LATIN AMERICAN VETERINARY CONFERENCE

# LAVC 2019

#APRENDOCONLOSMEJORES


**07 - 10 ABRIL, 2019 | 10AM-3PM**

**LA MEJOR CONFERENCIA DE LATINOAMÉRICA**

Puedes ver si un hombre es listo por sus respuestas.
Puedes ver si un hombre es sabio por su preguntas.

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# MEDICINA DE ANIMALES DE COMPAÑÍA

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# CASE STUDIES IN CANINE ANEMIA

## Yogi

7 year old MI Chow, examined for routine vaccinations. History of FUO 1 year ago. Pale pink MM; CRT 1 s; No fever; Poor hair growth from catheter site.

**Yogi**
**Complete Blood Count**

| Parameter | Value | Reference Range |
|---|---|---|
| RBC | 5.3 x $10^6$ /µl | 5-8 x $10^6$ /µl |
| Hematocrit | 34.1 % | 37-52 % |
| WBC | 8.9 x$10^3$/µl | 6-14 x$10^3$/µl |
| monocytes | 0.178 x$10^3$/µl | 0.13-1.15 x$10^3$/µl |
| lymphocytes | 0.623 x$10^3$/µl | 1.06-4.95 x$10^3$/µl |
| neutrophils | 7.9 x$10^3$/µl | 2.94-12.67 x$10^3$/µl |
| bands | 0.089 x$10^3$/µl | 0 x$10^3$/µl |
| eosinophil | 0.089 x$10^3$/µl | 0.07-1.49 x$10^3$/µl |
| reticulocytes | 10 x $10^3$/µl | 20-80 x $10^3$/µl |
| MCV | 64.3 | 63-75 fl |
| MCH | 22.3 | 13-18 pg |

**Yogi**
**Biochemical Profile**

| Parameter | Value | Reference Range |
|---|---|---|
| Total Protein | 7.9 g/dl | 5.4-7.8 g/dl |
| Albumen | 3.8 g/dl | 2.3-4.3 g/dl |
| Globulin | 4.1 g/dl | 2.5-5.5 g/dl |
| Glucose | 83 mg/dl | 65-140 mg/dl |
| Total Bilirubin | 0.4 mg/dl | 0.1-0.6 mg/dl |
| Alanine amino transferase | 19 IU/ml | 5-75 IU/ml |
| Sodium | 149 mEq/L | 139-154 mEq/L |
| Potassium | 4.7 mEq/L | 3.5-5.5 mEq/L |
| Creatinine | 0.9 mg/dl | 0.5-1.6 mg/dl |
| Blood urea nitrogen | 16.5 mg/dl | 8-25 mg/dl |
| Cholesterol | 600 mg/dl | 100-250 mg/dl |

Urinalysis 1.012 specific gravity

pH = 6.5

dipstick = negative

WBC = 2-4/hpf

RBC = 2-4/hpf

Is this anemia hemolytic, blood loss, bone marrow failure?

Is this anemia regenerative or nonregenerative?

What additional tests should be performed?

Jezabel

10 year old, FS, Mixed breed. Hit by car at 6 months of age. Referred for a diagnosis of aplastic anemia.

Thin body condition; Pale MM; Unremarkable physical examination.

**Jezabel**
**Complete Blood Count**

| Parameter | Value | Reference Range |
|---|---|---|
| RBC | 4.0 x $10^6$ /µl | 5-8 x $10^6$ /µl |
| Hematocrit | 16.9 % | 37-52 % |
| WBC | 20.5 x$10^3$/µl | 6-14 x$10^3$/µl |
| monocytes | 0.41 20-80 x $10^3$/µl | 0.13-1.15 x$10^3$/µl |
| lymphocytes | 5.12 20-80 x $10^3$/µl | 1.06-4.95 x$10^3$/µl |
| neutrophils | 14.5 20-80 x $10^3$/µl | 2.94-12.67 x$10^3$/µl |
| bands | 0.41 20-80 x $10^3$/µl | 0 x$10^3$/µl |
| reticulocytes | 7 x $10^3$/µl | 20-80 x $10^3$/µl |
| MCV | 57 fl | 63- 75 fl |
| MCH | 12.3 g/dl | 13-18 pg |
| nRBC | 3/100 | 0% |

**Jezabel**
**Biochemical Profile**

| Parameter | Value | Reference Range |
|---|---|---|
| Total Protein | 5.0 g/dl | 5.4-7.8 g/dl |
| Albumen | 2.5 g/dl | 2.3-4.3 g/dl |
| Globulin | 2.5 g/dl | 2.5-5.5 g/dl |
| Glucose | 120 mg/dl | 65-140 mg/dl |
| Total Bilirubin | 0.4 mg/dl | 0.1-0.6 mg/dl |
| Alanine amino transferase | 27 IU/ml | 5-75 IU/ml |
| Sodium | 145 mEq/L | 139-154 mEq/L |
| Potassium | 4.8 mEq/L | 3.5-5.5 mEq/L |
| Creatinine | 1.0 mg/dl | 0.5-1.6 mg/dl |
| Blood urea nitrogen | 40 mg/dl | 8-25 mg/dl |
| Phosphorus | 3.2 mg/dl | 2.6-6.0 mg/dl |

Urinalysis

1.034 specific gravity

pH = 7.5

dipstick = trace bili

WBC = 0-1/hpf

RBC = 1-2/hpf

few struvite crystals

Is this anemia hemolytic, blood loss, bone marrow failure?

Is this anemia regenerative or nonregenerative?

What additional tests should be performed?

Comet

Guide dog, 10 yr MC Lab. Previously healthy. Bad ears and aural hematoma.

Overweight, BCS7/9. Moderate yeast otitis, aural hematoma AS. Pretreatment blood tests.

**Comet**
**Complete Blood Count**

| Parameter | Value | Reference Range |
|---|---|---|
| RBC | 5.3 x $10^6$ /µl | 5-8 x $10^6$ /µl |
| Hematocrit | 33.9 % | 37-52 % |
| WBC | 24.5 x$10^3$/µl | 6-14 x$10^3$/µl |
| monocytes | 0.49 x$10^3$/µl | 0.13-1.15 x$10^3$/µl |
| lymphocytes | 4.9 x$10^3$/µl | 1.06-4.95 x$10^3$/µl |
| neutrophils | 18.6 x$10^3$/µl | 2.94-12.67 x$10^3$/µl |
| bands | 0.49 x$10^3$/µl | 0 x$10^3$/µl |
| reticulocytes | 150 x$10^3$/µl | 20-80 x $10^3$/µl |
| MCV | 78 | 63- 75 fl |
| MCH | 15 | 13-18 pg |
| MCHC | 35 | 30-38 g/dl |

**Comet**
**Biochemical Profile**

| Parameter | Value | Reference Range |
|---|---|---|
| Total Protein | 5.8 g/dl | 5.4-7.8 g/dl |
| Albumin | 2.9 g/dl | 2.3-4.3 g/dl |
| Globulin | 2.9 g/dl | 2.5-5.5 g/dl |
| Glucose | 120 mg/dl | 65-140 mg/dl |
| Total Bilirubin | 0.2 mg/dl | 0.1-0.6 mg/dl |
| Alanine amino transferase | 27 IU/ml | 5-75 IU/ml |
| Sodium | 149 mEq/L | 139-154 mEq/L |
| Potassium | 4.8 mEq/L | 3.5-5.5 mEq/L |
| Creatinine | 1.0 mg/dl | 0.5-1.6 mg/dl |
| Blood urea nitrogen | 15 mg/dl | 8-25 mg/dl |

Urinalysis

1.034 specific gravity

pH = 7.5

Bilirubin = trace to 1+

Few struvite crystals

1-2 WBC/ hpf

3-5 RBC/ hpf

Postoperative course

Excessive bleeding from hematoma repair; Required transfusion; Treated with cephalexin

Is this anemia hemolytic, blood loss, bone marrow failure?

Is this anemia regenerative or nonregenerative?

What additional tests should be performed?

Lady

1 year old, FS, Mixed breed dog

Red urine and vomiting for 1 day; 3 previous episodes of red urine and anemia; No travel history.

Pale pink MM; Lethargic; Unremarkable physical examination

**Lady**
**Complete Blood Count**

| Parameter | Value | Reference Range |
|---|---|---|
| RBC | 3.1 x $10^6$ /µl | 5-8 x $10^6$ /µl |
| Hematocrit | 25.6% | 37-52 % |
| Hemoglobin | 8.4 g/dl | 12-18 gm/dl |
| WBC | 34 x$10^3$/µl | 6-14 x$10^3$/µl |
| monocytes | 2.0 x$10^3$/µl | 0.13-1.15 x$10^3$/µl |
| lymphocytes | 0.3 x$10^3$/µl | 1.06-4.95 x$10^3$/µl |
| neutrophils | 25.5 x$10^3$/µl | 2.94-12.67 x$10^3$/µl |
| bands | 2.0 x$10^3$/µl | 0 x$10^3$/µl |
| reticulocytes | 372 x$10^3$/µl | 20-80 x $10^3$/µl |
| MCV | 83 fl | 63- 75 fl |
| MCH | 14 pg | 13-18 pg |
| nRBC | 3/100 | 0% |

**Lady**
**Biochemical Profile**

| Parameter | Value | Reference Range |
|---|---|---|
| Total Protein | 8.0 g/dl | 5.4-7.8 g/dl |
| Albumen | 5.6 g/dl | 2.3-4.3 g/dl |
| Globulin | 2.4 g/dl | 2.5-5.5 g/dl |
| Glucose | 72 mg/dl | 65-140 mg/dl |
| Total Bilirubin | 1.2 mg/dl | 0.1-0.6 mg/dl |
| Alanine amino transferase | 80 IU/ml | 5-75 IU/ml |
| Sodium | 148 mEq/L | 139-154 mEq/L |
| Potassium | 5.5 mEq/L | 3.5-5.5 mEq/L |
| Creatinine | 0.8 mg/dl | 0.5-1.6 mg/dl |
| Blood urea nitrogen | 23 mg/dl | 8-25 mg/dl |
| *hemolyzed serum | | |

<u>Urinalysis</u>

Color = port wine

Specific gravity = 1.050

4+ protein

4+ hemoglobin

4+ bilirubin

0-1 RBC/hpf

0-1 WBC/hpf

Is this anemia hemolytic, blood loss, bone marrow failure?

Is this anemia regenerative or nonregenerative?

What additional tests should be performed?

Theo

6 yr FS Welsh Terrier, vaccinated in March. In April PCV = 10%. Bone marrow aspirate found erythroid hypoplasia. Treated with prednisone, amoxicillin/clavulanic acid, anabolic steroids and two transfusions. Referred to AMC in May.

Pale pink MM; CRT 1s; No fever; Weak.

**Theo**
**Complete Blood Count**

| Parameter | Value | Reference Range |
|---|---|---|
| RBC | 3.1 x $10^6$ /µl | 5-8 x $10^6$ /µl |
| Hematocrit | 20.2 % | 37-52 % |
| WBC | 11.4 x$10^3$/µl | 6-14 x$10^3$/µl |
| monocytes | 0.23 x$10^3$/µl | 0.13-1.15 x$10^3$/µl |
| lymphocytes | 1.8 | 1.06-4.95 x$10^3$/µl |
| neutrophils | 9.12 | 2.94-12.67 x$10^3$/µl |
| bands | 0.23 | 0 x$10^3$/µl |
| reticulocytes | 1.0 | 20-80 x $10^3$/µl |
| MCV | 63 | 63- 75 fl |
| MCH | 15.7 | 13-18 pg |
| MCHC | 32.1 | 30-38 g/dl |

**Theo**
**Biochemical Profile**

| Parameter | Value | Reference Range |
|---|---|---|
| Total Protein | 5.8 g/dl | 5.4-7.8 g/dl |
| Albumen | 2.9 g/dl | 2.3-4.3 g/dl |
| Globulin | 2.9 g/dl | 2.5-5.5 g/dl |
| Glucose | 120 mg/dl | 65-140 mg/dl |
| Total Bilirubin | 0.2 mg/dl | 0.1-0.6 mg/dl |
| Alanine amino transferase | 27 IU/ml | 5-75 IU/ml |
| Sodium | 149 mEq/L | 139-154 mEq/L |
| Potassium | 4.8 mEq/L | 3.5-5.5 mEq/L |
| Creatinine | 1.0 mg/dl | 0.5-1.6 mg/dl |
| Blood urea nitrogen | 15 mg/dl | 8-25 mg/dl |
| | | |

Urinalysis

1.036 specific gravity

pH = 6.5

dipstick = negative

WBC = 2-4/hpf

RBC = 2-4/hpf

Is this anemia hemolytic, blood loss, bone marrow failure?

Is this anemia regenerative or nonregenerative?

What additional tests should be performed?

Pinkie

7y FS Pitbull. Rescued from Georgia 5 years ago. Vaccinated 2 years ago. Goes to Connecticut on the weekends. 2 weeks ago, PU/PD. 1 week ago lethargic. 4 days ago vomited 1x. 2 days of discolored urine and feces.

Physical examination. Icteric, pale. No petechiae. BCS 6/9. Abdominal discomfort with organomegaly.

| | 12/25/16# |
|---|---|
| Hct | 36.7 |
| Hb | 12.1 |
| MCV | 73 |
| MCHC | 33 |
| Reticulocytes | 160K |
| WBC | 4.4 |
| Neutrophils | 2.9 |
| Bands | 44 |
| Lymphocytes | 1.2 |
| nRBC | 28 |
| Platelets | 130 |

#stomatospherocytes

## Chemistry panel 12/25/16

| | | | |
|---|---|---|---|
| Glucose | 99 | Total protein | 5.5 |
| BUN | 13 | Albumin | 2.9 |
| Creatinine | 0.6 | Globulin | 2.6 |
| SDMA | 23 | ALP | 284 |
| Phosphorus | 3.3 | ALT | 84 |
| Calcium | 9.0 | AST | 33 |
| Sodium | 146 | Total bilirubin | 3.0 |
| Potassium | 4.1 | Cholesterol | 112 |
| Chloride | 106 | Spec cPL | 51 |

## Urinalysis (cystocentesis) 12/25/16

| Dipstick | | Sediment | |
|---|---|---|---|
| Color | Orange | WBC | none |
| Clarity | Clear | RBC | none |
| Specific Gr | 1.045 | Bacteria | none |
| pH | 7.5 | Epithelial cells | none |
| Protein | 2+ | Mucus | none |
| Glucose | negative | Casts | none |
| Ketones | negative | Crystals | none |
| Blood | 3+ | | |

Is this anemia hemolytic, blood loss, bone marrow failure?

Is this anemia regenerative or nonregenerative?

What additional tests should be performed?

# FELINE LOW GRADE ALIMENTARY LYMPHOMA

## DISEASE EVOLUTION

In the feline leukemia virus era which occurred prior to the mid 1980's, most lymphoma was found in young cats and involved the cranial mediastinum. With the advent of FeLV testing and vaccination programs, gastrointestinal lymphoma has become the most common form of feline lymphoma. Around 2000, several research publications identified a cluster of lymphoma in the small intestine composed of small lymphocytes infiltrating the intestinal wall. This lymphoma was slowly progressive and minimal treatment appeared to result in prolonged survival.

## LOW GRADE ALIMENTARY LYMPHOMA (LGAL)

Multiple terms have been used to describe LGAL:

- Small cell GI lymphoma
- Mucosal [T cell] lymphoma
- Intestinal small cell lymphoma
- Intestinal T cell lymphoma
- Epitheliotrophic small T cell lymphoma
- Enteropathy associated T cell lymphoma

Based on a recent publication from Japan, LGAL currently appears to be the most common form of feline lymphoma.

## Clinical presentation

The typical cat with LGAL has a median age of 12y and there may be a male prediction for the disease. The clinical signs of LGAL are vague and nonspecific. The clinical signs of LGAL also mimic signs of common feline diseases such a chronic kidney disease, hyperthryroidism, pancreatitis and inflammatory bowel disease.

| Clinical signs: 56 cats low grade alimentary lymphoma | Pope 2015 |
|---|---|
| Vomiting | 24% |
| Weight loss | 21% |
| Anorexia | 20% |
| Diarrhea | 10% |
| Lethargy | 9% |
| Increased LEs | 5% |

Physical examination will reveal weight loss and possibly thick GI loops and abdominal mass, commonly enlarged lymph nodes.

## Diagnostic Evaluation

The purpose of the diagnostic evaluation of a cat suspected to have LGAL is three fold:

1. Rule out common causes of clinical signs
    a. Intestinal parasites
    b. CKD
    c. Hyperthyroidism
    d. Pancreatic disease
2. Provide supporting evidence of a diagnosis of LGAL
3. Obtain a definitive diagnosis of LGAL

## Components of a diagnostic evaluation

1. CBC
2. Biochemical profile
3. Urinalysis
4. T4
5. Fecal
6. Trypsin like immunoreactivity
7. Feline pancreatic lipase
8. B12, folate

9. Retroviral testing
10. Diagnostic imaging
11. Histopathology
    a. PARR

**OBTAINING A BIOPSY**

Tissue samples adequate to diagnose LGAL can be obtained via endoscopy, laparoscopy or exploratory laparotomy. The key to making a diagnosis is to sample as many segments of the bowel as possible since LGAL is not uniformly distributed throughout the intestine. Most common locations are jejunum and ileum. The jejunum cannot be reached via endoscopy. Thus if endoscopy is used to obtain biopsies, both upper and lower intestine should be biopsied. While veterinarians worry about post-operative complications from intestinal biopsies in cats with intestinal neoplasia, reports of complications are uncommon.

**INTERPRETING THE BIOPSY**

In some cats, routine H&E staining will be sufficient to differentiate inflammatory bowel disease from LGAL. In others, the pathologist will recommend additional testing using PARR – PCR for antigen receptor rearrangement. PARR does not determine phenotype, but instead identifies clonal rearrangements of the T cell receptor gamma gene or the immunoglobulin heavy chain gene. Clonal or oligoclonal rearrangements of the T cell receptor gamma gene are found in LGAL, but not in inflammatory bowel disease. The utility of flow cytometry for the diagnosis of lymphoma in cats is less well defined than in dogs.

**TREATMENT OF LGAL**

The goals of treatment are twofold.

1. Treat the lymphoma
2. Manage associated conditions such as pancreatitis, microbiome changes, hypocobalaminemia, hypereosinophillia
3.

The optimal treatment for LGAL is unknown but by convention, prednis(ol)one and chlorambucil are administered. Current wisdom on treatment suggests a 12 month course of therapy. If the LGAL appears to be in remission, then a drug holiday is prescribed with careful monitoring and treatment again at the time of relapse.

Chlorambucil is traditional chemotherapy drug of the alkylating agent class. Administration to cats has been associated with bone marrow suppression, including irreversible thrombocytopenia, Fanconi syndrome and myoclonus.

Glucocorticoid therapy has been associated with an increased risk of infection, diabetes and congestive heart failure. Compounded cholorambucil is not recommended unless no other treatment options are available.

Optimal dosing of chlorambucil and prednisone have not been studied. Common doses of chlorambucil include 1.4 mg/kg given q 14 days or divided over 2-3 days per week. A dose of 20 mg/m$^2$ q 14 days has also been recommended. A CBC should be monitored every 4-6 weeks while the cat is being treated with chlorambucil with particular attention paid to the platelet count. Biochemical profile should be monitored approximately every 3 months unless the clinical condition requires more frequent monitoring. The author monitors B12 and abdominal ultrasound every 6 months for monitor response to therapy and define remission.

## REMISSION AND SURVIVAL

Defining remission is difficult in LGAL and is based on resolution of clinical signs, weight gain and resolution of intestinal thickening or lymphadenopathy based on palpation or ultrasound. Cats that have resolution of clinical signs are the cats most likely to have prolonged survival. Reports of median survival typically exceed 2 years.

## MANAGEMENT OF RELAPSE

Because common feline diseases can mimic relapse of LGAL, recognition of relapse can be complicated. When clinical signs recur or diagnostic testing reveal relapse, chemotherapy is reinstituted. Many cats on a drug holiday will respond to chlorambucil a second time. Oral cyclophosphamide and lomustine have also been used in relapsed cases. The ultimate cause of death in cats diagnosed with LGAL is more often than not a second tumor, another chronic feline disease and much less often LGAL.

# FIVE CHEMOTHERAPY DRUGS I CAN'T LIVE WITHOUT AND YOU SHOULDN'T EITHER

The important cancers of dogs and cats treated with chemotherapy include lymphoma, mast cell tumors and osteosarcoma. In order to treat these tumors, the small animal practitioner needs a pharmacy including chemotherapy agents known to be efficacious against these tumors. This presentation will focus on commonly used chemotherapy agents and their successful use in dogs and cats. Successful use requires not only the selection of the appropriate drug, but monitoring based on the adverse event profile of the drug and an understanding of the drug's mechanism of action. Clinical practices to ensure patient and medical staff safety will also be discussed.

## WHAT DRUGS MUST I ABSOLUTELY HAVE IN MY PHARMACY?

The practice of veterinary oncology requires the use of drugs effective for treatment of lymphoma, mast cell tumors and osteosarcoma. Some drugs will be used as a single agent and they may also be combined to create a multiagent protocol. The drugs I would choose include doxorubicin, cyclophosphamide, chlorambucil, vincristine, carboplatin, toceranib phosphate and vinblastine.

## GENERAL GUIDELINE FOR CHEMOTHERAPY DRUG USE

All chemotherapy drugs have the potential to cause hematologic toxicity, some more than others and some patients may be extremely sensitive to a particular drug. To monitor for hematologic toxicity, a CBC is performed immediately before each treatment. If the neutrophil count is less than 2000/µl, chemotherapy administration is delayed. Other blood tests performed prior to chemotherapy administration are based on a drug's adverse event profile. To mitigate gastrointestinal toxicity, prescriptions for nausea and diarrhea medications are dispensed and owners instructed to give the medications at the first sign of toxicity. Exposure to chemotherapy agents can impact human health, chemotherapy drugs should be diluted and reconstituted in a biological safety cabinet using closed transfer devices and personal protective equipment in accordance with laws and safety guidelines.

