hospital.

If you notice that someone is struggling to reach something up high and you know where there’s a step stool, go help them. Be observant and take that initiative. If you see that someone is setting up for an IV catheter and looks like they are waiting for someone to help them, be the person to offer the help. Don’t just keep ignoring them. Take the initiative to help your teammate and they will be a better teammate to you in the future. “Did you eat lunch” is a simply check in with a team member and can mean so much.

Observing if your teammate needs help, whether it be physical or emotional help is important to being a good teammate. If you sense that they need some type of physical help in doing a task you need to take the initiative to help them even if it might be somebody you don’t always get along with. It’s your job to do so. If you ignore them that’s going to just breed further
resentment. If you see someone needs emotional help reach out to them. For some personalities it’s really hard to do so but recognize that just checking in it sometimes all the help someone needs.

Be Engaged

If you are not engaged in your job then others will disengage with you. Maybe you are in engaged teammate but you know somebody who is completely disengaged. Starting off a conversation with “you just don’t seem that into your job today” or “what’s going on, you don’t seem to want to be here” can go a long way.

There will be days that you are disengaged. It’s important to let the team know that you’re having one of those days or recognize that you are when someone approaches you. It’s okay to tell your team “I’m exhausted today because I didn’t get enough sleep and I’m sorry that I’m not cleaning as much as I should.” If this behavior occurs every day then it’s a symptom of a larger problem. However, being a good teammate means you most of the times fully engaged.

If you come to work and practice amazing medicine, but sit down in between patients and ignore your team or you don’t perform the menial tasks that are part of your job, you are still disengaged. You must be fully engaged in the job entirely. No one likes taking out the trash. Doctors are not usually big fans of staying on phone calls with clients for hours at times. When a technician or receptionist looks at a full trashcan and decides to ignore it they are disengaged. When a doctor complains they don’t want to talk to a client or they want someone else to talk to them, they are disengaged. Passing on your lack of engagement to others is not being a good teammate. It’s okay to ask for help on days that you are struggling with engagement, but if it becomes a consistent theme then you need to talk to your supervisor or manager and figure out what will get you back on track.

Don’t Gossip & Assume Good Intention

Just don’t do it. When team members gossip it breeds distrust. The trust in a team comes from a respectful and healthy relationship. It’s okay to make mistakes. Everyone does. However, if people gossip about the person who made the mistake behind their back and that individual finds out it becomes a very bad team. Even if the person doesn’t find out, anyone who makes a future mistake will assume that they too will be the brunt of gossip.

A good team is built on trust. Gossip is defined as talking about someone when they are not present. Gossipping makes people feel uncomfortable and they will shut down and become resentful. The person who is gossipping requires attention or acknowledgment of what they are saying. It is hard for those who are listening to the gossip to disagree with the gossiper. Disagreeing with someone who is gossipping creates conflict. No one likes conflict when they have to work in a team environment. So, even if individuals disagree with the gossip up they are often times left with just agreeing to get through the situation. Gossipping makes everyone except for the person who is doing it uncomfortable.

Since most gossip is about something someone did wrong or how someone is bad or how something is annoying, the best rule of thumb is to “Assume Good Intention”. If all team members can assume good intention from clients and each other and it will make for a better team environment. Assuming good intentions and not gossiping go hand-in-hand.

Getting off the phone and complaining about a client who called in for a silly question about their cat’s medical health and about how much time they took out of your day is gossiping. It’s also not assuming good intention. The client had good intention. They were worried about
their cat. You work in veterinary medicine. You share a same love of animals as that client. Their only intention is to do right by their cat. Maybe they don’t have all the answers or maybe they’re not going about it the right way but the end result is they are trying to have good intention for their cat. When you get off the phone and talk about how the client is “stupid” and “annoying” and “wasted 15 minutes of your day” that is the opposite of assuming good intention. It also is gossiping. It is unlikely that your coworkers want to hear you go on and on about the client on the phone. They have other things to worry about. The reason why you are upset and gossiping in a negative way about that client is because you did not assume good intention. Take a moment to have compassion for them and assume good intention.

This same scenario can be used with your coworkers. The doctor wasn’t trying to make your life harder because they forgot to write a prescription that you asked them to do three times. They were busy and they had good intention doing other things. Maybe they simply forgot. It was not however their personal vendetta against you to not write the prescription. Don’t gossip about it. Assume good intention.