## DOXORUBICIN

Doxorubicin's broad antineoplastic profile puts it on my list of important chemotherapy drugs. Doxorubicin is effective in treating both lymphoma and osteosarcoma which are important tumors in dogs and cats. In dogs, it can induce remission and prolong survival when used as a single agent. In addition to lymphoma and osteosarcoma, it is also effective against hemangiosarcoma, mammary gland cancer and thyroid cancer. Doxorubicin is a component of the VAC chemotherapy protocol for sarcomas. Administration of doxorubicin requires placement of an IV catheter to prevent extravasation which is an adverse event to be avoided at all costs. Administration of doxorubicin should always be observed by the veterinarian or technician in case the infusion requires abrupt discontinuation to prevent extravasation. Infusion over 30 minutes (as compared to a rapid bolus infusion) decreases adverse events since the peak blood concentration [$C_{max}$] is lower with a 30 minute infusion and toxicity is related to $C_{max}$. Prophylactic administration of maropitant for 4-5 days after doxorubicin infusion decreases the occurrence of both vomiting and diarrhea. Should extravasation occur, the infusion should immediately be discontinued, the catheter left in place and any drug in the subcutaneous space aspirated. Cold compresses should be applied. Intravenously administered dexrazoxane at 10x the doxorubicin

dose should then be infused through a separate catheter within 6 hours of extravasation to prevent serious tissue ulceration. In some cases multiple doses of dxrazoxane have been administered. Exact dosing schedule is unknown.

**VINCRISTINE**

Vincristine's utility in lymphoma and as a single agent against transmissible venereal tumor plus its ease of administration puts it on my list of important chemotherapy drugs. It is a component of most multiagent chemotherapy protocols for lymphoma in both dogs and cats. Vincristine is a component of the VAC chemotherapy protocol for sarcomas and is also used as a component of initial therapy for immune mediated thrombocytopenia. Because of the small volume administered [<1ml in dogs and <0.3 ml in cats] placement of an intravenous catheter is not necessary; vincristine can be infused through a "butterfly" infusion set as a rapid bolus. Keep in mind vincristine is a vesicant and should not be extravasated. Should extravasation occur, the infusion should immediately be discontinued, the catheter left in place and any drug in the subcutaneous space aspirated. Warm compresses should be applied. Treatment with hyaluronidase helps to ameliorate cutaneous ulcer formation. Gastrointestinal toxicity is most common with vincristine, but is typically mild and responds to maropitant or metronidazole.

**CYCLOPHOSPHAMIDE**

Because cyclophosphamide is available in both 25 and 50 mg tablets and an injectable solution and can be used to treat lymphoma, mast cell tumors and is frequently used as rescue therapy for feline relapsed small cell gastrointestinal lymphoma, it makes my list of important chemotherapy drugs. Cyclophosphamide is a component of the VAC chemotherapy protocol for sarcomas. Cyclophosphamide is not a vesicant and it can safely be administered subcutaneously, intravenously through a butterfly infusion set as a rapid bolus or orally. One of the metabolites of cyclophosphamide can cause a sterile cystitis in dogs if they are not allowed to urinate frequently for the first 24 hours following administration. To promote urination, furosemide [2.2 mg/kg IV] can be administered following cyclophosphamide and through the same catheter. Sterile cystitis from cyclophosphamide occurs rarely in cats. If cystitis occurs, the diagnosis of sterile cystitis is one of exclusion. Urinalysis, urine culture, radiography or ultrasonography are necessary to rule out bacterial cystitis and urolithiasis. Anti-inflammatory drugs may improve the dogs comfort, but complete resolution requires weeks. When dispensed to owners for home administration, owners should not crush or dissolve tablets in water, should wear gloves and wash their hands after administration. Gastrointestinal toxicity is typically mild and responds to maropitant or metronidazole. Neutropenia usually occurs within 5-7 days after administration and resolves within a week.

**CHLORAMBUCIL**

Because of its ease of administration, limited adverse event profile and utility in treating feline gastrointestinal small cell lymphoma, chlorambucil makes my list of important chemotherapy drugs. Closely related to cyclophosphamide, chlorambucil has also been used to treat mast cell tumors, indolent lymphoma in the dog and as an immunosuppressive agent in cats. This drug is typically dispensed for home administration. When dispensed to owners for home administration, owners should not crush or dissolve tablets in water, should wear gloves and wash their hands after administration. Multiple dose regimens have been recommended. Some regimens use pulse therapy every 7-14 days; others use continuous administration. Because the adverse event profile is limited, cats with stable medical conditions need a CBC every 4-6 weeks and a chemistry profile approximately every 12 weeks. If neutropenia or thrombocytopenia occur, chlorambucil should be immediately discontinued as permanent bone marrow damage can occur.

## CARBOPLATIN

Although several chemotherapy agents have shown equal efficacy in treating canine osteosarcoma, carboplatin, used as a single agent has the lowest adverse sent profile. In addition, it can be administered as a 20-30 minute infusion, is not a vesicant and does not require pre- and post-administration fluid diuresis. Some oncologists administer this drug as an intracavitary infusion for malignant effusions. Thus, it makes my list of important chemotherapy agents in veterinary oncology. The major adverse event is neutropenia. The nadir in dogs is approximately 14 days following administration and in cats 14-25 days. Unlike cis-platin, carboplatin is not nephrotoxic, but carboplatin is excreted by the kidneys and will have increased toxicity in pet with decreased renal function.

## TOCERANIB PHOSPHATE - PALLADIA®

Also known as a small molecule inhibitor, tyrosine kinase inhibitor or a signal transduction inhibitor, toceranib phosphate is the newest drug on my list. A related drug mastinib [Kinavet® or Masivet ®] is not fully approved in the United States and consequently, oncologists in the USA, have limited experience with that drug as they do with toceranib. Toceranib is approved for use in dogs with mast cell tumors, but oncologists are using it in cats and tumors other than mast cell tumors, such as carcinomas. It has rapidly become an important drug in veterinary oncology. Most veterinary oncologists are successfully using toceranib at approximately 2.7 mg/kg PO every other day which is less than the label dose. When dispensed to owners for home administration, owners should not crush or dissolve tablets in water, should wear gloves and wash their hands after administration. Because toceranib is orally administered on a continuous basis, it should be discontinued at the first sign of an adverse event such as loss of appetite, vomiting or diarrhea. Toceranib can cause a mild neutropenia, but treatment is not typically delayed because of neutropenia and over time, the count will increase. Toceranib can cause a protein losing nephropathy and hypertension. Intermittent monitoring of urine protein to creatinine ratio and blood pressure are warranted. If adverse events occur, dosage can be decreased to 2.4 mg/kg every third day.

## VINBLASTINE

I know I said five, but I just need one more. Related to vincristine and having a similar mechanism of action, vinblastine is commonly used in the treatment of canine mast cell tumors. Another reason it makes my list of important chemotherapy drugs is it can be used in place of vincristine in lymphoma protocols if vincristine toxicity is unacceptable. Administration does not require placement of an intravenous catheter; it can be infused through a “butterfly” infusion set as a rapid bolus. Keep in mind vinblastine is a vesicant and should not be extravasated. The major adverse event with vinblastine is neutropenia, which occurs more often and to a greater degree than with vincristine. Gastrointestinal toxicity is typically mild and responds to maropitant or metronidazole.

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# When should the vet say YES to immunohistochemistry? Active learning handout

**TABLE 17-2 Markers Used for the Differential Diagnosis of Major Tumor Categories**

| Tumor Tissue | Markers |
|---|---|
| Adrenal | Cortex: Melan-A, inhibin-alpha, calretinin<br>Medulla: PGP 9.5, chromogranins, synaptophysin |
| Endocrine tumors (generic) | Chromogranin A, synaptophysin, PGP 9.5, neuron specific enolase (NSE), S100 |
| Epithelial vs. mesenchymal | Cytokeratins (epithelial), vimentin (mesenchymal), E-cadherin (epithelium), p63 (basal cells, myoepithelium) |
| Leukocytic | CD45 (panleukocytic), CD18 (with emphasis in histiocytic), CD11d (dendritic cells), E-cadherin (Langerhan's cells), lysozyme (histiocytes), myeloid histiocytic marker (histiocytes, myeloid cells) |
| Liver | Hep Par 1 (hepatocytes), cytokeratin 7 (bile duct epithelium) |
| Lymphoid | CD3 (T-cell), CD79a and CD20 (B-cell), CD45 and CD18 (panleukocytic), MUM1 (plasma cells) |
| Mast cell tumors | CD117, tryptase, OCT3/4 |
| Melanocytic tumors | Melan A, S100, NSE |
| Muscle differentiation | Actin muscle (all muscle), smooth muscle actin (smooth muscle), myoglobin (skeletal muscle), actin sarcomeric (striated muscle), desmin (all muscle), calponin (smooth muscle, myofibroblast, myoepithelium) |
| Neurogenic tumors | S100 (neurons, glial cells), neurofilament (neurons), GFAP (glial cells), glut1, nerve growth factor receptor (perineural cells) |
| Pancreas (endocrine) | Insulin, glucagon, somatostatin, synaptophysin, PGP 9.5, chromogranin A |
| Squamous vs. adenocarcinoma | Squamous cell carcinoma (CK5, p63); adenocarcinoma (CK7) |
| Testis and ovary | Sex cord–stromal tumors (inhibin-α, NSE); germ-cell tumors (calretinin, KIT, PGP 9.5) |
| Thyroid | Thyroglobulin (follicular cells), calcitonin (medulla, C-cells), TTF1 (follicles and medulla) |
| Urinary tumors | Uroplakin III, cytokeratin 7, COX-2, COX-1 |
| Vascular tumors (endothelium) | Factor VIII–related antigen, CD31 |

*Raskin and Meyers Canine and Feline Cytology 2nd, 2010 ed. P 409*

## *Questions to be answered during the presentation*

## Tucker – Havanese with intraocular mass

1. What tests are indicated before treatment is initiated?

_____ _____ _____ _____ _____

2. What is/are the next step(s)?

_____ _____ _____

3. What tumors should be included on the DDx based on the biopsy result?

_____ _____ _____ _____ _____

4. Given the list of DDx, is it important to know the exact histology of the tumor?
    1. Yes or No?
    2. Why?

5. Write down the expected median survival for each of the Ddx and a general comment about the treatment of each.

_____ _____ _____ _____ _____

6. What IHC stains should be requested for each of the DDx in this case?

_____ _____ _____ _____ _____

7. What is the diagnosis in this patient? _____

## Madison – Soft coated wheaten terrier with a splenic mass

1. What would you recommend as the next diagnostic steps in this case?

_____ _____ _____ _____ _____

2. What tumors should be included on the DDx based on the biopsy result?

_____ _____ _____ _____ _____

3. What IHC stains should be requested for each of the DDx in this case?

_____ _____ _____ _____ _____

4. Given the list of DDx, is it important to know the exact histology of the tumor?
    a. Yes or No?
    b. Why?

5. Write down the expected median survival for each of the Ddx and a general comment about the treatment of each.

_____ _____ _____ _____ _____

## Muchacho – mixed breed dog with liver masses

1. What tumors should be included on the DDx based on the biopsy result?

_____ _____
_____

_____ _____
_____

2. Given the list of DDx, is it important to know the exact histology of the tumor?
    a. Yes or No?
    b. Why?

3. Write down the expected median survival for each of the Ddx and a general comment about the treatment of each.

_____ _____
_____

_____ _____
_____

4. What IHC stains should be requested for each of the DDx in this case?

_____ _____
_____

_____ _____
_____

5. What is the diagnosis in this patient? _____

# MANAGING CHEMOTHERAPY TOXICITY

The goal of treating a pet with chemotherapy is to prolong a good quality of life while decreasing tumor related symptoms. This is challenging for the veterinarian because of the wide range of adverse effects attributed to chemotherapy drugs. Some of these adverse effects can be prevented or at least minimized by interventions at the time of chemotherapy administration. Practicing these preventive measures will help to make chemotherapy safe, effective and successful. In other cases, despite our best efforts to prevent toxicity, it occurs. In these cases, it is important to respond appropriately and quickly to minimize the risk to the patient and the cost to the owner. Minimizing the risk requires well trained front desk and technical staffs, and knowledge of the expected effect of the drugs to recognize and respond to changes in a chemotherapy patient's clinical status.

## COMMON CHEMOTHERAPY TOXICITIES

Chemotherapy toxicity can be divided into 3 main categories:

1. Neutropenia, which may lead to fever, infection and sepsis.
2. Gastrointestinal toxicity, inappetence, nausea, vomiting or diarrhea
3. Other toxicities. These are specific to each drug and require an understanding of the idiosyncrasies of each agent being administered. They include doxorubicin cardiac toxicity, CCNU hepatotoxicity, cyclophosphamide induced sterile hemorrhagic cystitis, to name a few.

## PREVENTING CHEMOTHERAPY TOXICITY

The old adage, "An ounce of prevention is worth a pound of cure" still holds true today for chemotherapy toxicity. It is essential to monitor and prevent toxicity since once some toxicities occur, there is no successful treatment and they are rapidly fatal. Doxorubicin cardiotoxicity and CCNU hepatotoxicity are examples of this. Preventing toxicity also helps to maintain a good quality of life for the pet. Maintaining a good quality of life during chemotherapy is essential for nearly every pet owner. If the veterinarian allows chemotherapy to cause a poor quality of life for the pet, owners will often discontinue therapy despite tumor remission. Finally, treatment of toxicity can be very expensive for the pet owner. The unanticipated expense of treating toxicity, coupled with the expense of chemotherapy is another reason pet owners discontinue treatment or euthanize the pet despite tumor remission.

One method to minimize the risk of neutropenia in chemotherapy patients is to carefully adhere to treatment protocols and dosages of chemotherapy drugs. Pets should be weighed before each treatment to allow dose adjustments for increased or decreased weight. Calculations should be checked and doubled checked to prevent a math error from causing an overdosage. Technical staff should also double check the volume of drug administered to ensure proper dosing. Prior to administration of any chemotherapy drug, a CBC should be obtained. If the neutrophil count is less than 1500 neutrophils/μl, chemotherapy should be delayed until the count rises above this level. If the neutrophil count is repeatedly low following administration of a particular drug, the dosage of that drug should be decreased by 10-25%. Preventing infection in neutropenic chemotherapy patients also relies on adherence to aseptic technique during drug administration. If the neutrophil count is adequate, but the pet is not feeling well or has a fever, chemotherapy should be delayed and the cause of the illness investigated.

Below is a table outlining some interventions designed to prevent various chemotherapy toxicities from occurring.

| Drug | Potential Toxicity | Prevention intervention |
|---|---|---|
| L-asparaginase | Hypersensitivity | Repeat administrations, administered diphenhydramine &glucocorticoids |
| Multiple drugs | Vomiting, nausea | Administer maropitant with chemotherapy, dispense tablets to administer at home |
| Cyclophosphamide | Sterile hemorrhagic cystitis | Give 2.2 mg/kg IV of furosemide with cyclophosphamide |
| Cis-platin | Nephrotoxicity | Administer 0.9% NaCl fluid diuresis, prevent vomiting with antiemetics |
| CCNU | Hepatotoxicity | Routinely monitor liver enzymes. Discontinue if elevated. |
| Multiple drugs | Infection | Wash hands. Aseptic technique. Monitor CBC prior to chemotherapy. Delay chemotherapy if cytopenic. |
| Doxorubicin | Cardiac toxicity | Administer as slow infusion. Monitor cardiac function via echocardiography. |

## RESPONDING TO CHEMOTHERAPY TOXICITY

**The first responders in the case of chemotherapy toxicity are the front desk staff who receive a telephone call 3-10 days following chemotherapy administration from a worried owner. Some of these calls can be prevented if the owners and front desk staff are given some simple instructions.**

1. 1 episode of diarrhea or 1 episode of vomiting does not require a telephone call.
2. Anorexia of > 24 hours duration requires a telephone call.
3. Bloody urine, frequent urinations or staining to urinate; severe vomiting, vomiting with blood or the inability to keep any food or water down; profuse diarrhea or bloody diarrhea requires a telephone call to schedule a clinic visit that day.
4. A visit to the emergency room should be made if the pet cannot walk, is extremely listless or has a rectal temperature above 103.5.
5. Swelling, pain or licking at the site of chemotherapy administration requires a visit within 24 hours.

## HISTORY AND PHYSICAL EXAMINATION OF THE SICK CHEMOTHERAPY PATIENT

The history should be reviewed for the most recent drug administration and the toxicity of that drug reviewed. The dosage administered should be checked to ensure toxicity is not due to over dosage. A complete physical examination, including body temperature should be performed. Special attention should be paid to injection/catheter sites, incisions, lymph nodes, abdominal pain, rectal examination and lung sounds since these sites may be site of infection.

Laboratory testing is critical to appropriate management of chemotherapy toxicity. A CBC should always be performed to determine if neutropenia should be addressed. If the pet has a fever, a urinalysis and urine culture should be performed since infection is common in the bladder, especially in pets on prednisone therapy. A negative urine culture in the presence of

lower urinary tract signs following administration of cyclophosphamide suggests sterile hemorrhagic cystitis. If there are any signs of respiratory tract infection, a thoracic radiograph is indicated since pneumonia often occurs in association with chemotherapy. For those pets with diarrhea, a fecal cytology may reveal *Clostridium* overgrowth or the presence of *Campylobacter*. Diarrhea with fever suggests a systemic infection and fecal culture should be considered. Any swelling, enlarged lymph node, incisional discharge or new mass should be aspirated and submitted for cytology and culture.

When faced with a sick chemotherapy patient, it is easy to focus on the chemotherapy agent and forget basic principles of patient management. The basic principles of managing a pet with chemotherapy toxicity are the same as managing any sick pet. Aseptic technique should be used when performing any invasive procedure such as catheter placement. Vomiting pets should be made NPO and treated with antiemetics. When vomiting resolves, a bland diet should be instituted. Dehydrated pets need fluid replacement. Hypoglycemic pets require glucose supplementation. Pets with electrolyte abnormalities require electrolyte supplementation. Anemic and bleeding pets need an assessment of coagulation and appropriate treatment with blood products. Keeping these common principles in mind will resolve nearly all of the common chemotherapy complications.

## CHEMOTHERAPY SPECIFIC PATIENT MANAGEMENT

### Neutropenia

Antibiotic therapy is controversial in neutropenic chemotherapy patients. Those that are neutropenic, without fever, do not require antibiotic therapy, but antibiotic therapy should be considered in those with profound neutropenia, < 500 neutrophils/μl. All pets with fever or with evidence of infection, purulent discharge, radiographic pulmonary infiltrate, pyuria or cytological evidence of infection should be treated with antibiotics. Antibiotic treatment should be based on results of culture and sensitivity, but until that information is available, empiric therapy is indicated. In dogs, broad spectrum antibiotics such as potentiated sulfonamides, cephalosporins or penicillins should be considered. Enrofloxacin should be reserved for severe infections when indicated by sensitivity testing. Antibiotic therapy is more difficult in cats because of the side effects of appropriate antibiotics in cats. These include foaming and frothing from potentiated sulfonamides, anorexia, vomiting and diarrhea from penicillins and cephalosporins and blindness from enrofloxacin. Cofovecin does not have as broad a spectrum as the other antibiotics listed, but it makes up for that in convenience and can be used in neutropenic cats. Fortunately, cats seem to get fever and infection from chemotherapy much less frequently than dogs do.

### Extravasation

Chemotherapy extravasation is a situation requiring special care. Drugs known to cause skin sloughing following extravasation include: doxorubicin, vincristine vinblastine, nitrogen mustrard, mitoxantrone and actinomycin D. Swelling, pain or licking a previous site of chemotherapy administration should raise suspicion of an unrecognized extravasation if one of these drugs was the most recently administered drug.

If the extravasation is recognized at the time of drug administration, the infusion needle/catheter should be left in place and as much of the drug as possible should be aspirated. There are many recommendations but little scientific information on the management of drug extravasation. Local infusion of saline to dilute the drug has been recommended, as has the infusion of lidocaine alleviate the pain associated with extravasation. Cold compresses of the

extravasation site are recommended except in the case of vincristine extravasation (See paragraph below). The pet should be discharged with an E-collar to prevent self-mutilation. Some also recommend the topical application of Synotic® and Banamine® to the extravasation site.

Specific recommendations for vincristine extravasation include application of warm compresses for 15 minutes QID and local administration of 300 units of hyaluronidase at the extravasation site weekly until the tissues are healed.

Specific recommendations for doxorubicin extravasation include intravenous administration of dexrazoxane at 10 times the doxorubicin dosage. No other medications are recommended with dexrazoxane.

# PANCEATIC AND HEPATIC TUMORS: DIAGNOSIS AND MANAGEMENT

**ABSTRACT**
Pancreatic and hepatic tumors are uncommon tumors of the dog and cat. In general, tumors of these two organs are advanced at the time of diagnosis and carry a poor prognosis. This presentation will focus on one treatable pancreatic tumor: insulinoma and one treatable hepatic tumor: massive hepatocellular carcinoma. Treatment of insulinoma requires first a diagnosis of an insulin producing tumor and second management of hypoglycemia, using chemotherapy and other drugs to prevent seizures. If surgically resectable, dogs suffering from massive hepatocellular carcinoma can have a prolonged survival.

## PANCREATIC TUMORS

Pancreatic tumors of the dog and cat are uncommon and are derived from either the endocrine or exocrine cells of the pancreas. In cats, exocrine pancreatic carcinoma is the most common tumor of the pancreas, while β cell tumors (insulinoma) are most common in the dog.

### Clinical signs

Clinical signs of pancreatic tumors are typically vague: weight loss, vomiting and anorexia and not specific for either exocrine or endocrine tumors. Signs such as biliary obstruction, abdominal distension and effusion occur due to a space occupying mass. Endocrine pancreatic tumors may autonomously secrete hormones resulting in a paraneoplastic syndrome such as hypoglycemia from a β-cell tumor or insulinoma. Endocrine pancreatic tumor may simultaneously produce multiple hormones. Other disorders of the pancreas occurring concurrently include pancreatitis and exocrine pancreatic insufficiency.

### Exocrine pancreatic adenocarcinoma

Diagnosis of exocrine pancreatic adenocarcinoma is most often made in the late stages of the disease. There is no effective treatment other than surgical excision of the tumor. Because metastatic disease is typically widespread at the time of diagnosis, reported survival times are very short.

### Beta cell tumors - insulinoma

This tumor most frequently occurs in older, large breed dogs. Only a very few cases of insulinoma have been reported in cats. Hypoglycemia is a common presenting complaint. Differential diagnosis for hypoglycemia include:

Insulin excess
- Hepatic tumors
- GI tumors
- Beta cell tumors

Insulin increase
- Xylitol toxicity
- Insulin overdose

Glucose metabolism abnormalities
- Hepatic failure
- Hypoadrenocorticsm
- Sepsis

Lower motor neuron disease

Spurious hypoglycemia

| Clinical signs in 128 dogs with insulinoma (Goutal, JAAHA 2012) | #dogs | percent |
|---|---|---|
| Seizures | 128 | 63 |
| Weakness | 80 | 39 |
| Collapse | 65 | 32 |
| Posterior weakness | 52 | 25 |
| Ataxia | 38 | 19 |
| Muscle fasciculations | 36 | 18 |
| Depression, lethargy | 36 | 18 |
| Bizarre behavior | 28 | 14 |
| Polyphagia | 18 | 9 |
| PU/PD | 14 | 7 |
| Weight gain | 13 | 6 |

**Diagnostic testing**

Hypoglycemia (glucose **<**70 mg/dL or <3.9 mmol/L) raises the suspicion for insulinoma, but can also be seen with other disorders. Low fructosamine concentration (mean 202+/-31 µmol/L) has also been reported in dogs with insulinoma. Various ratios of insulin to glucose have been proposed as diagnostic tools for insulinoma, but all lack specificity. Most useful may be an inappropriately elevated insulin level with concurrent hypoglycemia. Ultrasound and CT scanning are useful in detecting the primary tumor and metastatic lesions.

**Surgical treatment**

Surgical excision is the treatment of choice for insulinoma. Because of the high rate of metastasis, liver, regional lymph nodes and any suspected metastatic lesions should be biopsied at the time of abdominal laparotomy. Depending on the dog's conformation and the location of the tumor, laparoscopic techniques may be used for insulinoma resection. Post operative complications include: pancreatitis, diabetes mellitus, exocrine pancreatic insufficiency.

**Medical treatment of insulinoma**

For dogs presenting with seizures due to hypoglycemia, medial therapy is directed at increasing the blood glucose while diagnostics testing is performed. Medical therapy of insulinoma is selected for dogs that do not undergo surgery either because of owner preference or comorbidity that precludes surgery. Dogs that have already undergone surgery, but have residual or recurrent tumor are also candidates for medical therapy. Three different classes of medical therapy may be used: dietary, glucocorticoids, chemotherapy agents and agents that suppress insulin secretion. In refractory cases, multiple therapies administered simultaneously may be required to control hypoglycemia.

| **Emergency therapy** | | | | |
|---|---|---|---|---|
| Class | Therapy | Route | Dose | frequency |
| Increase blood glucose | dextrose | IV | 5-10% to effect | Bolus followed by CRI |
| Induce insulin resistance | Dexamethasone | | 0.5 mg/kg | |
| Insulin inhibitor | Octeotide | SQ | 20-40 ug/kg | |
| Insulin inhibitor | Glucagon | IV | 5-12 ng/kg/min | |

| **Ongoing therapy** | | | | |
|---|---|---|---|---|
| Class | Therapy | Route | Dose | frequency |
| Dietary | Diets with complex carbohydrate, high fat/protein | PO | | 4-6 times daily |
| Induce insulin resistance | Prednisone | PO | 0.5-4 mg/kg | Q 12 hr |
| Inhibts insulin secretion | Diaoxide | PO | 5-40 mg/kg | Q 12 hr |
| Insulin inhibitor | Octeotide | SQ | 2-4 ug/kg | Q 8-12 hr |
| Destroy β-cells | Streptozotocin | IV infusion following saline diuresis | 375-400 mg/m2 < 15kg<br>500 mg/m2 >15kg | Every 2-3 weeks |
| Uknown | Palladia | PO | 2.7 mg/kg | Q 48 hr |

**Survival time in dogs with insulinoma**
Dogs with insulinoma managed surgically have a longer survival than those managed medically: in one study 381 days versus 74 days. Dogs with insulinoma can have prolonged survival times despite the presence of metastatic disease: in one study 20 months versus 6 months. Because survival time can be long with a combination of surgical and medical treatments, euthanasia is not necessary due to the presence of metastatic disease.

**HEPATIC TUMORS**
Metastatic tumors to the liver are far more common than primary hepatic tumors in dogs which comprise about1% of canine tumors. Metastatic disease to the liver is less common than primary hepatic tumors in the cat. Hepatic tumors can be classified into 4 major categories based on tissue of origin: hepatocellular, biliary, neuroendocirin and mesenchymal. In general, benign hepatic tumors such as the heptatic adenoma and hepatic cystadenoma of the cat carry a relative good prognosis. Malignant tumors of the liver are usually advanced by the time of diagnosis and there are few treatment options. The one malignant hepatic tumor which can have a good prognosis is the massive hepatocellular carcinoma of the dog. This tumor has a low metastatic rate and a low rate of recurrence following successful resection.

**Diagnostic Testing and Imaging**
Occasionally a liver mass can be identified with palpation, but more typically laboaotry abnormalities are identified. Most laboratory testing in dogs with hepatocellular carcinoma is nonspecific and suggests inflammation (leukocytosis and anemia) and hepatic disease (elevated liver enzymes). Further evaluation of physical examination or laboratory abnormalities with diagnostic imaging will identify hepatic parenchymal disease. If clinical suspicion is high for hepatic neoplasia, three view thoracic radiographs should be obtained.

**Surgical excision and outcome**
Liver lobe resection is the treatment of choice for solitary hepatic tumors. Intraoperative mortality is related to hemorrhage, vascular compromise of adjacent liver lobes, hypoglycemia and loss of hepatic function. A greater complication rate is seen in dogs with right sided tumors compared to left sided tumors due to the proximity of the caudal vena cava. Successful resection of massive hepatocellular carcinoma in dogs can result in prolonged survival compared to dogs not undergoing surgery (median survival >1460 days versus 270 days).

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# WHEN SHOULD THE VET SAY YES TO IMMUNOHISTOCHEMISTRY?

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An accurate diagnosis is critical to cancer patient management. Most often, the diagnosis of a tumor is made based on histopathologic examination of a biopsy specimen. Pathologists are trained to recognize the specific expected pattern and cell features of various tumors. Based on the location of the tumor and microscopic features, the pathologist creates a list of differential diagnoses and then narrows down the list to a final diagnosis, based on the appearance of the cells and stroma.

**WHEN DOES THE PATHOLOGIST RECOMMEND IHC?**

If the biopsy sample demonstrates overlapping features between more than one tumor type or if the tumor appears to be highly unusual for the tissue of origin, additional diagnostics can be helpful for differentiation and confirmation of the final diagnosis. Veterinary pathologist's histopathology reports frequently contain a recommendation for additional testing on tumors. In the past, stains like Giemsa were used to confirm a mast cell tumor diagnosis or Congo red O for the presence of amyloid. Today, pathologists are increasingly recommending immunohistochemistry (IHC) to confirm various tumor diagnoses.

**WHAT IS IHC?**

Immunohistochemistry is a very descriptive term. First, immune indicates an antigen-antibody reaction. The antibody used in IHC is selected to target a protein found in a specific tumor type. An example of the antigen-antibody reaction familiar to many veterinarians is the use of CD20 testing for B cell lymphoma in the dog. CD20 occurs only on B lymphocytes and not T lymphocytes. Histo indicates the test is performed on tissue rather than a direct smear of tumor cells or a blood film. Finally, chemistry specifies an enzymatic reaction catalyzing a color change reaction. The antibody is tagged with the enzyme and when the enzyme binds to the protein in the tumor, the color change indicates a positive test.

**HOW CAN IHC HELP?**

The decision to pursue pathologist recommended IHC should be based on the impact a more specific histologic diagnosis will have on patient management. IHC is an expensive test, and before agreeing to the pathologist's recommendation, the pet owners should be consulted regarding their ultimate goals for their pet. In many cases, results of IHC will allow the pet owner to have a better understanding of their pet's prognosis and the veterinarian will able to choose the most efficacious treatment. The case presentations to follow use actual patient biopsy information to demonstrate the clinical utility of immunohistochemistry in oncology patients.

**COMMONLY USED IHC MARKERS IN VETERINARY PATIENTS**
**RASKIN AND MEYERS CANINE AND FELINE CYTOLOGY 2ND, 2010 ED. P 409**

**TABLE 17-2 Markers Used for the Differential Diagnosis of Major Tumor Categories**

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|---|---|
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| Epithelial vs. mesenchymal | Cytokeratins (epithelial), vimentin (mesenchymal), E-cadherin (epithelium), p63 (basal cells, myoepithelium) |
| Leukocytic | CD45 (panleukocytic), CD18 (with emphasis in histiocytic), CD11d (dendritic cells), E-cadherin (Langerhan's cells), lysozyme (histiocytes), myeloid histiocytic marker (histiocytes, myeloid cells) |
| Liver | Hep Par 1 (hepatocytes), cytokeratin 7 (bile duct epithelium) |
| Lymphoid | CD3 (T-cell), CD79a and CD20 (B-cell), CD45 and CD18 (panleukocytic), MUM1 (plasma cells) |
| Mast cell tumors | CD117, tryptase, OCT3/4 |
| Melanocytic tumors | Melan A, S100, NSE |
| Muscle differentiation | Actin muscle (all muscle), smooth muscle actin (smooth muscle), myoglobin (skeletal muscle), actin sarcomeric (striated muscle), desmin (all muscle), calponin (smooth muscle, myofibroblast, myoepithelium) |
| Neurogenic tumors | S100 (neurons, glial cells), neurofilament (neurons), GFAP (glial cells), glut1, nerve growth factor receptor (perineural cells) |
| Pancreas (endocrine) | Insulin, glucagon, somatostatin, synaptophysin, PGP 9.5, chromogranin A |
| Squamous vs. adenocarcinoma | Squamous cell carcinoma (CK5, p63); adenocarcinoma (CK7) |
| Testis and ovary | Sex cord–stromal tumors (inhibin-α, NSE); germ-cell tumors (calretinin, KIT, PGP 9.5) |
| Thyroid | Thyroglobulin (follicular cells), calcitonin (medulla, C-cells), TTF1 (follicles and medulla) |
| Urinary tumors | Uroplakin III, cytokeratin 7, COX-2, COX-1 |
| Vascular tumors (endothelium) | Factor VIII–related antigen, CD31 |

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# PHIL FOX

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# CARDIOMIOPATÍA FELINA - CÓMO DIAGNÓSTICAR Y MANEJAR

OVERVIEW

Cardiomyopathy is the most common form of feline heart disease and accounts for 95% of cardiac morbidity and mortality. Cardiomyopathies represent a diverse and heterogeneous group of heart muscle disorders not caused by valvular, vascular, congenital, or systemic conditions. Clinical phenotypes often change (remodel) over time and some hearts express attributes that overlap with other diseases. In humans more than 1500 mutations have been detected in HCM. In the cat only two have been identified. Many affected cats remain asymptomatic for life, although substantial proportion develop cardiac morbidities.

TERMINOLOGY AND CLASSIFICATION Diagnostic classification can be complicated. Structural and functional phenotypes can change over time, may overlap with other diseases, and some cases do not conform to strict definitions! Phenotypes can change over time, may overlap with other diseases, and some cases do not conform to strict definitions. Four classic forms of cardiomyopathy (CM) help provide the best "snapshot" of cardiac structure: 1. Hypertrophic (HCM)- hypertrophied, non-dilated LV (IVS or LV wall at end diastole ≥ 6mm thick) in absence of clinical disease capable of inducing the magnitude of LV hypertrophy (no aortic stenosis, severe systemic hypertension, or hyperthyroid state). Many cases of HCM have the additional distinction of dynamic left ventricular outflow tract obstruction during systole, termed hypertrophic obstructive cardiomyopathy (HOCM). Often, this distinction is vague because at rest such cats may not display dynamic obstruction whereas with excitement, this feature becomes apparent. 2. Restrictive (RCM) a. Classic, nonendomyocardial form: Severe, bi-atrial dilation in absence severe volume overload (eg, no shunts or severe Mitral or Tricuspid regurgitation); relatively normal LV and RV cavities; normal or mild LV hypertrophy; and restrictive diastolic LV filling (eg, high E:A ratio [>2.5:1] and reduced mitral E deceleration time [<65msec]). b. Endomyocaridal form: Prominent endocardial scarring (hyperechoic echo lesions) bridging the ventricular septum and LV free wall, or obliterating or partially attenuating the LV apical region, and/or mid-left ventricular region; mild to moderate LVH; severe LAE; Doppler echo findings of diastolic dysfunction. 3. Dilated (DCM)- LV dilation (LVs>12mm, LVd>20mm), systolic failure (%FS<25%), thin LV walls. 4. Arrhythmic cardiomyopathy (also termed arrhythmogenic RV cardiomyopathy [ARVC] or dysplasia [ARVD])- severe RVE, often with thin RV walls, abnormal RV pectination, RA enlargement, and variable LA and LV changes. Many affected cats have substantial tricuspid regurgitation.

CLINICAL FINDINGS Systolic heart murmurs are very common in cats with some estimates that up to 40% of normal cats may have a heart murmur. Most but not all cats with cardiomyopathy have heart murmurs. Gallup sounds including third and fourth heart sounds are sometimes detected in cardiomyopathic cats even in preclinical stages, and the presence of these sounds are never normal. Some affected cats will have arrhythmias and in fact, infrequent ventricular premature complexes are relatively common in cats with preclinical as well as decompensated disease.

Clinical signs are apparent when a cat decompensates, including acute respiratory distress due to CHF, acute paralysis from arterial thromboembolism, or occasionally, sudden death. Pulmonary edema is the most common manifestation, followed by pleural effusion, with pericardial and abdominal effusion occurring much less frequently.

DIAGNOSIS

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Test for Discriminating Cardiac vs Respiratory Cause of Dyspnea- Thoracic radiography documents changes consistent with CHF (e.g., cardiomegaly and patchy, diffuse or focal pulmonary interstitial and alveolar infiltrates), detect effusions, masses, and other non-cardiac conditions. Thoracic radiography can indicate changes in cardiac silhouette and helps to document CHF and distinguish non-cardiac conditions, but does not substitute for echocardiography. Echocardiography is the gold standard for assessing cardiac structure and function and characterizing the form of underlying myocardial disease. Heart murmur is not a sensitive marker of heart disease and some studies report that up to 40% of normal, healthy cats have soft heart murmurs. Gallop heart sounds may be detected by auscultation and are never normal. A fourth (S4) gallop sound may be detected in some cats with hypertrophic cardiomyopathy, while a third (S3) gallop sound is usually associated with dilated cardiomyopathy. Atrial or ventricular premature complexes are often detected however overall, electrocardiography is insensitive for detecting heart disease. Noninvasive blood pressure measurement identifies systemic hypertension which can increase left ventricular wall thickness, especially with chronic renal failure and hyperthyroidism. Serum T4 (in cats older than six years of age) and PCV are important. High sensitivity and specificity using a commercial blood test to measure the cardiac biomarker, NTproBNP has made this useful an adjunct test to help differentiate cardiac vs non-cardiac causes of respiratory distress. Moreover, assessment of NT-proBNP concentration in combination with conventional evaluation such as radiography and electrocardiography has been reported to significantly improve the accuracy and confidence of general practitioners to distinguish cats with primary respiratory disease from those with

CHF. Diagnostic accuracy is improved when NTproBNP assay is used in conjunction with other tests such as physical examination, ECG, radiography, and echocardiography. The snap test was designed to differentiate cats with moderate to severe LVH from cats with normal or equivocal or mild LVH, but was not designed to diagnose CHF and should be avoided for this specific application. Serum troponin, if elevated, can sometimes infer myocarditis but sensitivity and specificity for this application it is uncertain.

THE PRECLINICAL (ASYMPTOMATIC) CAT Cats with preclinical hypertrophic cardiomyopathy are at substantial risk for developing cardiac morbidity and mortality. The epidemiology of preclinical HCM has recently been described from 1730 cats (1008 HCM/HOCM and 722 apparently healthy cats without heart disease (Fox et al., REVEAL Study. JVIM, 2018). During the study period, CHF, ATE, or both occurred in 30.5% and cardiovascular death in 27.9% of 1008 HCM/HOCM cats. Risk assessed at 1, 5, and 10 years after study entry was 7.0%/3.5%, 19.9%/9.7%, and 23.9%/11.3% for CHF/ATE, and 6.7%, 22.8%, and 28.3% for cardiovascular death, respectively. There were no statistically significant differences between HOCM compared with HCM for cardiovascular morbidity or mortality, time from diagnosis to development of morbidity, or cardiovascular survival. Cats that developed cardiovascular morbidity had short survival (mean+/-standard deviation, 1.3+/-1.7 years). Overall, prolonged longevity was recorded in a minority of preclinical HCM/HOCM cats with 10% reaching 9-15 years. Thus,preclinical HCM/HOCM is a global health problem of cats that carries substantial risk for CHF, ATE, and cardiovascular death.

Unfortunately, there is no current evidence that treating asymptomatic cats prevents cardiac disease progression, reduces risk of cardiac morbidity, or prolongs cardiac survival. Nevertheless, certain findings merit concern for increased risk of cardiovascular morbidity and such risk factors provide grounds for treatment deliberation.

POTENTIAL CARDIOVASCULAR RISK FACTORS Risk factors that predispose to morbidity and mortality are beginning to be clarified but more work remains in order to develop accurate, actionable, and effective risk stratification. However, certain myocardial structural or functional abnormalities as listed below, may predispose to adverse outcome, providing raison d'être for pharmacologic intervention. Efficacy remains unproven.

Myocardial Infarction This is inferred by thinned, hypokinetic LV wall segments seen by echocardiography. Such cases have used ACEI or beta-blockers based upon the use of these drugs in humans to mitigate ventricular remodeling and reduce mortality. Tachyarrhythmia Rapid tachyarrhythmias can reduce cardiac

filling, promote ischemia, and result in hemodynamic instability. Sustained tachyarrhythmias are usually associated with myocardial disease (myocyte necrosis, fibrosis, inflammation, interstitial matrix changes). Antiarrhythmic therapy is administered in selected cases to control ventricular rate.

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Severe LV Hypertrophy Cats with greatly increased LV mass (diastolic septal or LV wall thickness > 8mm) may be at increased risk for cardiovascular events. Severe Left Atrial Dilation This contributes to blood stasis and thrombus formation. Restrictive LV Filling Pattern (Restrictive Physiology) Doppler echocardiographic evidence of a restrictive trans-mitral filling may suggest end-stage diastolic dysfunction and carries poor prognosis. This physiology may occur in any form of cardiomyopathy. Spontaneous Echo Contrast ("Smoke") Associated with blood stasis and presage increased thromboembolic risk, this finding warrants consideration for antiplatelet drugs. Myocardial Failure In some HCM and RCM and in DCM cats LV contractility is reduced (e.g., fractional shortening <25%; LV end-systolic dimension >12 mm). Potential therapies include oral taurine supplementation, ACEI, pimobendan, and treatment of tachyarrhythmia if present. Arrhythmic Right Ventricular Cardiomyopathy Cats with advanced structural lesions (e.g., severe RV/RA dilation, ventricular tachycardia) are at risk for CHF. ACE inhibitors and pimobendan should be considered with advanced lesions. "Malignant" Familial History of Sudden Death (High Risk Genotype) Pedigrees may be identified with a documented heritable pattern of HCM and severe morbidity and mortality (e.g., Maine coon cats, others). More aggressive monitoring and focused, individualized therapies should be considered. Hypertrophic Obstructive Cardiomyopathy (HOCM) by itself does not confer higher risk than cats with the non-obstructive form of Hypertrophic Cardiomyopathy (HCM) and thus, HOCM cats do not automatically merit more aggressive therapy.

GOALS FOR MANAGING HEART DISEASE There is no single test that reliably identifies the failing heart (heart failure is a syndrome, not a disease). Diagnosis requires an integrated approach that synthesizes findings from medical history, clinical signs, imaging, and clinical testing. Management goals directed to reduce morbidity, assure quality of life, and prolong survival.

Managing Acute Congestive Heart Failure with Predominantly Pulmonary Edema Pulmonary edema is life threatening. • Diuretics represent the cornerstone for acute, emergency management and are administered as intermittent IV bolus is or by constant rate infusion. An initial IV bolus of furosemide (1- 2 mg/kg IV) is given and repeated if needed in 1-2 hrs; 1 mg/kg IV is administered every 8-12 hours until evidence of reduced lung crackles, improved breathing rate and effort are observed, at which time furosemide dose is briskly reduced. Alternatively,

furosemide is administered by continuous infusion (0.25 – 0.35 mg/kg/hr) following an initial IV bolus. There is no proof that IV bolus or continuous infusion is superior. • Thoracocentesis is performed when substantial pleural effusion is present • Some clinicians add pimobendan, 1.25 mg Q 12 hours while others reserve this for resistant or recurrent CHF. • Supplemental oxygen (40-60% O2-enriched inspired gas) improves pulmonary gas exchange. • Trans-dermal 2% nitroglycerin ointment, ¼ to ½ inch q 6hr can be added for the first day or two in severely affected cases safely, although this therapy has become less popular. • Clopidogrel (18.75 mg daily) is administered to cats judged to be at risk for thromboembolism (eg, large atrium, blood stasis, myocardial failure). Aspirin is judged to be less effective but in cats in which oral medication is difficult, it can be administered (10-20 mg q 3 days). • Angiotensin converting enzyme inhibitors (ACEI) such as enalapril [1.25-2.5mg q 24 hr] can be added, usually at first recheck if renal function is normal.

• Diagnostic tests should include a CBC/differential and biochemical profile (with T4 when cats are greater than seven years of age). Renal function and electrolytes should be tested at least every day during hospitalization since acute kidney injury and electrolyte loss can occur owing to the sensitivity of cats to furosemide. ECG is performed if rhythm disturbance is detected • Systolic blood pressure should be monitored during hospitalization • Diagnosis should be confirmed via echocardiography

• Radiographic clearing of alveolar infiltrates usually occurs usually by 24 to 36 hrs post therapy in first time heart failure cases. • Dehydration, azotemia, and hypokalemia can result from over-diuresis. Close monitoring of



creatinine and electrolytes is important. Appetite stimulants should be administered if anorexia is present.

Managing Acute Heart Failure Associated with Systolic Dysfunction (eg, DCM) Although uncommon, some cats present with CHF associated with reduced LV contractility and LV dilation. Taurine deficiency, once common, has become an exceedingly rare and etiology is usually unknown. In some cases, DCM may develop as an end-stage consequence of HCM or RCM.

Decompensated cats present with pulmonary edema, effusions or both in conjunction with hypothermia and often, cardiogenic shock. Therapies include the following:

• Pimobendan (1.25 mg Q 12 hours) • Dobutamine (2-5 mcg per kilogram per minute constant rate infusion) is added if cardiogenic shock is present • Judicious furosemide administration is titrated to patient needs and briskly reduced or stopped once pulmonary edema as resolved. • Centesis it is performed as needed if plural, pericardial, or abdominal effusion is present and it is interfering with breathing or cardiac function. • Clopidogrel (1/4 of a 75 mg tablet orally every 24 hours) because heart failure cats are at risk for thromboembolism • (Generalized support is added including supplemental oxygen, assessing kidney function and electrolyte concentrations • Supplemental feeding via nasoesophageal tube can be considered if anorexia persists despite appetite stimulant medication.