Remember ONE Team
You are part of one hospital team. Within the hospital team there may be smaller teams. There may be the front office team or the management team, but regardless you all work in the same hospital. You are all striving for the same goal. No team is better than the other so please, don’t start the team wars.

If a team member is struggling in a different department or area of the hospital you don’t normally work, but you’re able to help them even if it’s not the best help, do so. They are your coworker. If you see the front office staff struggling to answer the phones, answer a phone. You may not know the answer to the client’s question, but that’s okay. You can put them on hold or explain to them that the front office is busy and you’re going to try to get the answer for them. It’s okay to say that you don’t normally work in a certain area of the hospital but you’re doing your best to help.

Be respectful of the fact that that individual has to do their main job to do. If the team member is constantly being pulled away from their main job then it will cause more stress within their team. It’s important to remember that each team member has a very specific job within the hospital in order for the hospital to function best. Most of that team members job must be dedicated to their original job description. It’s okay to ask for their help, but don’t be upset if they truly can’t because there is a more pressing issue in their team that they need to deal with. The person who has declined to help another area of the hospital should provide a reason OR provide a timeline that they could be able to help them. “I’m just finishing up with this patient and then I can come over in about five minutes to help restrain that dog.”

Ultimately it is important to remember that every job is important in that hospital. There is not one that is more important than the other. Doctors would not have appointments if the front office did not make them. Technicians would not have patient orders if doctors did not provide them. Front office would not have phones to answer if doctors did not see patients. Remembering that you are all part of the same hospital is important so that you can help each other when time allows. It is every single team members job to help each other out.

Create Moments of Laughter & Fun
The best team member is a fun team member. For those that are introverted this doesn’t mean you have to be the life of the party. However, even an introvert knows what is fun. Maybe
it simply bringing in some chocolate or its playing a good song. Maybe it’s printing out a picture of a unicorn and putting someone’s name underneath it. Maybe it’s wearing a silly hat or breaking out into crazy dance moves. And it could be as simple as laughing over something that is not going quite as planned. “Today really stinks like the biggest pile of stinky poop, right” “Yes, it smells like HGE met IBD”

If you do not have fun then you likely will not last in that particular job for very long. It can be argued that you spend more time with those that your job then you do with your family and friends. It’s important to have fun with them. If you notice a team member struggling, hitting the keys of the keyboard in an angry fashion or maybe just not talking like they usually do, put a candy bar in front of them. That usually gets them to smile.

There has to be silly moments of laughter and fun throughout the day. The best teammate ensures those moments happen.

Ending The Day With a Unicorn Flying By

There has to be a good end to the day. A good teammate will take in the day and be good to their coworkers on the way out. Say goodbye. Don’t just walk out the door. Even though veterinary medicine a shift work, it is very rare that the team members leave exactly at the time they are scheduled to. Don’t be the team member that runs out the door exactly at 5:00 PM.

If your hospital works on multiple shifts, potentially 24 hours or even evening shifts, set the next shift up for success. You should leave the end of your shift as if a unicorn ran by and made everything perfect the way you would want it when you came in for your shift. Set the next team up for success and that will make you a good team member. Remember that even though you may not work with the next shift they are still part of your team.

End on a high note. It might have been a terrible day but you all stuck it out and no one ran out of the hospital crying. It’s okay if that was the only good thing that happened. Laugh and say “Today was not a good day, but we all stuck it out and no one ran out of the building with their hands above their heads screaming.” That’s a positive end to the day. Ideally the wins for the day will be bigger. It may be a simple “good job everyone” or “see you all tomorrow” or “I can’t wait to see Mrs. Smith’s new puppy tomorrow”. Regardless, there should be some conclusive statement that is overall positive to end the day from every team member.

Remember that if you are the team member who didn’t stock the drawer or left the trash overfilling, it will either be there for you the next day or your teammate who comes in for the next shift is not going to be happy. End the day with a unicorn not a pile of trash.

A Good Team Member

A good team member is one that is engaged, comes in on time, helps out their fellow team members, doesn’t gossip, smiles, and create moments of laughter. Just think about someone who does all those things and you likely want them as part of your team. Recognizing that there are so many types of personalities out there and realizing that none of them are better than the other is important. By understanding a little bit about personalities and assuming good intention while being kind you can be an amazing team member. Happiness and laughter means that when you go home at the end of the day you don’t spend an hour venting to your family and friends. It means you have an easier life that can be more enjoyable. Being a good team member means that you want your job to be enjoyable so that you can go home stress-free and enjoy the other parts of your life. If everybody could have that mindset we would have great teams in every hospital.