• Diuretics I reduced to the lowest effective dose, pimobendan his continued, and consideration is given to adding an ACEI. Many supplement the diet with taurine, 250 mg twice daily if they cannot obtain a blood taurine level.

• For refractory effusions, judicious use of hydrochlorthiazide (6.25mg q 24-48 hrs) and an ACE inhibitor (enalapril, benazepril, ramipril, etc) it is considered when renal function is preserved and patient status is stable.

• Long-term prognosis is guarded. Historically, taurine deficiency was the most common cause of DCM. Following the reported link with dietary taurine deficiency in 1987, taurine related DCM is now rare. However, cases of idiopathic DCM are still detected

Managing Chronic Heart Failure Chronic therapy is individualized to maintain a congestion-free state; prevent arterial thromboembolism; halt, slow, or reverse myocardial dysfunction (theoretically); promote quality of life; and prolong survival. It is essential to identify and treat contributory diseases (e.g., systemic hypertension, hyperthyroidism, and anemia) and other comorbidities if present. Complete database is helpful including comprehensive clinical pathology testing.

Furosemide is decreased to the lowest effective dosage. Some cats remain stable on 1- 2 mg/kg PO given daily or every other day while in others, diuretics may need to be used twice daily. For cats that have the obstructive form of hypertrophic cardiomyopathy (HOCM), recent data shows that these cats are at no greater risk compared to HCM. There is no data to suggest that beta blocker therapy is beneficial and thus, these agents are not routinely recommended to treat HOCM anymore. The use of pimobendan is controversial with some

clinicians prescribing it long term and others not prescribing it until recurrent heart failure. Animals should be reevaluated every 3 to 4 months to assess overall health and renal function, heart rate and rhythm, and once or possibly twice yearly, repeat echocardiogram to look for change of significant remodeling. Affected cats are at risk for recurrent heart failure and thromboembolism.

RECURRENT OR RESISTANT HEART FAILURE Comprehensive patient evaluation helps to identify and manage renal failure, hyperthyroidism, anemia, arrhythmias, and other systemic or metabolic conditions that can trigger or predispose to cardiac decompensation.

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• Diuretic resistance may occur as heart failure progresses, and upward furosemide dose titration may be indicated. • Some cats appeared to respond favorably when furosemide is substituted for with torsemide, starting at 0.1 mg per kilogram orally daily and titrating the dose upward or to twice daily administration. This therapy is individualized to each cat based upon its renal status, appetite, and in consideration of other drugs being given. • Addition of a second diuretic (e.g., thiazide-5 to 10 mg every other day) is reserved for cases of persistent diuretic resistance that did not respond to torsemide. • Arterial blood pressure and thyroid status should be reassessed periodically as well as CBC/deaf and biochemical profile to check for comorbidities and treatable conditions.

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FELINE THROMBOEMBOLISM

Thrombosis is clot formation within a cardiac chamber or vascular lumen. Embolization results from dislodgement of a clot fragment or other foreign material into a vessel.

Pathogenesis Thrombosis requires one or more of the following conditions: 1) local vessel or tissue injury, 2) circulatory stasis, and 3) altered blood coagulability. The cardiomyopathies predispose to LA or LV endothelial injury and blood stasis from atrial dilation and impaired function. Together, these factors predispose cats to thromboembolism. Moreover, collateral circulation is modulated by vasoactive



substances (e.g., serotonin and others) released by the clot as well as by endothelial substrates. These chemicals decrease collateral circulation and exacerbate ischemia. Clinical Signs Clinical consequences depend upon: 1) site of embolization, 2) severity and duration of occlusion, 3) degree of functional collateral circulation, 4) state of myocardial function, and 5) development of serious complications. CHF (dyspnea, tachypnea, anorexia) or syncope may

occur concurrently. Clinical signs result from CHF and specific tissues or organs that are embolized (e.g., azotemia from renal infarction, bloody diarrhea from mesenteric infarction, posterior paresis from saddle embolus). More than 90% of affected cats present with lateralizing posterior paresis caused by a saddle clot at the distal aortic trifurcation. Clinical signs are characterized by the 4 P's: Paralysis; Pain; Pulselesness (lack of palpable femoral arterial pulses); and Polar (e.g., cold distal limbs and pads) extremities. Anterior tibial and gastrocnemius muscles become firm from ischemic myopathy by 10 to 12 hours post aortic embolization. These muscle groups begin to soften 24 to 72 hours later. Acutely affected cats drag their back legs by flexing and extending the hip, but cannot flex and extend the hock. Invariably, one leg is more severely affected. Nail beds are cyanotic and distal limbs are swollen. Embolus to a single brachial artery (usually right front leg) may cause monoparesis. When intermittent claudication occurs, arterial pulses may be palpated, foot pads feel warm (normal), and nail beds are not cyanotic. This frequently precedes severe subsequent thromboembolism. Less common sites include renal, mesenteric, pulmonary, coronary, and cerebral arteries (embolic "showers"). Most cats are clinically dehydrated and hypothermic.

Diagnostic Workup for ATE Thoracic radiographs, ECG, echocardiogram, biochemical profile, and urinalysis provide the initial data base. Affected cats have creatine phosphokinase enzymes elevated shortly after embolization; BUN/creatinine, serum alanine aminotransferase and aspartate aminotransferase (SGOT) elevate by 12 hours of presentation, and peak by 36 hours post embolization. Hyperglycemia, mature leukocytosis, lymphopenia, and hypocalcemia may be present. Acute hyperkalemia can result from skeletal muscle reperfusion injury downstream from the embolus. Hypokalemia accompanies anorexia and diuretic therapy. Coagulation abnormalities may occur. Echocardiography characterized heart structure and function and detects intracardiac and vascular thrombi. Spontaneous echo contrast ("smoke") in the LA or LV is associated with blood stasis, and is a harbinger for increased thromboembolic risk. Scintigraphy, MRI, high definition CT, and angiography are rarely required but may have clinical application in selected patients.

Treatment Goals for ATE Therapies are directed to 1) manage concomitant CHF or serious arrhythmias (especially associated with hyperkalemia), 2) patient support (nutritional supplementation, correct hypothermia, prevent self-mutilation), 3) acute pain amelioration, 4) measures to limit thrombus growth/ formation, 5) critical monitoring, and 6) prevention of repeated events.

Analgesia (ideally, u-antagonists) with close monitoring to prevent hypotension or hyperthermia): For acute ATE- • Fentanyl (2-4ug/kg IV bolus, then 2-5 ug/kg/hr Constant Rate Infusion) • For consideration if CRI not possible (hydromophone,

oxymorphone, methadone) • Other (less optimal) agents (buprenorphine, butorphanol) Antiplatelet aggregating drug therapy should be considered for: a) current or past thromboembolism, b) moderate to severe left atrial enlargement c) spontaneous echo contrast or thrombosis in the LA or LV, d) systolic atrial dysfunction. Present medications include: • Clopidogrel (Plavix)- 1.1-3.0 mg/kg PO q 24h for ATE prevention (generally, 1/4 of 75mg tablet daily); a single loading dose of 4-10 mg/kg may be useful for obtaining more rapid therapeutic plasma concentrations – Clopidogrel provides superior results vs aspirin to prevent repeated feline thrombosis. • Aspirin- historically used but has been shown to be less effective than clopidogrel. Effective doses have not been established but clinical dosing range from 10 to 20 mg every three days. • Results using dual therapy have not been documented. Antithrombotic Agents for active thromboembolism: Two particular expensive anticoagulant agents- enoxaparin and dalteparin- are commonly used with far greater safety margins vs unfractionated heparin; TID administration is optimal.

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• Lovenox (enoxaparin)- 0.8 mg/kg SC q6h is safe and well-tolerated but may not achieve antiXa levels considered therapeutic for people • Fragmin (dalteparin), 100 U/kg q 12-24hrs SQ or have been used relatively safely. • Rivaroxaban (Direct factor Xa inhibitor) - 1-2 mg/kg/d q 24 hr

Less accepted and more risky therapies: • Fibrinolytic therapy using tissue plasminogen activator (tPA) has received less attention and some have reported untoward results, especially reperfusion injury (1mg/kg, administering 10% as a slow IV bolus and the remainder by CRI over 1 hour). • Streptokinase and warfarin have fallen out of favor. Heart Failure and Arrhythmia Therapy: • As indicated per individual patient needs Supportive Care: • Close hospital monitoring • Physical therapy (gentle limb range of motion 28 hours after ATE if pain is controlled) • Appetite stimulants if needed

Critical Patient Monitoring Acute Care- Because reperfusion injury-induced hyperkalemia is common within the first 1 -2 days following embolization, continuous ECG monitoring is valuable during hospitalization. Renal infarction and azotemia may occur and periodic evaluation of creatinine, SDMA, and electrolytes are important. CHF accompanies ATE in many cases and thoracic radiographs should be performed if needed. Echocardiography can reveal cardiac thrombi in some cases and helps to guide overall cardiac therapy. Anorexia should be managed pharmacologically, with appetite stimulants, or with feeding tubes.

Chronic Management- Establishment of a good appetite is a substantial benefit. Maintaining client communication is important and should emphasize being alert for signs of self-mutilation of the affected distal limb. Such cases may require protective bandage or E-collar. Long term outcome is generally guarded and recurrent thromboembolism should be anticipated. Recurrent thrombolism should be anticipated.

Time Course for Physical Recovery Acute pain is generally most severe during the first 24 hours. This is associated with muscle hypoxia and swelling that becomes confined by fascial sheaths. Muscle firmness accentuates from 4 to 6 hours post thrombosis and by 24 hours, cranial tibial muscles and gastrocnemius muscles are generally very firm and painful to palpation. Toes and toe pads in affected limbs are swollen and nail beds are cyanotic. These muscle groups begin to soften as soon arterial blood circulation becomes reestablished and sometimes, limbs will become softer and more supple 24 to 48 hours post thrombosis. Occasionally, muscle groups will harden further over the first 48 hours and this is generally a poor prognostic sign. Reperfusion typically begins approximately 24 hours post embolization and can result in rapid and severe hyperkalemia. In catss who avoid reperfusion injury, affected cats typically show progressive improvement between 1 to 3 weeks following thrombosis. Initially, cats may be able to bear some weight on one rear leg while dragging the other rear leg when trying to ambulate. Range of motion is confined to flexion and extension of the hips initially. Progressively, hock function develops. In the majority of cases that resolve, animals are left with neuromuscular deficits in one or both rear limbs defined as being able to walk adequately but having the appearance of being “down in the hock.” Special care must be taken to avoid self-mutilation which can appear at first as subtle signs of excessive licking between digits of affected limbs.

Indicators of a Relatively Favorable Prognosis-Arterial TE 1. Resolution of CHF and/or control of serious arrhythmias, 2. Lack of LA/LV thrombi or spontaneous echo contrast, 3. Reestablished appetite, 4. Relatively normal BUN/creatinine/ electrolytes, 5. Return of limb viability/function (e.g., loss of swelling; return of normal limb temperature; return of motor ability), 6. Return of femoral arterial pulses and pink nail beds, 7. Lack of self- mutilation. Indicators of a Poor to Grave Prognosis- Arterial TE 1. Refractory CHF or development of malignant arrhythmias, 2. Acute hyperkalemia, 3. Hypothermia, 4. Declining limb viability (e.g., progressive hardening of gastrocnemius and anterior tibial muscle group; failure of these muscles to soften 48-72 hours after presentation; distal limb necrosis), 5.

Multiorgan/multisystemic embolization (CNS signs, bloody diarrhea, acute renal failure), 6. History of previous embolic episodes, 7. LA/LV thrombus or spontaneous echo contrast, 8. Rising BUN, creatinine, 9. Hypothermia, 10. Severe LA enlargement with tachyarrhythmia. References

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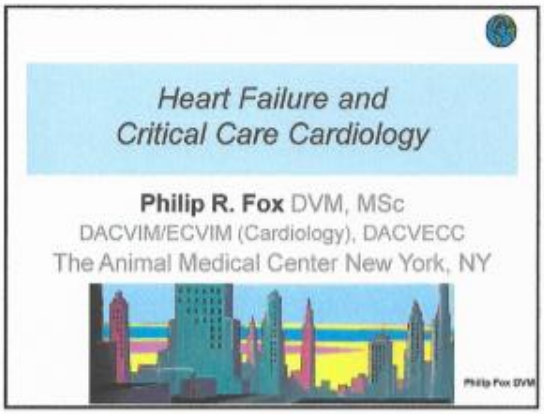
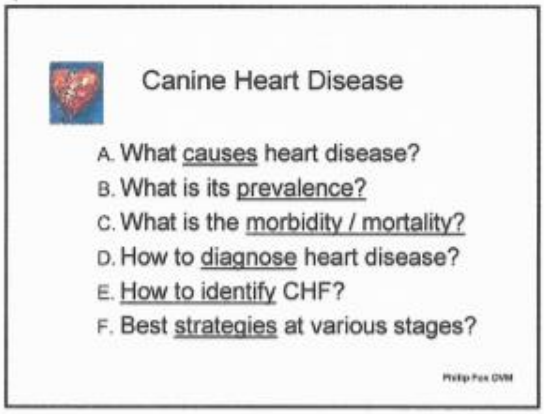
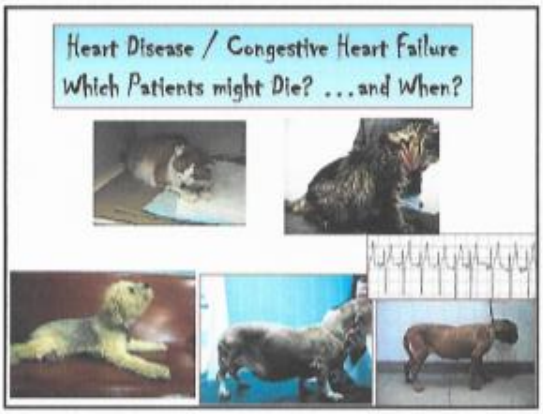
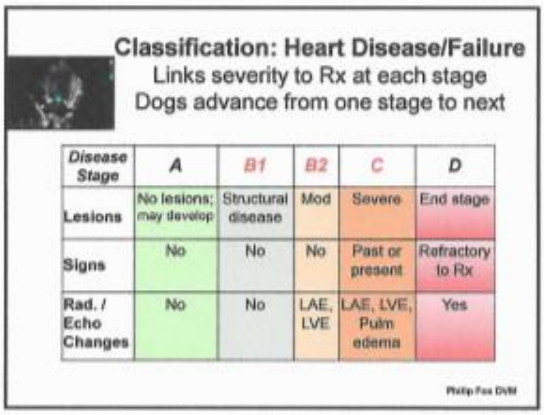
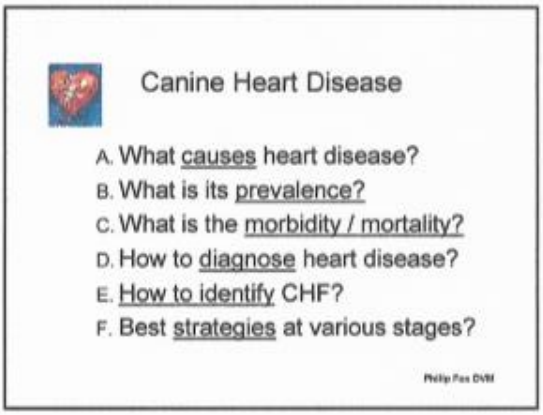
# CUIDADOS CRfTICOS EN CARDIOLOGfA. (CRITICAL CARE IN CARDIOLOGY)

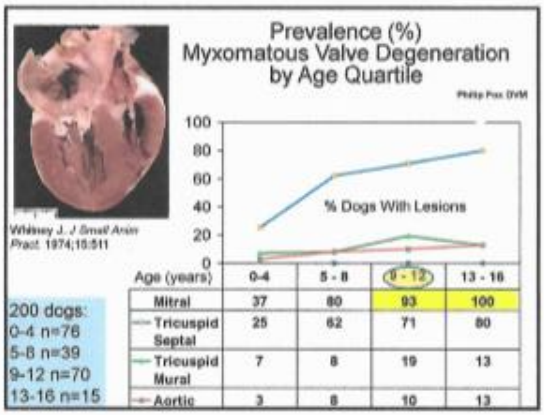


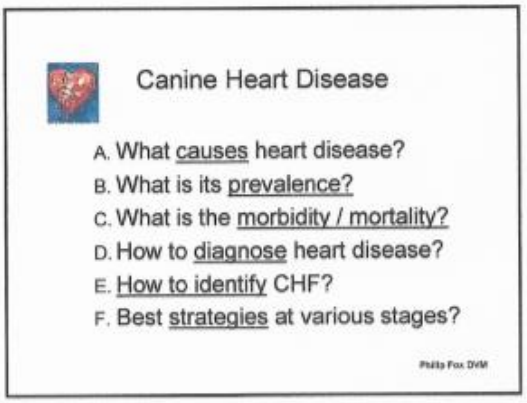




Canine Heart Disease
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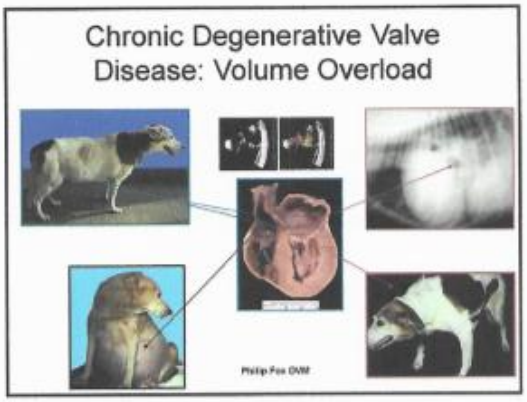
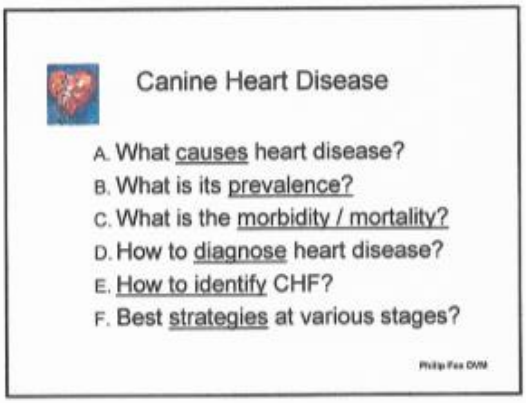
F. Best strategies at various stages?


Chronic Degenerative Valve Disease: Volume Overload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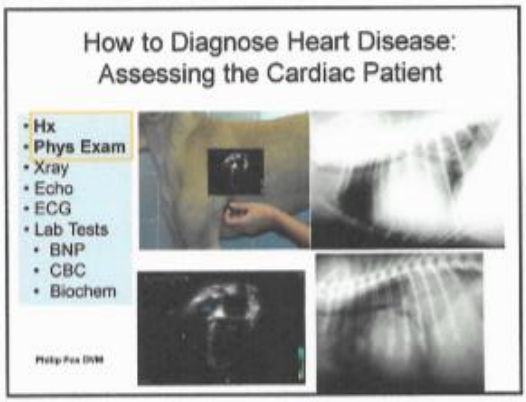
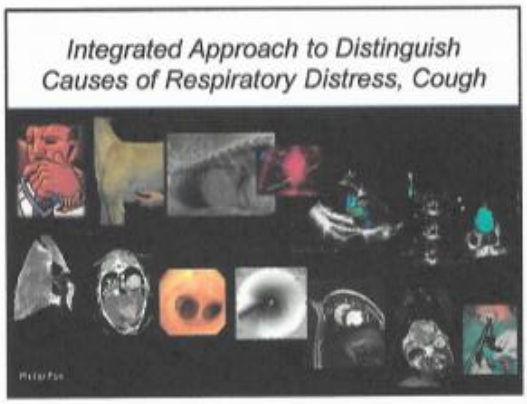
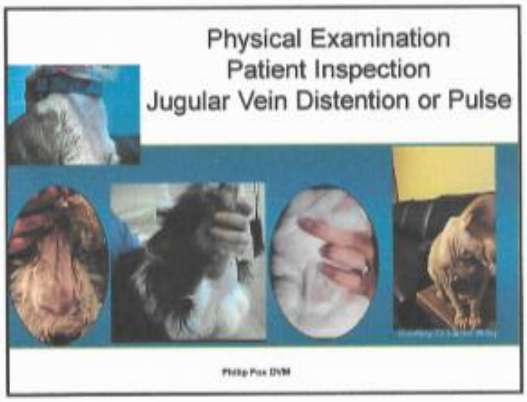
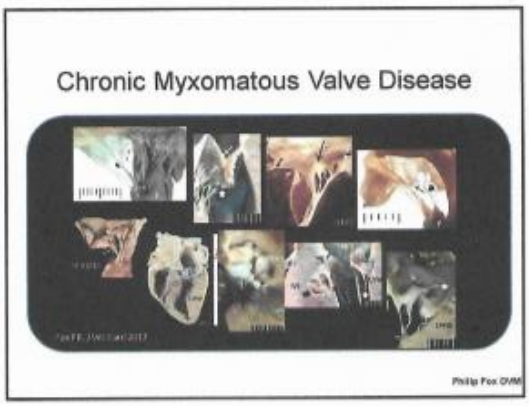
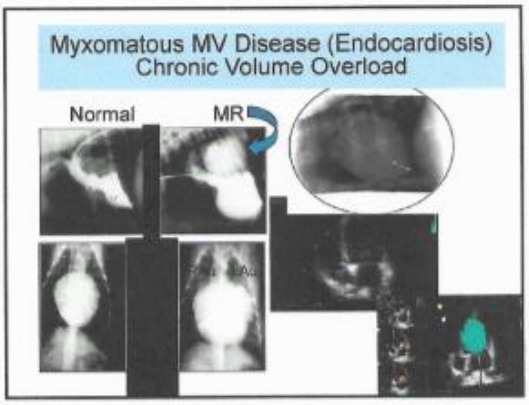
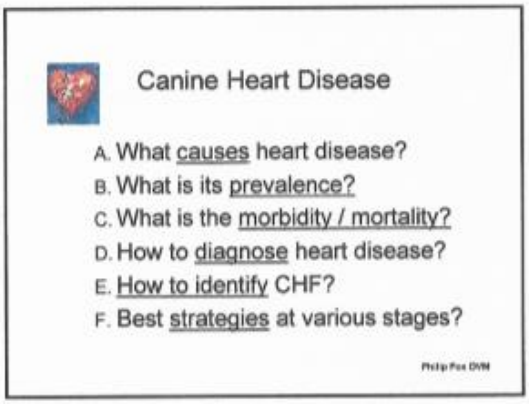

How to Diagnose Heart Disease: Assessing the Cardiac Patient
Hx
Phys Exam
Xray
Echo
ECG
Lab Tests
BNP
CBC
Biochem


Integrated Approach to Distinguish Causes of Respiratory Distress, Cough


Physical Examination
Patient Inspection
Jugular Vein Distention or Pulse


Chronic Myxomatous Valve Disease
Philip Fox DVM


Myxomatous MV Disease (Endocardiosis)
Chronic Volume Overload
Normal
MR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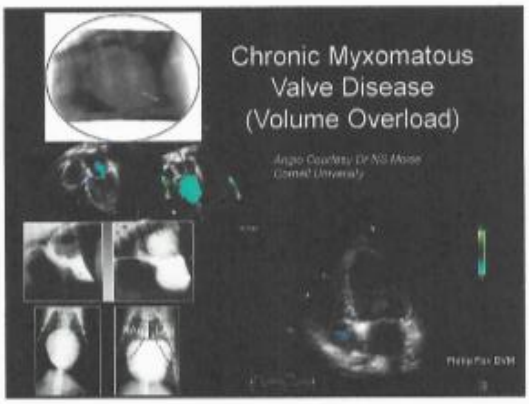
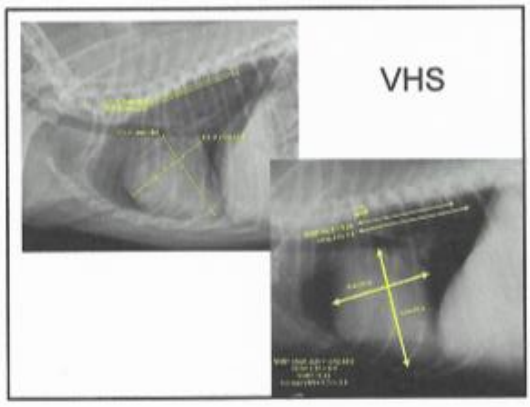
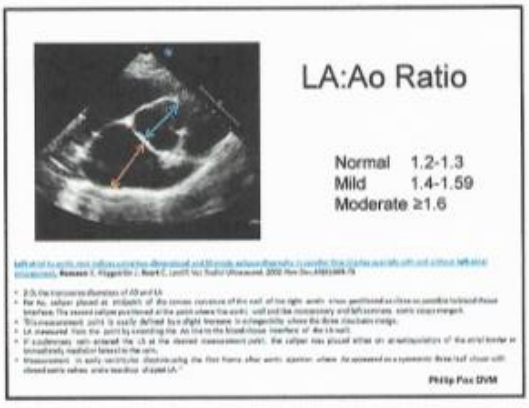
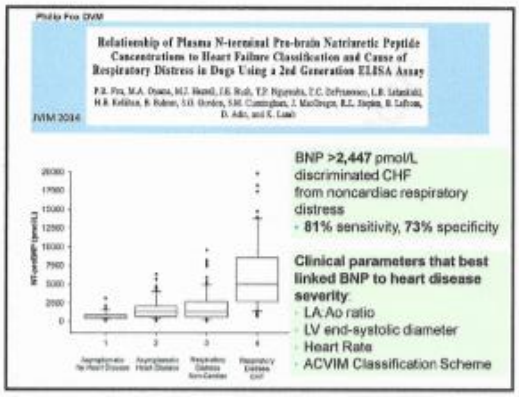
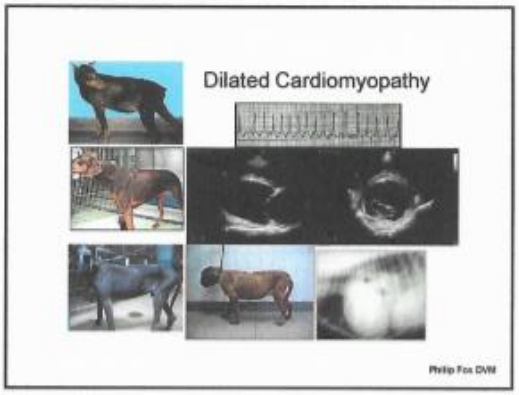
Philip Fox DVM

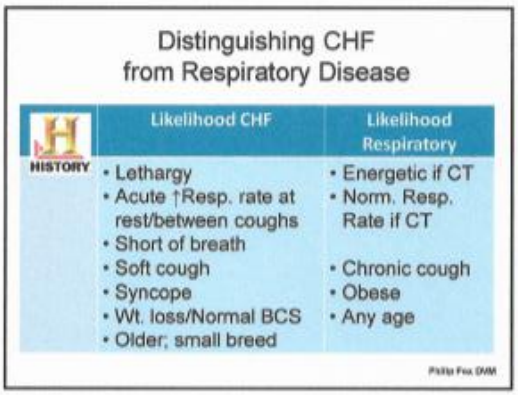

Chronic Myxomatous
Valve Disease
(Volume Overload)

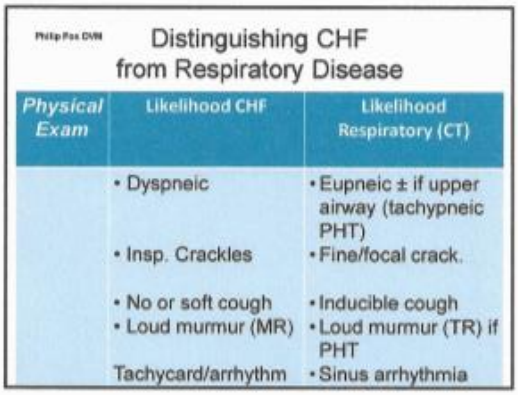

VHS

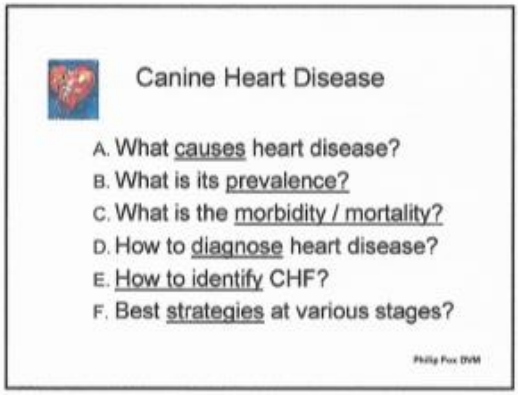

LA:Ao Ratio
Normal 1.2-1.3
Mild 1.4-1.59
Moderate ≥1.6
Philip Fox DVM


Relationship of Plasma N-terminal Pro-brain Natriuretic Peptide Concentrations to Heart Failure Classification and Cause of Respiratory Distress in Dogs Using a 2nd Generation ELISA Assay
JVIM 2014
BNP >2,447 pmol/L discriminated CHF from noncardiac respiratory distress
81% sensitivity, 73% specificity
Clinical parameters that best linked BNP to heart disease severity:
LA:Ao ratio
LV end-systolic diameter
Heart Rate
ACVIM Classification Scheme


Dilated Cardiomyopathy
Philip Fox DVM


Distinguishing CHF from Respiratory Disease
HISTORY
Likelihood CHF
Likelihood Respiratory
• Lethargy
• Acute ↑Resp. rate at rest/between coughs
• Short of breath
• Soft cough
• Syncope
• Wt. loss/Normal BCS
• Older; small breed
• Energetic if CT
• Norm. Resp. Rate if CT
• Chronic cough
• Obese
• Any age


Philip Fox DVM
Distinguishing CHF from Respiratory Disease
Physical Exam
Likelihood CHF
Likelihood Respiratory (CT)
• Dyspneic
• Insp. Crackles
• No or soft cough
• Loud murmur (MR)
Tachycard/arrhythm
• Eupneic ± if upper airway (tachypneic PHT)
• Fine/focal crack.
• Inducible cough
• Loud murmur (TR) if PHT
• Sinus arrhythmia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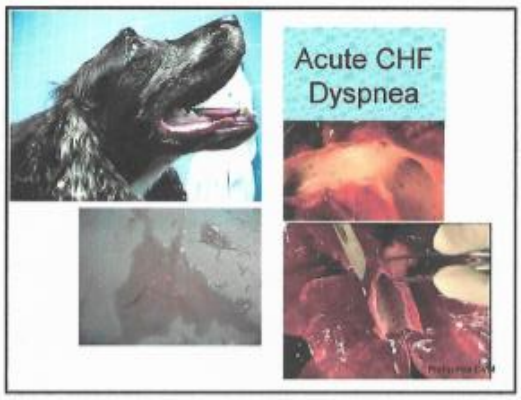
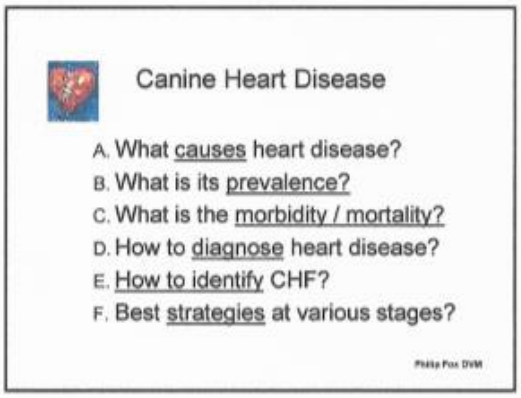
Congestive Heart Failure


Acute CHF
Dyspnea


Congestive Heart Failure
Breathing Patterns
Inspiratory and Expiratory Effort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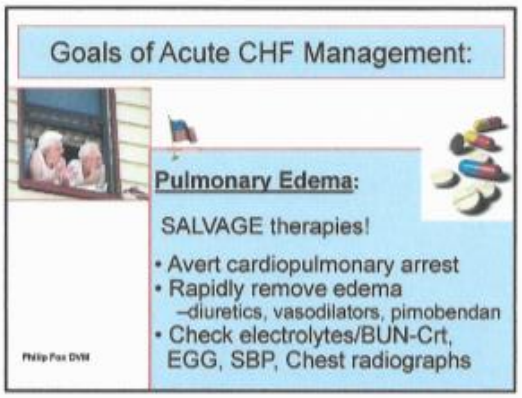
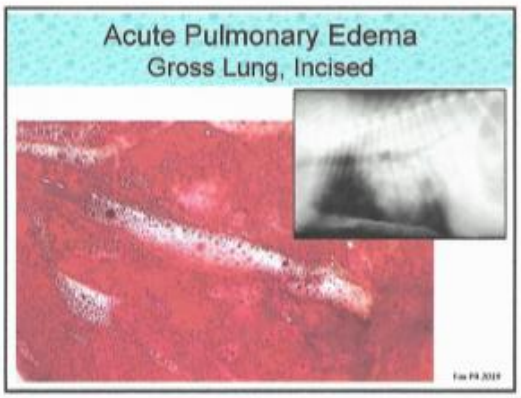
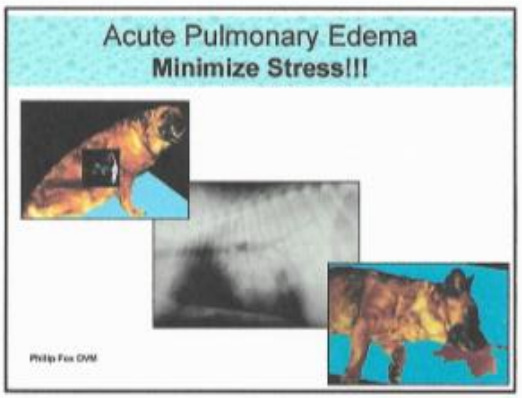

Goals of Acute CHF Management:
Pulmonary Edema:
SALVAGE therapies!
• Avert cardiopulmonary arrest
• Rapidly remove edema
–diuretics, vasodilators, pimobendan
• Check electrolytes/BUN-Crt,
EGG, SBP, Chest radiographs


Acute Pulmonary Edema
Gross Lung, Incised

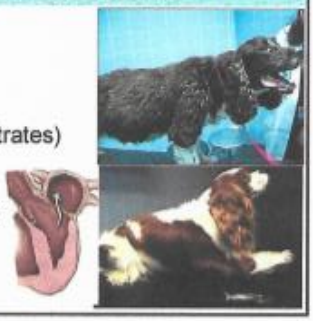

Acute Pulmonary Edema
Minimize Stress!!!

## Acute Pulmonary Edema
### Drug Considerations

***FOH-PA***

- Furosemide
- Oxygen
- Hydralazine (Nitrates)

- Pimobendan
- Antiarrhythmics



## Acute Pulmonary Edema
### Management:

Reduce Preload:

**IV Furosemide** 2-4mg/kg IV
- 1-2 mg/kg in 1 hr, then q4-8h

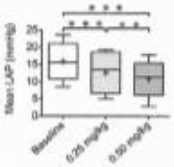
- Initial Bolus, then 0.25-.35mg/kg/hr CRI
- Adjust dose to Clinical Endpoints
  1. Breathing (Resp Rate, Effort)
  2. Lung Sounds
  3. Crt/BUN, Electrolytes, Systolic BP
  4. Body wt

*AVOID Hypotension and Renal Failure*

## Acute Pulmonary Edema
### Management:

Inodilator Therapy

**Pimobendan**
0.5mg/kg PO q-12 hrs
Suzuki S. JVIM 2016




Significantly reduces LAP
- 1 day later (0.5mg/kg), vs
- 4 days later (0.25mg/kg)

## Cardiogenic Pulmonary Edema
### Acute Management:

↓↓Resistance to LV Ejection (Afterload)

2. **Oral Hydralazine**
- 0.75-1.5 mg/kg PO q 8 hrs, or
- **0.5mg/kg q 1 hours**

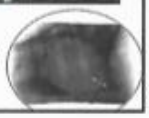
Titrate-
SBP >85mmHg, ↓ resp. rate, ↓ lung crackles

AVOID HYPOTENSION

## Cardiogenic Pulmonary Edema
### Acute Management:

↓Resistance to LV Ejection (Afterload)

1. **Sodium Nitroprusside** 2-15ug/kg/min IV CRI
- Start at 2ug/kg/min
- ↑ by 1ug/kg/min/30 min
- Titrate to ↓ RR and dyspnea, reduce lung crackles
- Maintain SBP>85mmHg



AVOID Hypotension, Renal Failure

## *Cardiogenic Pulmonary Edema*
### *Acute Management:*

**Positive Inotropes**

Pimobendan
0.25-.3mg/kg q12h

**Dobutamine**
5-15ug/kg/min CR

**Digoxin**
0.005 mg/kg q12h

**Nutriceuticals**

## Cardiogenic Pulmonary Edema
*No Money, No Problem (kind of)*

| | | |
|---|---|---|
| ↓ Preload | • Furosemide<br>• 1mg/kg IV q 1 hr | Maintain SBP > 85mm Hg |
| ↓ Afterload | • Hydralazine<br>• 0.5 – 1 mg/kg q 1 hr | |
| ↑ Contractility | • Pimobendan<br>• 0.5mg/kg q 8 hrs | |
| Recheck hourly!!!! | • Systolic BP; HR/RR | |

Titrate to ↓ resp. rate, ↓ lung crackles

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## Cardiogenic Pulmonary Edema
**Monitor:**

**AVOID Hypotension, Renal Failure**
- Systolic blood pressure
- Creatinine, $K^+$ $Na^+$ $Cl^-$
- Monitor ECG
- Chest Radiographs/Lung US

Perform: Echo

## Goals of Chronic Therapy:

- Reduce morbidity
- Improve survival
- Enhance quality of life

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## ACE Inhibitors

**Indications**
- Counter RAAS activation

**Administration**
- Enalapril, Benazepril
- (0.5mg/kg q12-24h)

**Considerations**
- DCM (Dobermans) delays onset CHF
- Chronic MVD- small or no benefit in volume overload (SVEP, Vetproof)

**Monitoring**
- Rare side effects without diuretics
- AKI with overdiuresis
- Re✓ 3-7d post Rx, 1-3 months, q 12 months- or following increased diuretic dose

## Spironolactone

**Indications**
- Adosterone antagonist (RAAS)
- Promotes fluid retention, vascular & myocardial remodeling
- Elevate despite ACEI

**Administration**
- Given with ACEI and diuretics
- 2 mg/kg q12h PO

**Monitoring**
- Rare side effects

**Considerations**
- Strong efficacy data in people
- Uncertain benefit, dogs

## Chronic Management

1. Client Monitoring
   - Teach resp. rate (normal < 30)
   - Anorexia, weakness, cough, syncope
2. DVM Monitoring
   - Radiographs
   - Creat./lytes/SBP/ECG
   - Echo (if symptoms)
3. Expect recurrences
   - Risk/Life expectancy
   - Reset concept of maximal dosages
     *Lasix, Spironolactone, ACEI, Amlodipine*
4. Quality of Life
   - Coughing- manage
   - Cardiac cachexia- nutritional consult

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## Home Care Focus

- Home monitoring
  - Heart rate/rhythm?
  - Breathing rate
  - Body weight
- Compliance
- Diet
- Activity
- Quality of life
  - Appetite / treats
  - Urinary continence
  - Medication interval
  - Activity
  - Costs
  - Recheck frequency
  - Advice

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## Primary Care Focus

- Accuracy of diagnosis
- Comorbidities
- Prognosis 3-18 months post 1st CHF
- Evidence-based practice guidelines
  - At every stage of disease (interface w/ specialist care)
- Clinical monitoring
  - Renal function / electrolytes
  - Body weight (expect cachexia)
  - ECG / radiographs
  - Arterial blood pressure
- Follow-up phone care / reminders
- Emergency service / advice

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## Pulmonary Hypertension Cardiac vs Respiratory Disease

| TR Velocity (m/s)- estimated PA systolic | Asympt. No Heart Disease | Asympt. Heart Disease | Resp. Distress Lung or Airway | Resp. Distress CHF |
|---|---|---|---|---|
| 2.8 - 3.5 Mild | 0 | 12(15%) | 15 (14%) | 20 (27%) |
| >3.5-4.3 Mod | 0 | 1 (1%) | 18 (17%) | 7 (9%) |
| **>4.3 Severe** | 0 | 1 (1%) | 9 (9%) | 9 (12%) |

**Sildenefil** 2-8mg/kg PO q 8-12 hours

Fox PR JVIM 2014

## Chronic Valvular Heart Disease Stage D (Refractory to standard Rx)

- Change furosemide to torsemide
- Maximize drug doses
- Dietary Management
- Off-label drug doses
  - Pimobendan q 8 hrs
  - Amlodipine; Digoxin

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## Chronic Valvular Heart Disease Stage D (**Refractory** to standard Rx)

**Reassess Diagnosis**
- Comorbidities?
- Pulmonary hypertension?
- Tachyarrhythmias?
- Mocardial failure?

**PHT and R CHF**
- Sildenefil 3-8mg/kg q8-12hr

Diuretic Resistance (ie Furosemide>6mg/kg/d)

Torsemide
- (0.1mg/kg q12-24h;
- tot. daily furosemide dose x 0.1 q24h)

Hydrochlorthiazide
- 6.25-12.5mg q 24-48 hr PO

Amlodipine 0.1mg/kg q12h PO, titrate q1wk to 0.4mg/kg q 12 hr

**Monitor** Creatinine, electrolytes, SBP, Body wt, QOL

## Cardiac Cachexia

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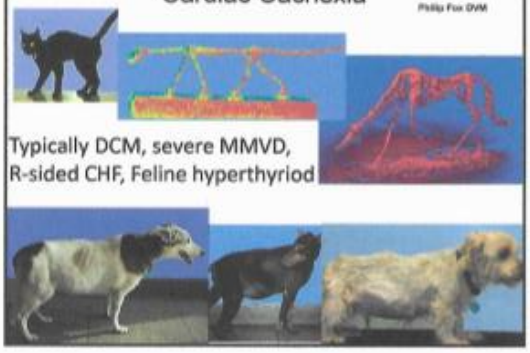

Typically DCM, severe MMVD, R-sided CHF, Feline hyperthyriod

## Chronic CHF Therapies

**First Line Drugs**
- Pimobendan
- Furosemide
- +/-ACEI
- +/- Spironolactone

**For Recurrent CHF**
- Torsemide
- Amlodipine

**For Comorbidities**
- Sildenefil
- Theopylline
- Hycodan

**Refractory Cases**
- Validate compliance
- Re-evaluate diagnosis
- Referral

## Arrhythmia Management Central Considerations:

**Does the arrhythmia:**

1. ***Trigger signs***? Syncope, weakness
2. ***Contribute to CHF***? Rapid AFib (>160bpm)
3. ***Have hemodynamic consequences*** (hypotension)
4. ***Pose risk of death*** (electrical instability)? V-Tach (rapid/sustained/ multifocal, R on T)

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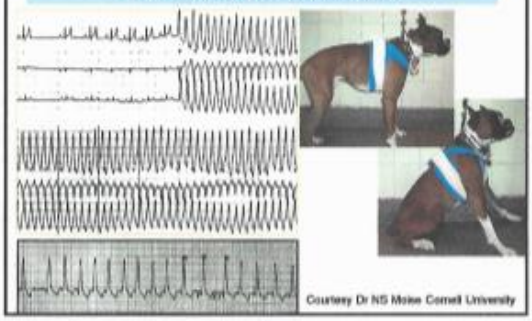
## Arrhythmia Management Clinical Assessment:



Courtesy Dr NS Moise Cornell University

"Sam" 3 year old boxer
Healthy with 1 "sibling," well vaccinated, current on heartworm, flea/tick prevention.

Courtesy Dr. Bruce Keene, NCSU

## Ventricular Tachycardia May Accompany CHF, other Diseases

For Unstable VT (electrical or hemodynamic) Treat IMMEDIATELY

Goals- Convert to sinus rhythm

IV Lidocaine
- Dog: 2.2 mg/kg IV (x4) 40-80 ug/kg/min CRI
- Cat: 1-2 mg IV slowly (10-30 ug/kg/min CRI)

Beta-blocker Esmolol (100-500ug/kg/min IV/CRI)
IV Procainamide 5-10 mg/kg IV slowly; 25-50 ug/kg/min CRI)
IV Amiodarone 5mg/kg IV bolus slowly
Oral Sotalol 1-2mg/kg q 12 hours
Oral Mexiltine 5-8mg/kg q 8 – 12 hours with sotalol

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- Resolve CHF (Furosemide, Pimobendan, ACEI)
- Treat underlying conditions
- Monitor ECG, electrolytes/ renal function, SBP

## Atrial Fibrillation: ECG Features

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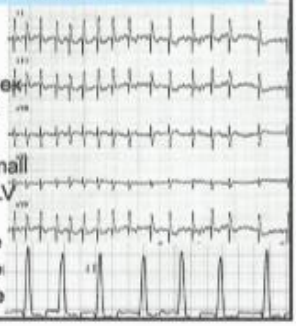
1. Rapid
2. Irregularly irregular
3. Variable QRS complex width and amplitude
4. No P Waves!
5. 'f' waves can be small
6. Large QRS when LV enlargement

**Ventricular rate = the most important facto when considering tre**



## Management of Atrial Fibrillation

HR < 140 = Monitor; HR >180: Treat IMMEDIATELY

**Begin IV Rx**
Diltiazem 0.1 mg per kg IV x 2-3 boluses
Diltiazem CRI 2-6ug/gk/min

Digoxin bolus (0.0025mg/kg IV)
Diltiazem bolus 0.1 mg per kg IV
Diltiazem CRI 2-5ug/gk/min

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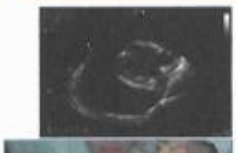
**To change from IV to oral**
Stop CRI x 6h, then Dilacor 2-5mg/kg PO q12h

**Begin as Oral Rx**
Diltiazem HCl 1-2mg/kg q 8h

Fox PR, 2009

| Reduce Ventricular Heart Rate (Atrial fibrillation/flutter) | | |
|---|---|---|
| Diltiazem | Diltiazem HCl<br>Dilacor | 1-2mg/kg q 8 hr PO<br>3-5mg/kg q 12 hr PO |
| Atenolol | | 1mg/kg q 12-24 hr PO |
| Esmolol | | .01-.05mg/kg IV<br>.025-.75mg/kg CRI |
| Digoxin | Tablet<br>Elixer | 0.01mg/kg q 12 hr PO<br>Subtract 10% |
| Amiodarone | | 10-30mg/kg/d PO loading x 4 d<br>5-15mg/kg/d PO maintenance |
| **Suppress Ventricular Arrhythmias** | | |
| Lidocaine | | 50-80 ug/kg/min CRI |
| Sotalol | | 40-80 mg q 12 hr PO |
| Procainamide | | 8-10mg/kg IV, 25-50ug/kg/min CRI |

## Cardiac Tamponade
## Pericardiocentesis

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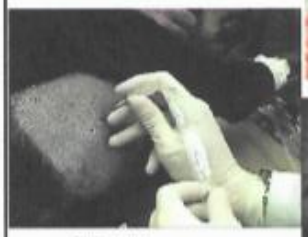
## Pericardiocentesis



Philip Fox DVM

# DIAGNÓSTICO POR IMÁGENES PARA PERROS Y GATOS CON TOS Y DISNEA. PARTE I & II.

**IMPORTANT CONSIDERATIONS 1. Chest radiography is generally the most useful single test to assess the coughing patient 2. A multimodal diagnostic approach is often required to provide a comprehensive evaluation. 3. Because respiratory distress has a myriad of causes, accurate diagnosis requires a systematic approach to evaluate the cardiorespiratory system, from the nares through the pharynx, large and small airways, lungs, interstitium, pleural space, pulmonary vasculature, and thoracic cavity. Clinical pathology, ECG, biomarkers, and other ancillary tests may provide useful information.**

**COUGHING 1. The cough results from sudden expiratory effort with noise coincident with expulsion of air. A number of factors can initiate the cough reflex throughout the upper and lower respiratory system (pharynx, larynx, tracheobronchial tree, and small airways). 2. Coughing may be occasional and of no clinical significance; in other cases coughing affects quality of life (to the animal and the owner), or is a harbinger of serious underlying disease. 3. Most coughs sound alike. More than one etiology may coexist.**

**DYSPNEA (RESPIRATORY DISTRESS) AND TACHYPNEA (RAPID BREATHING) 1. Dyspnea refers to difficult or labored breathing. Severity is judged by breathing effort, respiratory rate, rhythm, and character. Affected dogs display a standing or sitting posture with neck extended and elbows adducted. Cats rest on their sternum, may display nasal flaring, and with advanced states, open mouth breathing. 2. Tachypnea is increased breathing rate which may or may not be associated with a dyspnea. a. Common causes of acute dyspnea include trauma, pulmonary edema, pneumonia, airway obstruction, pneumothorax, pulmonary thromboembolism, pulmonary thromboembolism, and pleural space disease. Paroxysmal dyspnea suggests brady or tachy arrhythmias, especially with episodic weakness or syncope. Resolved dyspnea following cardiac drug therapy may suggest heart failure. b. Chronic dyspnea can occur from right-sided CHF, pulmonary hypertension, pericardial tamponade, broncho-interstitial disease, pleural effusion, anemia, neoplasia, hernia, and other causes. c. Inspiratory dyspnea (call stridor) suggests upper airway obstruction Expiratory dyspnea suggests lower airway obstruction, parenchyma lung disease, or effusion. Common causes include congestive heart failure, chronic obstructive lung disease, other parenchymal conditions, third space diseases or neuromuscular or musculoskeletal disorders. 3. Clients may confuse coughing with gagging, wheezing, labored breathing, and reverse sneezing. Some dogs wretch or vomit after coughing or vice versa and can be misinterpreted as gastrointestinal signs. Naso-pharyngeal diseases may induce gagging, stimulating cough; these cases may also exhibit nasal discharge, sneezing and snorting, ptyalism, or strider. Laryngeal diseases generally appears as strider.**

**CLINICAL APPROACH Accurate diagnosis is best facilitated when clinical signs are integrated with medical history, physical examination, radiographic findings, and results of multimodal imaging including as needed, as well as clinical pathology, since a broad range of conditions cause or contribute to coughing and dyspnea. The history and physical examination will help sort out the underlying cause, select cost-efficient diagnostic tests, guide treatment options, and assess response to therapy. Determining how to diagnose and manage the coughing or dyspneic animal and formulate differential diagnoses requires selecting the most optimal diagnostic or imaging technique to begin with, accurate interpretation to generate differential diagnoses, follow-up tests, and integration with the clinical data base.**

**2 KEEP IN MIND 1. Even if one particular condition appears to stand out from the others, a complete systematic search may identify additional or contributory factors. 2. Heart failure is not a disease, but a syndrome with highly variable clinical findings; no single feature is pathognomonic for CHF. 3. Integration of history, physical examination, laboratory and imaging tests help distinguish between heart failure and non-cardiac causes of respiratory distress.**

**DIAGNOSTIC IMAGING OPPORTUNITIES selecting the most optimal imaging modality helps screen for cardiopulmonary, systemic, and metabolic disorders and assist treatment response. Repeat radiographs (using the same radiographic technique and positioning) supply useful comparative data. Cross-sectional imaging of the chest, neck and head with CT, MRI, or ultrasonography identifies pharyngeal and nasal lesions and delineates mediastinal, hilar, pleural, in thoracic abnormalities. Diagnostic ultrasound is useful to assess cardiac structure and function, detect certain masses, evaluate for the presence and severity of pulmonary hypertension, help detect effusions, and provide information about lung parenchyma and infiltrates.**

**Role of Thoracic radiography Good quality chest films are essential for accurate diagnosis and effective management. The chest radiograph is the most useful first line diagnostic test if the animal can tolerate being positioned in VD or lateral recumbency. It portrays the cardiac silhouette, airways, and lung parenchyma and thus, provides unique information not obtainable by other imaging modalities.**

**Radiography- Technique Images should be exposed at peak inspiration. Poorly inflated lungs will appear increased in density- i.e., 'whiter'. Breed conformation, state of respiration, obesity, relative state of hydration, stage of cardiac cycle, positioning errors and effusions alter radiographic appearances. Over-exposure causes loss of important information; under exposure causes over interpretation of lung fields.**

**The patient should be correctly positioned (superimpose the spine and sternum on the VD/DV and adjust the animal in the lateral view so that the sternum and spine are equidistant to the table top, the costochondral junctions and ribs are superimposed, the**

**front legs are drawn forward). Align with the primary beam centered approximately at the 5-6th intercostal space. Oblique views will greatly distort the cardiac silhouette. Avoid motion artifact. The ventrodorsal (VD) radiograph is advantageous when pleural effusion is present, since free fluid gravitates along the paravertebral gutters, and does not superimpose over the heart- as occurs with the DV view.**

**Radiographic Interpretation One must consider technique, variations in organ size, and changes associated with breed, age, and body conformation.**

**Thoracic Wall The chest wall includes the spine, ribs, sternum and related soft tissues, and is framed by the caudal cervical vertebrae cranially, and diaphragm caudally. Evaluate symmetry in both views (altered by pectus excavatum, scoliosis, trauma).**

**Mediastinum These are potential spaces between cranial and caudal pleural cavities. In the cranial mediastinum lie the heart, ascending aorta, main pulmonary artery, cranial vena cava, thoracic duct, nerves, trachea, esophagus, lymph nodes, and thymus. In the caudal mediastinum are the posterior vena cava, trachea, descending aorta, nerves, and lymph nodes. Because the mediastinum communicates with fascial planes of the neck and retroperitoneal space, pneumomediastinum may result in contrast and thus, visualization, of mediastinal structures, as well as subcutaneous edema or pneumoretroperitoneum. Widened cranial mediastinum may result from lymphadenopathy, thymoma, megaesophagus, neoplasia, or abundant mediastinal fat.**

**Pleural Space This potential space located between the parietal pleura and visceral (pulmonary) pleura is occupied by the lungs. Pleural thickening may allow visualization of pleural fissures. Diseases which increase pleural space opacity include pleural masses and effusions. Occasionally, effusion is loculated or**

**3 trapped and involves the region of a cranial lung lobe or right middle lung lobe. Small volumes of free pleural effusion may cause blunting (rounding) of the costophrenic angles, accentuation of pleural fissure lines, and might be best visualized on the DV projection. Chronic effusions may cause pleural fibrosis. Pneumothorax decreases pleural space opacity. Overinflation can mimic pneumothorax.**

**Diaphragm Altered diaphragmatic symmetry may occur with diaphragmatic or peritoneal pericardial diaphragmatic hernia. Diaphragmatic hernia and pleural effusion may obscure the diaphragmatic border. Diagnostic ultrasound can help clarify these issues.**

**Abnormalities in Cardiac Size and Shape The cardiac silhouette is affected by breed, body conformation, and disease condition. Overestimating heart size is common with barrel-**

**chested dogs. In deep-chested dogs the cardiac silhouette appears to be 'tall.' With obesity, pericardial fat can cause the cardiac silhouette to appear larger. The cardiac silhouette many assume a more horizontal position in geriatric cats and in barrel shaped dogs. Pleural effusions will obscure the cardiac silhouette relative to the degree of effusion. Cardiomegaly usually results from congenital or acquired lesions causing volume overload (e.g. valvular insufficiency or shunts), pressure overload (e.g., valvular stenosis), myocardial disease (e.g., cardiomyopathy), pericardial disease, or respiratory conditions (e.g., cor-pulmonale). The vertebral heart scale (VHS) is a validated technique to assess and monitor cardiac size. This scale, however, varies amongst certain breeds with bracheocephalic breeds noted for comparatively larger VHS scores.**

**Radiographic Lung Patterns. Radiographic vascular patterns • Cranial lung lobe vessels assessed from the lateral projection show that arteries are dorsal and veins are ventral to related bronchi. • Caudal lobar vessels assessed from the VD or DV view show arteries are lateral and veins are medial to associated bronchi. • Normally, arteries and veins are approximately the same size. • Hypervascularity refers to arteries and/or veins which may be enlarged together in states of increased pulmonary blood flow (left-to-right shunts), high output states (thyrotoxicosis, severe anemia, fluid overload), left-sided CHF from severe mitral insufficiency or canine dilated cardiomyopathy (i.e., chronic pulmonary venous dilation with secondary pulmonary hypertension). • Increased pulmonary artery size and shape suggest pulmonary hypertension (usually dirofilariasis; occasionally, right-to-left shunts, idiopathic pulmonary hypertension). Pulmonary venous congestion is associated with left-sided CHF. • Hypovascularity (hypoperfusion or under circulation) creates thin arteries, veins and radiolucent interstitium and may accompany low cardiac output [shock, dehydration, caval syndrome, cardiac tamponade, acute blood loss, restrictive pericarditis, hypoadrenocorticism, severe myocardial failure), or right to left shunts Alveolar lung patterns • Occur when there is alveolar collapse or when alveoli are filled with blood, pus, or water. Typical findings include 1) patchy, poorly defined, increased densities with fluffy, indistinct margins which tend to coalesce, 2) air bronchograms, and 3) silhouetting of pulmonary vessels and bronchial walls by lung alveoli and interstium containing fluid. Alveolar patterns are typically fluffy and indistinct and coalesce. Cranioventral distribution is most associated with bronchopneumonia; perihilar distribution (in dogs) is most associated with CHF. Noncardiogenic edema usually occurs in dorso-caudal lung fields but can be variable. Diffuse or patchy alveolar distribution may occur with bronchopneumonia, pulmonary edema, hemorrhage (often lobar), and atelectasis. Interstitial lung patterns • Show up as increased nodular densities having distinct, well defined margins (e.g., neoplasia, chronic granuloma (e.g., structured pattern), or as nonspecific, localized or generalized interstitial "grayness" (e.g., non-structured pattern typical of pulmonary edema, pulmonary fibrosis, some neoplasia, interstitial pneumonia or hemorrhage), and vasculature and bronchi are blurred. Bronchial patterns • Result when bronchial walls become more opaque when thickened or surrounded by fluid or cellular infiltrate. Bronchial disease may progress to bronchiectasis that appears as thin-walled, cylindrical or saccular bronchial dilation with enlarged bronchial lumens that lose their distal tapering; emphysema appears as saccular or coalescing airways.**

**4 Esophagus A small amount of gas is often present in the mid thoracic esophagus. Caudal thoracic esophagus may be visualized in left lateral recumbency as a soft tissue or fluid filled structure. Aerophagia or anesthesia can result in a gas-filled distended esophagus.**

**Trachea Collapsing trachea (often also referred to as large airway disease) is a dynamic condition that also includes large airways.**

**Spinal vertebrae Older dogs often have narrowing of the thoracic intervertebral disc spaces.**

**Sternebrea Pectus excavatum causes cardiac shift (VD or DV view). Sternal malformations may accompany other congenital anomalies such as peritoneopericardial diaphragmatic hernia.**

**ROLE OF COMPUTERIZED TOMOGRAPHY CT can demonstrate various lung disorders: lung cancer, pneumonia, emphysema, bronchiectasis, inflammation or other pleural diseases, and diffuse interstitial lung disease. CT angiography evaluates arteries, veins, and cardiac structures. CT is capable of identifying intra and extracavitary masses. CT uses shorter anesthesia time vs MRI and is less liable to motion artifact associated with MRI. CT images can often be postprocessed to highlight structures of interest.**

**ROLE OF MAGNETIC RESONANCE IMAGING (MRI) MRI produces detailed images of organs, soft tissue, bone, and internal structures. It can assess masses including pulmonary neoplasia which cannot be assessed adequately with other imaging modalities (typically CT). It helps determine tumor size, extent, and the degree of metastasis, assess cardiac anatomy and function and its structures, determine blood flow dynamics, display lymph nodes, assess vascular and lymphatic malformations, and assess extracardiac abnormalities (vertebrae, ribs, sternum, chest wall lesions. MRI- resonance angiography (MRA) is helpful to assess vasculature. Disadvantages of MRI include its longer anesthesia time vs CT and is relatively uncommonly used for cardiac diagnosis.**

**ROLE OF ECHOCARDIOGRAPHY Color-flow Doppler, 2-dimensional and M-mode echocardiography provide safe, reliable, and noninvasive information on cardiac structure and function. The echo should never replace the thoracic radiograph when the former is indicated. Echo will not usually provide information about the cause of coughing, but certain findings if present can lend support to respiratory disease (eg, pulmonary hypertension), impingement by left atrial dilation of the mainstem bronchi that helps confirm radiographic findings. Standard 2-Dl and M-mode echocardiography evaluates cardiac chamber anatomy and motion and function.**

**Doppler Echocardiography Doppler echocardiography permits evaluation of blood flow velocity and direction within the heart and great vessels. The Doppler shift is greatly influenced by transducer frequency. The higher the transducer frequency (e.g., 7.5MHz vs 2.5MHz), the lower the velocity of blood flow which can be measured. Sound waves which strike RBC's moving toward the transducer are reflected off the RBC's at a higher frequency. This is displayed as a spectral recording above the baseline as a positive Doppler shift. Conversely, sound waves which strike RBC's moving away from the transducer are reflected back at a lower frequency. This is displayed as a spectral recording below the baseline as a negative Doppler shift. The intercept angle, theta influences the accuracy of Doppler echo**

**gradients. It represents the angle between the ultrasound beam and the moving red blood cells (RBC's). When Doppler echo beam alignment is parallel to moving RBC's, blood velocity is most accurately measured. If the intercept angle is wide, there will be a greater reduction in measured blood flow velocity compared with true velocity. Practically speaking, angles > 25o generally yield unacceptable quantitative estimates of velocity. In contrast, 2-D and M-mode echocardiographic beam should be perpendicular to tissue interfaces for ideal imaging. Estimation of Pressure Gradients • The gradient (i.e., pressure drop) across an obstruction may be calculated by the simplified Bernoulli equation which approximates the pressure gradient across an obstruction (e.g.,**

**5 across a stenotic valve): pressure gradient = 4 x velocity2. Pulsed-wave (PW) Doppler echo uses the same transducer to alternate between sending and receiving sound waves. This provides Doppler shift data selectively along the ultrasound beam at any given range (known as range resolution). PW Doppler echo has limited ability to measure high blood flow velocities as occur frequently with acquired or congenital valvular diseases. Continuous-wave (CW) Doppler echocardiography uses separate transmitting and receiving transducer crystals to enable ultrasound waves to be continuously transmitted and received. CW Doppler echo accurately measures high blood flow velocities but is unable to selectivity sample at a given location and lacks depth discrimination. The CW beam measures Doppler shift information all along the ultrasound beam. Color-flow (CF) Doppler echocardiography • Combines the anatomic image of the two-dimensional or M-mode echocardiogram with Doppler blood flow characteristics to create a spatially correct, dynamic image. Blood flowing towards the transducer is coded red, and blood flowing away from the transducer is coded blue. Blood flow velocity is indicated by the intensity of the color. Slowly moving blood is colored darker; faster moving blood is colored more brightly. Noninvasive assessment of diastolic function • Various indices assessed by Echo and Doppler echocardiography provide important information about left ventricular (LV) and RV status in certain patients. Diastolic dysfunction is common in heart disease, particularly in feline cardiomyopathy and older cats. Mitral inflow velocity patterns, tissue Doppler parameters, strain and strain rate assessments, and a variety of other modalities are increasingly measured in conjunction with standard Dopplerderived indices and parameters. Standard imaging planes (also called views) are designated based upon 1) transducer location (also called "windows"), 2) spatial orientation of imaging plane, and 3) recorded structures. For example, right parasternal long axis describes a view recorded with the transducer positioned on the right parasternal location and the imaging plane oriented parallel to the LV long axis. • Right Parasternal Location- Two principal imaging planes are:1) long-axis views, and 2) short axis views. M-mode echocardiogram is derived from either the long-axis or short axis views. When recording the M-mode from short axis views, one must transect the heart in the true minor axis, avoiding angled/oblique views. • Long-Axis Views- Two standard views include: 1) a four-chamber view with the ventricles (cardiac apex) displayed to the left and atria (cardiac base) displayed to the right, and 2) a LV inflow-outflow view obtained by slight clock-wise transducer rotation showing the LV outflow tract, Ao valve and root. • Short-Axis Views- These are obtained by rotating the transducer (and beam plane) 90o from long-axis views, then angling the beam from apex (ventral) to base (dorsal) to obtain a series of progressive views at LV apex, papillary muscles, chordae tendineae, mitral valve, and Ao valve, respectively. • Left Cranial Parasternal Location- This is located between the left 3rd and 4th intercostal spaces between the sternum and costochondral junctions. Long-Axis Views A series of views may be obtained with the beam plane oriented**

**approximately parallel with the long axis of the body and heart. • Left Caudal (Apical) Location- This location is close to the sternum between the 5th-7th ICS. • Left Apical Four and Five Chamber Views- A four-chamber view of the heart oriented vertically may be obtained with the left heart appearing to the right and right heart to the left, and the ventricles in the near field. A left ventricular outflow region may be brought into view by tilting the beam slightly cranial from the four-chamber view. A five-chamber view is denoted when all four cardiac chambers, both atrioventricular valves, and the aortic valve appear in one plane. • Left Apical Two-Chamber Views- When the beam plane is nearly perpendicular to the long axis of the body and parallel to the long axis of the heart, a two-chamber long axis view is obtained of the left atrium, mitral valve, and left ventricle.**

**Cage-side Lung Ultrasound • Increasingly, this has been shown to provide reliable and accurate assessment for diagnosing lung infiltrates including pneumonia and pulmonary edema in emergency settings. Advantages are its fast, non-invasive, and radiation-free method to provide ancillary diagnosis.**

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# LA HISTORIA Y EXÁMEN FÍSICO - LOS SECRETOS DEL ÉXITO. PARTE I & II

DO FIRST THINGS FIRST 1. Observe the dyspneic patient as soon as it is presented to determine if it needs immediate intervention. 2. Triage or stabilize, then, conduct a more comprehensive evaluation. 3. As soon as possible, ask owner- what their observations and concerns are – what is the emergency? 4. For non-emergency visits, start with a well-planned set of questions to learn a. What is the reason for the visit, b. Chief concerns of the pet owner?– onset of signs, their related chronology, and severity, c. Are there precipitating factors such as exercise, cough, excitement, etc., and c) has this pet been treated for this condition before? If so, with what drugs (and doses) and has been the response (or lack of response) to therapy. 5. Have any diagnostic tests been performed recently at other veterinary hospitals, do they have these results with them, or can they provide you with contact information to acquire this data?

FREQUENTLY ASKED QUESTIONS 1. What causes coughing and breathing distress? These have many etiologies, especially cardiopulmonary conditions, but everything from foreign bodies to allergies should be considered. a. Use a consistent, detailed diagnostic approach to generate differential diagnoses and guide diagnostic testing and risk assessment. 2. Is there one best test to start with? a. Not really. A chest radiograph is the best test to start with in general, when coughing is a major complaint (echocardiography is an insensitive test to identify and discriminate between causes of coughing) and it is also one of the first tests to consider when respiratory distress is present (assuming pet is stable enough). b. Lung ultrasound examination can be considered if the animal is too unstable for thoracic radiographs – or, performed in addition to chest radiographs. c. Comorbidities are common. A complete systematic search may identify additional or contributory factors even if one particular condition appears to stand out from the others,. 3. What is the best test to detect heart failure? a. Heart failure is not a disease, but a syndrome with highly variable clinical findings, and no single feature is pathognomonic. Diagnosing CHF is aided by integrating the history, physical examination, diagnostic imaging (most importantly, chest radiographs and echocardiography), and selected clinical pathology tests to distinguish between cardiac and non-cardiac causes of respiratory distress, or to identify and assess contributions of these conditions to clinical signs.

OVERVIEW Cough or respiratory distress are common presenting problems. Improving your medical history and physical examination skills will help you detect the underlying cause(s) of the symptoms, choose the most cost-efficient diagnostic tests tailored to that patient, assess prognosis, guide treatment, and gauge response to therapy.

Remember – cardiorespiratory distress has many potential causes. One must be thorough and consider conditions throughout the cardiopulmonary system. Comorbidities are common so don't stop your evaluation if you identify what appears to be a major disease or condition!.

The medical history and examination are the bedrock upon which all diagnoses and therapies are based. To be successful, one must adapt a consistent and systemic approach to evaluate the cardiorespiratory system from the nares through the pharynx, large and small airways, lungs, pleural space, mediastinum,

pulmonary vasculature, and heart. This will facilitate detection of masses, tumors, foreign bodies; certain parasites; toxins, inflammation, and irritants; congenital heart disease, CHF and arrhythmias.

HISTORY take your time and be thorough. The medical history helps reveal conditions and associated diseases causing clinical signs. It is also an indispensable aid to establish a trusting doctor-client relationship.

The history may capture irrelevant facts, but offers a glimpse of the client's emotional state, health care experience, observational skills, and also gives the client the satisfaction of being heard. Remember – the pet owner will not always volunteer all relevant information due to incomplete or misinterpretation of clinical signs, emotional status, and denial of serious illness). It is your role to uncover this information.

Signalment Many diseases have age, breed and sex predilections that assist diagnosis.

Past History Review any available diagnostic tests and procedures (radiographs, ECG's, echocardiograms, clinical pathology) from other veterinary practices before the visit if possible. Congenital heart disease may be implied if siblings, dam or sire are also affected. Drugs may have been already prescribed, and knowledge of doses, compliance and therapeutic response can offer valuable insights. Knowledge of past medical and surgical conditions, body condition, travel history, diet, and vaccination status provide important background data regarding the state of health and illness.

Comprehensive Current Cardiopulmonary History Ask the owner if they have noticed rapid breathing (tachypnea), dyspnea, excitement related respiratory induced breathing distress, exercise intolerance, syncope, coughing, or cyanosis. These signs can result from both cardiac and respiratory disease. The following historical information can imply certain disease states: 1. Dyspnea. □ Acute dyspnea can attend pulmonary edema, pneumonia, airway obstruction, pneumothorax, pulmonary thromboembolism, exacerbation of pulmonary hypertension, foreign body, trauma. □ Chronic, progressive dyspnea may occur with right-sided CHF, pericardial disease, bronchial or parenchymal lung disease, pleural effusions or pleural space diseases, anemia, or neoplasia. □ Inspiratory dyspnea suggests upper airway obstruction. □ Exertional dyspnea suggests lower airway obstruction and can also be associated with organic cardiac disease (e.g., CHF) or severe respiratory disease. □ Dyspnea at rest can indicate pneumothorax, pulmonary thromboembolism, pneumonia, CHF, or severe pleural space

disease (such as effusions).  Paroxysmal dyspnea in a pet without other respiratory signs may suggest brady- or tachyarrhythmias, especially when accompanied by episodic weakness or syncope.  Resolved dyspnea following cardiac drug therapy supports CHF.  Cats with pulmonary edema will display acute tachypnea, flaring nostrils, and open mouth breathing. 2. Cough  Most coughs sound alike and more than one etiology may coexist.  Dogs with pulmonary edema – ▪ Coughing will not always occur. ▪ Acute, edema-related cough or respiratory distress is generally a recent, rapidly progressive finding, often 1-2 days duration; coughing when occurs, is relatively soft, accompanies tachypnea at rest, and exertional dyspnea (in contrast to large airway disease, below). ▪ When edema is fulminate, soft, short coughs may yield small quantities of frothy, pink-tinged edema foam from the mouth or nares; affected dogs often extend the neck, are in duress, and gasp for air. ▪ Cardiogenic pulmonary edema frequently results from left-heart volume overload (mitral regurgitation due to chronic, myxomatous valve disease [or left to right shunting PDA, a rare occurrence]), or from dilated cardiomyopathy. ▪ Large airway disease induced-cough is harsh, resonant, 'dry,' 'goose honking'; chronic; paroxysmal; elicited by excitement/activity. Persists for years. Dogs usually have normal exercise capacity. Impingement of the left main stem bronchus by an enlarged left atrium from chronic mitral regurgitation may contribute to chronic coughing.

 Cats rarely cough with pulmonary edema- rule out asthma, bronchial disease, parasites 3. Syncope.  Can result from transient loss of consciousness from inadequate cerebral blood flow.  May follow coughing or excitement in small breed dogs with chronic, severe mitral regurgitation, who's paroxysmal cough is immediately followed by transient collapse ('cough syncope').  Other cardiac causes include severe sub-aortic stenosis (SAS) or pulmonic stenosis (PS), severe pulmonary hypertension (PHT), right-to-left cardiac shunts (tetralogy of Fallot, patent ductus arteriosus [PDA]), and tachy- or bradyarrhythmias (e.g., sick sinus syndrome or SA node dysfunction, high grade AV block), or hypertrophic obstructive cardiomyopathy (feline).  Noncardiac causes include upper and lower airway disease, pulmonary hypertension, and parasites such as heartworm and other long parasites. 4. Shortness of breath, weakness, exercise intolerance.  Decompensated heart failure causes lack of exercise ability, lethargy, or fatigue. So can obstruction to ventricular outflow, cardiac tamponade, severe SAS, PS, PHT, and arrhythmias. Other disorders can be causative including anemia, systemic and metabolic diseases (e.g., hypotension, hypoadrenocorticism), neuromuscular and orthopedic diseases, and a host of respiratory diseases.

PHYSICAL EXAMINATION Perform a complete review of all systems including HEENT (head, eyes, ears, nose, throat), neurologic, gastrointestinal, urinary, endocrine, hematologic, vascular, musculoskeletal, cardiac, and respiratory systems. • Inspect the patient at rest and during activity (assess respiratory rate and effort) • Check mucus membrane color and refill time • Examine the oropharynx (most require sedation for thorough evaluation) • Palpate the neck for tracheal conformity and masses • Look at the external jugular veins for distension or pulsation • Palpate the precordium (detect thrills; assess precordial thump and point of maximal impulse) • Auscultate the heart. Use both the bell and diaphragm (assess all four valve areas) • Auscultate all lung regions (over both sides of the thorax) • Palpate abdomen (assess for organomegaly, hydroperitoneum, masses) • Palpate femoral arteries. Assess pulse pressures (strength, regularity, contour [normal, hypokinetic, hyperkinetic]) • Assess body score. Note obesity or cachexia (cardiac cachexia is common in advanced acquired heart disease)

Auscultation Develop a systematic approach. Listen to both sides of the chest at the heart base and apex. Auscultation should not be limited to these sites only. At the heart base (left side) is the: 1. Pulmonic area- left 2nd to 4th ICS; 2. Aortic area- left 4th ICS just dorsal to the pulmonic area. At the left heart apex is the is the mitral valve area usually located at the left 5th ICS at the CCJ (may be more sternal in cats or change slightly with different breeds). At the right heart apex is the tricuspid valve area- right 3rd to 5th ICS at the CCJ (cat- right 4th or 5th ICS toward the sternum).  Palpate left and right precordium to detect thrills (vibrations) and assess the cardiac apex beat.  Apply the stethoscope bell with light pressure to collect low frequency sounds (S3 and S4, diastolic murmurs of (aortic or pulmonic regurgitation). Apply the diaphragm firmly to collect high frequency sounds (S1 and S2, systolic clicks, high pitched murmurs).  Begin at the left apex (S1 is normally loudest). Inch forward, then dorsally. Factors that increase heart sound loudness include a thin chest, sympathetic stimulation, thyrotoxicosis, and anemia; circumstances that decreases loudness include obesity, pericardial/pleural effusions, intrathoracic masses, pneumothorax, abdominal herniation into the chest or pericardium, and systolic failure.  Simultaneously palpate the femoral arterial pulse to help time events (a peripheral pulse occurs just after the 1st heart sound).  Pulse deficits suggest an arrhythmia.  Vagal maneuvers might slow heart rate during tachycardia.  Utilize selective listening. Focus on one part of the cardiac cycle at a time. Listen separately to the 1st heart sound (S1), then the 2nd heart sound (S2), the systolic interval, then the diastolic interval.  Determine the intensity, quality, and splitting of each sound.

 Listen to the systolic and diastolic intervals in order to detect additional heart sounds or murmurs.

Heart Sounds These are associated with the CARDIAC CYCLE which encompasses: A) contraction (systole) when the ventricles eject blood, and B) relaxation (diastole) when ventricular chambers fill.  Ventricular systole follows closure of mitral and tricuspid valves (related to S1). When ventricular pressure increases and exceeds aortic and pulmonic pressure, aortic and pulmonic valves open, causing rapid ejection of blood. Later is systole ejection is reduced and ultimately stops.  Ventricular diastole follows closure of aortic and pulmonic valves (related to S2).  Following the early diastolic filling phase, atrial contraction occurs, contributing up to 20-25% of ventricular filling. S1 occurs at the beginning of ventricular systole. S2 occurs at the end of ventricular systole. The period between S1 and S2 represents ventricular systole; that following S2 and up until the following S1 represents ventricular diastole.  Third (S3) and fourth (S4) heart sounds are referred to as gallop sounds.  S3 is low frequency, heard best with the bell, and is associated with early diastolic, rapid ventricular filling.  Causes include 1) high cardiac output states (anemia, hyperthyroidism, large left-to-right shunts [e.g., PDA, VSD), 2) rapid ventricular filling (severe MR, TR, AI), and 3) myocardial failure (DCM).  S4 is a low frequency sound associated with decreased ventricular compliance. It follows atrial contraction just before S1 and is called an atrial or presystolic gallop. A left-sided S4 sound is most commonly detected with feline hypertrophic cardiomyopathy, in less commonly, severe systemic hypertension, AS. Isolated S4 can be related to 2nd or 3rd degree AV block.  Ejection sounds and clicks are systolic high-pitched sounds heard best with the diaphragm.  Mid-systolic clicks can be associated with mitral valve prolapse.

Absent or Decreased Respiratory Sounds  Air or fluid in or around the lungs; fluid or organs occupying the thoracic cavity  Severe obesity  Over inflation (severe emphysema)  Reduced airflow to part of lung

Adventitious Breath Sounds  These abnormal sounds are heard over the lungs and airways.  Sounds fine and coarse crackles (sometimes called rales); wheezes (sometimes called rhonchi). ▪ Crackles – discontinuous, brief, focal or diffuse, popping sounds, most commonly during inspiration. They occur often when air opens closed air spaces (e.g. – pulmonary edema) ▪ Wheezes – continuous, musical, high or low pitched, usually accentuated during expiration (e.g. – narrow airways such as with lower airway disease)

Upper Airway Sounds  Stridor – high-pitched, wheezes like sound associated with blocked airflow in the pharynx or upper airway (e.g. – laryngeal paralysis, mass, foreign body)

References: 1. Sisson, D; Ettinger, SJ. The Physical Examination. In: Fox, PR; Sisson, DD; Moise, NS. eds: Textbook of canine and feline cardiology principles and clinical practice (2nd ed). Philadelphia, WB Saunders, 1999;46-64. 2. Fox PR, The History. In: Fox, PR; Sisson, DD; Moise, NS. eds: Textbook of canine and feline cardiology principles and clinical practice (2nd ed). Philadelphia, WB Saunders,1999;41-45.

# Acute Pancreatitis

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

## PATHOPHYSIOLOGY

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

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

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

ligament may be present. Gastric and duodenal ileus are common.

**DIAGNOSIS**

Animals with acute pancreatitis are usually presented because of depression, anorexia, vomiting, and in some cases, diarrhea. In severe cases shock and collapse may be present. In other cases the signs are very vague to almost nonexistent. Cats with mild pancreatitis are often presented with a vague history of being inappetent. Some animals with severe pancreatitis will exhibit signs of cranial abdominal pain and even a "praying" position. Pain may or may not be evident. Patients in shock may not show any signs of pain until perfusion is restored with fluid therapy. Occasionally the only clinical signs the patient exhibits are from systemic complications. Physical examination should include careful auscultation, palpation and visual inspection of the animal. Lack of gastrointestinal sounds is consistent with ileus, which may be localized or generalized. The right and left cranial abdominal quadrants should be individually evaluated using palpation underneath the rib cage. Large dogs may need to have their front feet placed on a stool or chair to shift abdominal contents caudally. The umbilicus should be closely inspected since masses involving the umbilicus have been associated with pancreatic neoplasia. A rectal examination should be performed to evaluate for evidence of diarrhea as well as the presence of blood. Vomitus should also be evaluated for blood.

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

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

Ultrasonic interrogation of the cranial abdomen will be helpful but is operator

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

**MEDICAL MANAGEMENT**

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

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

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

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

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

Nutritional support ideally should begin within 12 hours of admission. Partial parenteral formulas can be given by peripheral catheter. ProcalAmine (B. Braun Medical), which is a hyperosmolar solution containing 3% amino acids, 3% glycerol and maintenance concentrations of electrolytes, is an excellent partial parenteral nutritional support product. It is

given at a rate of 0.5 mL/kg/hr as a constant rate infusion. Maintenance fluids to which 3% amino acids and 3-5% dextrose are added can be used instead of commercially prepared solutions.

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

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

**INDICATIONS FOR SURGERY**

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

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

# Toxicologic Emergencies

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

## HISTORY AND CLINICAL SIGNS:

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

## DIAGNOSIS:

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

## TREATMENT OVERVIEW

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

## INDUCING VOMITING

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

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

## GASTRIC LAVAGE AND ACTIVATED CHARCOAL

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

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

## SKIN CONTAMINATION

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

**AIRWAY AND BREATHING**

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

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

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

**CIRCULATION**

Patients that are hypotensive may require crystalloids and colloids for resuscitation. Animals that are significantly anemic should receive red cells. Patients with coagulopathies should received fresh whole blood (if also anemic) or fresh frozen plasma. Patients that are hypoalbuminemic may require a combination of synthetic colloid and albumin replacement depending on the serum albumin concentration. Blood pressure and perfusion status should be returned to normal. Some toxins may cause hypotension by depressing cardiac function or by causing excessive vasodilation. In this case positive inotropic drugs, □□blockers, antiarrhythmics, or vasopressors may be indicated depending on the toxin. Patients that are dehydrated should have their fluid deficit calculated and administered over an 8-12 hour period.

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

Severe bradycardia (heart rates less than 50-60 beats per minute) with concurrent heart blocks, or bradycardia associated with hypotension should be treated with atropine or glycopyrrolate. Bradycardia

associated with normal to high blood pressure should not be treated with anticholinergic drugs.

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

**SEIZURE MANAGEMENT**

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

**MANAGEMENT OF STUPOR AND COMA**

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

Mannitol may be useful in helping treat cerebral edema.

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

**MANAGEMENT OF TREMORS**

Tremors are best controlled by use of intravenous methocarbamol, diazepam or midazolam. Constant rate infusions may be required to control the tremors. Dosing should be adjusted to ensure the patient does not become anesthetized. If general anesthesia is necessary to control the motor movement the patient should be intubated to help protect the airway.

**MANAGEMENT OF TEMPERATURE ABNORMALITIES**

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

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

**ANTICOAGULANT RODENTICIDE**

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

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

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

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

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

oral medications the vitamin K1 can be given orally.

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

**PYRETHRIN**

*Source:* Insecticides especially flea products

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

*History and Clinical Signs:* Pets have usually been exposed to topical or premise spray products. Clinical signs include depression, muscle fasciculations, salivation, vomiting, bronchospasm and ataxia.

*Treatment:* Skin decontamination should be performed if this was the route of exposure. Vomiting can be induced if the patient ingested the toxin within the previous 1-2 hours and the animal is neurologically stable and able to protect its airway against possible aspiration and the product did not contain petroleum distillates. Atropine can be used to control salivation as long as the patient is not tachycardic. Most patients recover within 24-48 hours with supportive care.

**METALDEHYDE**

*Source:* Slug or snail bait

*Mechanism of Toxicity:* Unknown

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

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

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

**GARBAGE**

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

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

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

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

**CHOCOLATE**

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

*History and Clinical Signs:* Vomiting and diarrhea may be present that are not direct causes of the theobromine but are related to the dietary indiscretion. Pancreatitis may be seen depending on the type of chocolate that was eaten. Clinical signs include cardiac abnormalities (tachycardia, arrhythmias), central nervous system excitement (hyperactivity, tremors, seizures), panting, and urinary incontinence.

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

**ETHYLENE GLYCOL**

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

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

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

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

*Treatment:* Vomiting should be induced within 30 minutes; after that time it is not likely to be effective due to the raid absorption rate. Activate charcoal is not effective. Treatment includes treatment and monitoring as for any renal failure patient. A central line and a urinary catheter are advised in order to be able to monitor

central venous pressure and urine output respectively. Primary treatment involves administration of an antidote, either ethanol, which acts as a competitive substrate for alcohol dehydrogenase, or 4-methylpyrazole, which is an alcohol dehydrogenase inhibitor. Ethanol has many side effects; therefore; 4-methylpyrazole is preferred. The prognosis is excellent if dogs are treated with 4-methylpyrazole within 5 hours and cats within 3 hours. Dialysis is always advised but is probably unnecessary if 4-methylpyrazole is being administered early. Dialysis is continued until the ethylene glycol test is negative which usually requires 24-32 hours of continuous dialysis.

**ETHANOL**

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

**ACETAMINOPHEN**

*Source:* Prescription and over-the-counter drugs

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

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

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

**STRYCHNINE**

*Source:* Pesticide

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

*History and Clinical Signs:* Early signs included anxiety and restlessness. Tonic muscle contractions of the extensor muscle groups become evident. A risus sardonicus

is evident from facial muscle contraction. Muscle contractions are worsened by external stimuli. Tetanic contractions of the respiratory muscles can lead to apnea.

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

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

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# ASSESSMENT OF SUFFERING IN ANIMAL CRUELTY CASES: A NEW ROLE FOR VETERINARIANS

**SUFFERING**

Many animal cruelty laws animal suffering as an element of the crime, sometimes defined as 'unjustifiable' or 'unnecessary' in the statute. It is the degree of this suffering that can determine the level of charges filed and impact the sentencing. There are five freedoms recognized for animals from the Farm Animal Welfare Council in 2009 that provide the basis for animal suffering: freedom from hunger and thirst; discomfort; pain, injury or disease; to express normal behavior; and from fear and distress. Veterinarians are considered the experts on the animal's condition, including pain and suffering (see Pain section below), and are often asked to provide time estimates for the length of any negative or adverse conditions, physical or environmental, which are a component of the length of suffering. In addition to pain, it is important to recognize there are other forms of suffering that have can have mental and physical effects including stress, boredom, distress, and emotional maltreatment.

Suffering has been defined as different unpleasant states that one would avoid or remove themselves
from if they could. Suffering also has been defined as an unpleasant state of mind that disrupts the quality of life. This mental state is associated with unpleasant experiences, including pain, malaise, distress, injury, and emotional numbness and must be either severe or prolonged. Causes of suffering include hot or cold environments, lack of food or water, confinement, space restriction, lack of social companions, lack of stimulation, injury, and disease. There are physiological and behavioral manifestations of suffering as well such as increased corticosteroid levels (stress), respiratory rate, heart rate, or blood pressure; vocalizing; and the sudden release of urine or bowels (fear reaction). These manifestations must be contextually evaluated, as some of these same responses can result from pleasurable experiences.

Animals may have severe or prolonged experiences of fear, pain, hunger, boredom, thirst, and so on. Suffering can be further defined by looking for evidence that the animal attempted to or would have taken steps to change the situation, either by escaping or to gain access to something wanted or needed (Dawkins 2005). Comparison of the animal's behavior after removal from the situation can reveal the extent of the suffering. It should be considered that the animal may be too weak to exhibit the behavior of escape, avoidance, or to otherwise seek change.

Learned helplessness may occur in animals that have been subjected to prolonged abuse. Learned helplessness refers to a condition in which the animal will not escape from a negative situation even when able to do so. This occurs in animals that have been subjected to prolonged abuse without any opportunity to escape or effect change. They "learn" that they are "helpless" to change their situation. Eventually, when presented with an opportunity to escape or effect change, the animal will not attempt to do so.

**STRESS**

Stress may be defined as an abnormal or extreme adjustment in physiology and/or behavior in response
to prolonged or intense aversive stimuli. To recognize stress, the veterinarian must have an understanding and appreciation of the physical, psychological, and behavioral needs of the animal. These needs are affected and determined by the species, gender, reproductive status, age, and environment. They include appropriate space, ability to locate to a safe area, light, suitable bedding, environmental enrichment, sanitary environment, appropriate food, and clean water.

An animal's response to stress is usually to develop coping behaviors such as hiding or escaping. The
animal's ability to cope varies with the individual animal and type of stressor. The unpredictability of the stressor may induce chronic fear and anxiety. Depending on the severity of the stressor and the

animal's coping ability, the animal may adapt over time and the stress response may no longer be activated.

The psychological impact of stress on housed cats is primarily caused by the lack of opportunity for active behavioral coping responses. The impact of the stressor is directly related to the degree the cat can exert a behavioral response to the stimulus. The most severe stress response is when the stressor is perceived as uncontrollable or inescapable. This is especially important in hoarding situations and whenever cats are housed with unfamiliar dogs.

Several factors affect the stress response, including novelty, severity, predictability, chronicity, and duration. The animal's prior experiences, socialization, personality, and genetics affect the individual stress response. Multiple stressors can have a cumulative effect. The physiological effects of stress are compounded by poor nutrition.

**Physical Manifestations of Stress**

Acute stress causes the release of epinephrine and norepinephrine through the activation of the sympathetic branch of the autonomic nervous system. This catecholamine release can be triggered by several different stimuli in dogs and cats. However, in cats, apprehension is the most potent stimulus for its release. Triggers for apprehension can be anything unfamiliar to a cat presented in any form, including visual, auditory, and olfactory stimuli.

Persistent stress causes the activation of the hypothalamic-pituitary-adrenal (HPA) response pathway
causing glucocorticoid secretion. Under chronic stress, the glucocorticoid secretion reduces over time and the animal actually becomes more sensitized to new stressors. When a chronically stressed animal is stimulated by a new stressor, the HPA system responds. Chronic activation of these pathways can have deleterious effects on the body, including insulin resistance, mental depression, increased susceptibility to infection, peptic ulcers, decreased reproductive capacity, promotion of dehydration, and sudden death. The pathology of disease of the urinary bladder, gingiva, lung, gastrointestinal tract, and skin may be affected by the increased endothelial and epithelial permeability caused by the stress response pathways. The metabolism may be altered because of chronic stress, resulting in weight loss, lack of normal growth, and abnormal behavior that may be harmful to the animal.

Acute or chronic stress can have potentially irreversible effects on the animal's health. Stress has behavioral, endocrine, and immune effects. Higher levels of prolactin are seen in dogs with chronic stress and high anxiety while lower levels are seen with acute fearful and phobic events. Hyperglycemia and increased lactate are seen in stressed cats. Acute stress, including fear and anxiety, can result in decreased appetite, anorexia, vomiting, diarrhea, and/or colitis along with anxiety and displacement behavior. Recurrent or chronic stress results in alteration of the immune system, inflammation, increased sensitivity to pathogens, cellular aging, neurologic disease, and respiratory disease (especially cats). Acute or chronic stress can cause urinary tract disease due to altered bladder permeability and is linked to feline interstitial cystitis. It can also cause dermatologic conditions as a result of increased immune cells in the skin, increased opioid levels which potentiate pruritis, and increased epidermal permeability. Chronic stress can alter the bacterial flora, decreased gastric emptying time, increased colonic activity, and increased intestinal permeability to antigens. This can result in inflammatory bowel disease, gastrointestinal reflux, heartburn, and stress induced hypersensitivity. Anorexia, pica, polyphagia, and polydipsia may also be seen. Behavioral manifestations of chronic stress include anxiety disorders, panic disorders, phobias, and compulsive disorders.

Stress can produce primary physical injury or secondary to stress induced behaviors. Escape behaviors can result in worn teeth from chewing on tethers or barriers due separation anxiety, phobias, and territory or barrier frustration. Stress can produce aggression and trauma such as maternal cannibalism. Frustration or conflict may lead to displacement behaviors that are out of context which may progress to compulsive disorders, such as self-mutilation, if the animal cannot achieve homeostasis. Anxiety can decrease the left brain perfusion that improves with behavior combined with anxiety drug therapy.

**BOREDOM**

Animals have an innate need to interact with their environment, explore, and play. Juvenile animals are
prone to develop arousing behavior that is part of the cognitive and neurological maturation. Confinement and lack of stimulation lead to another form of suffering, i.e. boredom, which has physical and psychological impacts on the animal. Prolonged confinement can lead to behaviors of self-mutilation, aggression to other animals, tenseness, restless, agitation, coprophagy, over-grooming or fur pulling, and licking, sucking, or chewing at cage surfaces. A study was conducted on the effect of feeding enrichment using the Kong™ feeding toy with kenneled military working dogs in the U.K. It was found that there was no negative affect on the overall working ability, health or behavior. The study did find there was a significant increase in the dog's ability to learn from being rewarded. Furthermore, the dogs showed an increase in cortisol levels when the feeding toy was removed and a decrease when it was re-introduced. To recognize boredom, one must understand that the criteria are fluid and changing for the animal. The degree of boredom for an animal is most evident when one observes the behavior after the environment is changed to enriched conditions.

**DISTRESS**

Consideration should be given to the distress of animals as a form of suffering. Distress may be conceived as the unpleasant affective state, akin to or the same as anguish, resulting from an inability to control or otherwise cope with or adapt to the unpleasant affect generated by altered or threatened homeostasis. Examples of distress are boredom, pain, thirst, hunger, loneliness, fear, and any function of how an animal copes with the unpleasant affect. The term 'affect' refers to any feeling, emotional or physical in origin. Evidence of unpleasant emotions in animals are fear, phobias, anxiety, separation anxiety, loneliness, boredom, frustration, anger, grief, helplessness, hopelessness, and depression.

**EMOTIONAL MALTREATMENT**

Emotional maltreatment refers to the link between emotional states and physical health. Emotions can
cause distress, anguish, and suffering. Long-term problems associated with emotional maltreatment may be separation anxiety, decreased learning, depression, difficulty with social interactions, or even physical manifestations of illness.

Because the idea of maltreatment in animals is analogous to children, the terminology associated with child maltreatment may be used. The US Department of Health, Education, and Welfare defines maltreatment as actions or inactions that are neglectful, abusive, or otherwise threatening to an individual's welfare. Note that the term maltreatment includes both neglect and physical abuse. Maltreatment should be considered from the perspective of the victim, i.e. the animal, in which the animal is harmed or at risk of harm.

Emotional suffering is generated along the same or similar pathways for physical pain where the same
drugs alleviate emotional and physical pain (see Pain discussion below). Studies have been conducted to determine which hurts more between physical and emotional pain. When the animals are presented with a choice to endure or relieve physical pain in response to separation anxiety, i.e. emotional suffering, they chose to endure the physical pain to alleviate the emotional suffering. A study of capuchin monkeys found they chose social companionship over food. There are reports of cats that have shown they will continue to enter a burning fire to retrieve their kittens despite enduring repetitive physical harm.

Traditionally, neglect is considered to be a passive act or act of omission by the caregiver to provide basic physical and emotional needs of a dependent being. Most animal cruelty laws include neglect as a form of animal cruelty. It is estimated that greater than 80% of cruelty cases are classified as neglect. Commonly, neglect has been characterized by a lack of intent considered a result of ignorance or poor judgment. However, a reasonable person standard should be applied which refers to what a reasonable person would think and do in a given situation. For example, when someone does not provide food or fresh water for an animal, a reasonable person would expect the result of death, or at minimum physical harm, due to imposed starvation and/or dehydration.

Sometimes proving intent by the abuser is required to meet the animal cruelty statute in certain states.

Physical and emotional abuse is considered an active maltreatment characterized by intent to harm. These overt acts or acts of omission also are characterized by the caregiver's knowledge that the action or inaction will result in harm to the animal.

There are four categories of maltreatment: emotional neglect, physical neglect, emotional abuse, and physical abuse. There can be crossover of neglect to abuse depending on the caregiver's intent and the animal cruelty laws.

**Emotional Neglect:**

An emotional need may be defined as any need that is signaled by an emotional affect. The emotional needs of animals have similar properties as physical needs and are shared regardless of species, gender, etc. The physical needs of animals include food, water, shelter, temperature regulation, oxygen, health care, and exercise. Failure to meet both emotional and physical needs of an animal will result in harm to the animal.

**Emotional Abuse:**

Emotional abuse may be defined as the deliberate infliction of emotional distress on another individual. It includes acts of commission or omission that have caused or may cause serious behavioral, cognitive, emotional, or mental disorders. A study was conducted in dogs on the physiological reactions to fear provocation, specifically assessing fear of floors and fear of gunshots. The dogs with fear of floors demonstrated higher heart rates than the fearless group. In the gunshot fear group, the study found elevations in heart rate, hematocrit and plasma cortisol, progesterone, vasopressin, and beta-endorphins than the fearless group with cortisol and progesterone the most drastically increased.

**Physical Abuse:**

Physical abuse can cause emotional maltreatment if it causes emotional distress. There is evidence that emotional maltreatment produces harm that is often worse than physical abuse. This is seen in children with long-term effects resulting from emotional maltreatment with similar findings in dogs. The harm depends on the animal's coping ability to the event. In animals, the long-term consequences may be seen as behavioral problems under otherwise normal conditions, similar to post-traumatic stress syndrome in humans.

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# FOLLOW THE CLUES: SUSPICIOUS INDICATORS AND COMMON FINDINGS OF ABUSE

## INTRODUCTION AND CONSIDERATIONS

There are numerous situations that may qualify as animal cruelty depending on the governing laws: starvation, dehydration, untreated medical problems, failure to provide relief from extreme environmental conditions, hoarding, embedded collars, physical or sexual abuse, poisoning, animal fighting, and so on. Physical abuse cases often have neglect as a component of the crime. Animal cruelty is basically any action or lack of action that results in unjustifiable or unnecessary suffering, illness, injury or death of an animal. It is important that veterinarians have an understanding of the animal cruelty laws to they can respond appropriately and assist the investigators and prosecutors in the potential case.

There are several considerations to first determine if the injury is a result of accidental versus non-accidental causes. The veterinarian must draw on their own experience with known accidental injuries and compare those findings to the evaluation. The information provided by the caregiver and/or the investigator is critical to properly evaluate a possible case of cruelty, whether the animal is alive or deceased. A necropsy should never be performed without investigation findings and crime scene information including photographs of the scene. The environment and husbandry for the animal directly affects the health of the animal and must be analyzed along with physical exam findings. Animal cruelty should be suspected in every case where the history, crime scene findings, and environmental conditions do not support the exam findings. Aberrant findings should not be disregarded for they are often the key piece of evidence that the injuries sustained are non-accidental. The goal of reporting suspected abuse is for an investigation to be conducted. It takes all parties to fulfill their role in the investigation to prove and disprove possible elements of the crime.

When examining an animal, there must be full documentation of all the findings. The exam should include written and photographic and/or video documentation. Make sure the evidence is photographed in situ prior to collection. All notes, recordings, photographs, and reports are considered evidence and will be reviewed by the investigator, prosecutor, defense attorney, and judge. Every effort should be made to collect evidence prior to treatment to prevent contamination of the evidence. After treating the animal, it is vital to document the process of the animal's recovery including weight gain and by repeating appropriate tests. As the animal recovers, the medical records and/or reports should include the timelines for treatments and assess the reasons for the animal's recovery.

### Forensic Necropsy Procedure Considerations

The necropsy procedure involves a process of documentation and examination of the external and internal body. Photography starts with the body still in the package or bag. Photos with and without a photo scale should be taken of any evidence where the size is important. The external body should be examined for trace evidence, foreign material, bodily fluids, and obvious area of trauma. External wounds or evidence of injury such as contusions should be shaved and measured. The necropsy may be performed in lateral or dorsal recumbency. The skin should be reflected to identify underlying injuries. The dissection, and opening of body cavities should be done based on the apparent injuries avoiding major blood vessels which can contaminate the field and distortion or alteration of wounds. Flap dissection should be used to analyze and follow wound tracks through tissue such as gunshot wounds or sharp force penetrating injuries. It is important to consider skin tension lines and avoid manipulation of skin or wound tracks which can distort the weapon characteristics. It is best to examine the skin and soft tissue wound characteristics first without manipulation and then with gentle manipulation to restore skin tension. Scotch tape may be used to re-appose the wound edges to discern blade characteristics such as serration. The use of a necropsy exam form and diagrams are recommended to ensure complete examination and documentation. The form also corresponds to the forensic report form making report writing easier. The deceased animal intake form is used to document case information when receiving the body. The evidence-chain of custody log and photo log are forms that should be used.

**TYPES OF ABUSE**

**Neglect:**

The legal definition of neglect varies by jurisdictions. It has traditionally been defined as a passive act or the lack of action that results in the neglect of an animal. It is critical for the veterinarian to understand the nuances of the laws including local, state, and federal, in order to properly assist the investigator and prosecutor on the case. Neglect can be anything the causes the animal to suffer. It can also be defined as anything that is inadequate or inappropriate for the animal taking into account environmental conditions, the species, gender, size, and age of the animal. Neglect can take many forms that negatively impact the animal's physical and mental well-being. These include the lack of or inappropriate: shelter, food, water, bowls for food and water, tethering, preventative health care, medical treatment, embedded collars, and heavy chains.

Another consideration in neglect is the mental well-being of the animal in the form of boredom, distress, and emotional maltreatment. Consideration must be given to the species, gender, breed, and age of the animal to determine what the mental needs of that particular animal are. Confinement and lack of stimulation leads to another form of suffering, boredom, which has physical and psychological impacts on the animal. The degree of boredom for an animal is most evident when one observes the behavior after the environment is changed to enriched conditions. Distress manifests as a result of how an animal copes with an unpleasant affect (physical or emotional) such as boredom, pain, thirst, hunger, loneliness, or fear. Evidence of unpleasant emotions in animals are fear, phobias, anxiety, separation anxiety, loneliness, boredom, frustration, anger, grief, helplessness, hopelessness and depression. Emotional maltreatment refers to the link between emotional states and physical health. Emotions can cause distress, anguish, and suffering. They can be associated with long term problems such as separation anxiety, decreased learning, depression, difficulty with social interactions, or even physical manifestations of illness.

**Starvation:**

Starvation is the process of the body consuming itself, both fat and protein, which causes vital members of the body to cease to function. It causes immune suppression making the animal more susceptible to infections. You need to get the initial body weight and record the body condition score. It is also important to show the subsequent weight gain in response to treatment, especially if the only treatment was giving the animal food and water. If the animal is wearing a collar and it is loose then you need to measure the circumference of the neck and the collar for comparison. This is especially important if the animal was tethered outside because at some point that collar had to fit or the animal would have got loose. If the collar is loose enough that the dog could slip out, then you have to question what prevented the animal from escaping. Usually it is because the animal was too sick or weak to escape and seek food and water.

It is important to run bloodwork on these cases as soon as possible after they are impounded and preferably prior to initiating treatment. Blood may be drawn at a shelter by the staff and then held pending the veterinarian's instructions. Findings on labwork in starvation cases depend on secondary infection and the state of starvation. They may include: prerenal azotemia, anemia, elevated liver enzymes, increased total protein, increased globulin, low albumin, very high CPK, monocytosis, leukocytosis, stress-leukogram, ketonuria, and electrolyte abnormalities. Low glucose may or may not be seen – the body is doing everything it can to maintain the blood sugar. In the terminal phase of starvation the glucose may be low. For cases of animals that have not eaten for 4-5 days or prolonged periods of time, inanition, it is possible to see slightly low AST, slightly low Calcium and/or a slightly elevated Total Bilirubin.

**Burns:**

Burns may be caused by a variety of methods including chemicals, thermal, scalding, and fire. The appearance of the burn provides several clues as to the cause of the burn. Burns are usually a patterned injury that reflects the cause of the injury. It is the proper interpretation of the burn patterns can reveal the exact nature of events which may support or refute the history. A determination of where the burn started on the body may be made when there are more severe burns confluent with more superficial burns. Splash or spill burns have trickle-like areas that are usually more superficial than where the liquid first contacted the body. A burn pattern that is evenly distributed with the same degree of injury is indicative of an even rate of burn.

**Blunt Force Trauma:**

With every animal cruelty case, one must consider the animal suffered blunt force trauma in addition to any other injuries. Contusions are very hard to see on the skin surface of animals unless there is light colored skin and the fur is parted all over the body to inspect for discoloration. It can take hours for bruising to show up on a live animal so re-inspection of the body should be done every few hours. In deceased animals, the skin should be reflected all over the body to reveal subcutaneous hemorrhage. Sometimes the hemorrhage is in the deeper muscle next to the bone, such as the rib cage, and does not extend to the subcutaneous layers especially if the survival period was very short after the injury. Careful dissection of the muscle layers can reveal the deeper evidence of trauma. The size and shape of the contusions can help determine what was used to cause the injury. There may be a denser area of hemorrhage with seepage into the surrounding tissues. It is the denser area that provides the clues to the cause. Petechiae may be seen on the pinnae and horizontal ear canal with blunt force trauma to the head. The petechia in the ear canal is a unique finding in dogs and cats due to the shape of their ear canal. Frank hemorrhage may be seen inside the ear due to a ruptured tympanic membrane. The common rule-out for any hemorrhage is clotting disorders which have a wide variety of causes so a full work-up should be conducted.

The causes of non-accidental injury are limited only by the perpetrator's imagination. To try and surmise the cause and/or weapons used, one must first examine the body for injury patterns. These will give the greatest clues as to the cause of injury. When weapons are used, either in penetrating or non-penetrating injuries, a corresponding weapon pattern may be found on the body. These can be in the form of distinct bruising, skin injury, or damage to bones. If a significant time period has elapsed since the injury occurred, the bruising may spread obscuring any distinct weapon patterns. The skin injury may present as patterned hair loss due to crushing forces, abrasions, or full-thickness defects. Bone fractures are caused by certain physical forces. Each fracture must be evaluated considering the type of force required to produce that particular type of fracture. In addition, the type of bone, the age of the animal, growth plate closures, the size of the animal, the density of the bone, and the location of the fracture are all factors in determining accidental versus non-accidental causes.

**Sexual Assault:**

In these cases you need to inspect the perineal area for evidence of trauma, abnormal swellings, contusions, or abrasions. Look for painful defecation, rectal or vaginal bleeding or abrasions. Use a UV light source to examine the fur and perineal area for bodily fluids and take samples. If the fluid is dried, moisten a cotton-tip applicator with distilled water and swab the area. Always take an additional control sample adjacent to the area of interest. Perform a vaginal exam to check the mucosa and cervical area for bruising or trauma. Take sterile swabs of the vaginal area for semen and STD's. Make a separate slide and examine the swab sample for sperm. Swab the gums, teeth and mouth area for possible DNA.

**Gunshots:**

There are seven main objectives when analyzing gunshot wounds: determining entrance and exit wounds, retrieving gunshot residue, retrieving the projectile, retrieving any bullet cartridge or casing, determining trajectory, determining gunshot range, recording injuries. There are some basic rules for determining entrance and exit wounds. In animals there is the advantage of fur being forced in or out, respectively. In general, entrance wounds are smoother and smaller than exit. Entrance wounds may have singed fur or skin indicating direction of travel. Abrasion rings may be found at entrance wounds where the bullet rubs raw the edges of the hole. The ring may be concentric or eccentric if the bullet entered at an angle causing a "bunching up" of skin. Entrance wounds may also have micro-tears at the edges if caused by a high velocity gun. If the bullet entrance is at an area of thick skin or it is a distant gunshot to the head the wound will usually have a stellar appearance. Contact gunshots produce splintered or star-shaped wounds because the bullet has a degree of wobble when first exiting the barrel of the gun. Exit wounds are usually larger and more irregular. They can be stellar, slit-like circular, crescent or completely irregular. "Shored" exit wounds have abraded margins because the skin was next to something firm when the bullet exited causing abrasions. Exit wounds through tight skin such as the head tend to be larger. Those through loose skin can be small and slit-like. When retrieving projectiles, care should be taken not to cause damage that will interfere with the rifling marks on the surface of the bullet. These marks can be matched to the gun it was fired from. Use your fingers or cotton wrapped forceps to grab the bullet. In shot gun injuries get a representative sample of the projectiles and any wadding if present. Place items in a paper envelope and then a small box for protection. Ejected cartridges and casing may contain fingerprints. Exercise caution not to compromise their integrity during collection. All animals with gunshot injuries should have full body radiographs. An exit wound does not necessarily

mean the bullet exited. The bullet could have propelled bone fragments and tissue out then rebounded back. Bullet emboli are possible.

Photograph each bullet wound before and after cleaning and shaving the wounds taking long range and close up views. Assign a number to each entrance wound and describe the location with a measurement to a landmark such as nipple, midline and the animal's muzzle. Describe the appearance of the wound, path of the missile, injuries produced and exit or lodgment site. Save any powder grains and describe such as flake, ball or cylindrical. Shave and note powder tattoo patterns, abrasion rings and muzzle imprints. When taking measurements, use a clock reference identifying the dorsal spine or head as 12 o'clock. Record the injuries created by the missile path.

**Considerations for Accidental Causes:**

For all trauma cases, the most common rule-outs are motor vehicle accidents (MVA) and dog attack. With MVA injuries, there should be certain findings that are supportive of this type of cause. There should be dirt and debris on the fur; skin abrasions from the animal sliding on pavement or dirt; the abrasions should be lateral on the down side and medial on the opposite side; and frayed nails (most commonly found with cats). These findings are in addition to any injuries sustained from being hit, rolled under, or run over by a car such as blunt force trauma and fractures. In dog attacks, there should also be supportive findings of the cause. There is often dirt and debris in the mouth where the animal was dragged and shake on the ground; head and oral trauma from being shaken by the neck or grabbed by the head; saliva on the fur which causes spiking of the fur; fur caught in the nails where the victim fought the attacker (especially cats); punctures of the skin which may be triangular or elliptical; and abdominal organ lacerations from compression and shaking with or without associated skin punctures.

**DETERMINING TIME OF DEATH**

Determining time of death is usually an estimate at best. It requires taking into account several exam findings in addition to eye witness statements. Rigor mortis, algor mortis, and gastric emptying time are all variable depending on the events prior to death and the environmental conditions. The most accurate time of death can be provided using insect evidence. Maggots can aid in determining TOD, location of death and provide DNA and toxicology evidence. Maggots can help determine the time of death by providing the post mortem interval. Other methods may be used to aid in the TOD such as vitreous potassium levels. New human research using decomposition scoring may be of value.

**DECOMPOSITION**

Decomposition involves the two processes of putrefaction and autolysis. Autolysis is a chemical process by the intracellular enzymes that causes the breakdown of tissue and organs. Heat accelerates autolysis while cold slows it down. Freezing can stop the process and in some cases significant heat can inactivate the intracellular enzymes. Organs that have higher enzymes will undergo autolysis faster, such as the liver and pancreas. Decomposition usually occurs in from 6 to 36 hours depending upon the condition of the animal and the environmental conditions of the exposed body. Microscopic exam may reveal autolysis of the tissues with no immune or inflammatory reaction. However, the presence or absence of an inflammatory reaction to an area of injury can help determine a time interval between injury and death. Depending on the cause of death or the type of injury hemorrhage, neutrophils, and/or edema fluid may be present with hours of the injury. The inflammatory responses may be affected by the age of the animal, the tissues affected, medications, and the health of the animal. An injury without an inflammatory response is indicative it occurred in close proximity to death. The nature of any inflammatory response may also determine a time interval such as in the case of peritonitis that resulted from intestinal rupture caused by blunt force trauma. The microscopic examination may have evidence of chronic inflammation including fibroblasts and hemosiderin. Putrefaction involves bacteria and fermentation and is often used interchangeably with the term decomposition. After death, the bacteria from the gastrointestinal tract spread throughout the body. Putrefaction is accelerated in animals that are septic prior to death and this process may continue even with refrigeration of the body. In addition to the body, the development of putrefaction is dependent on the environment. In high temperatures the rate of decomposition is accelerated and the body can reach an advanced state of putrefaction within 24 hours. In cold temperatures the rate slows down and may even stop in extreme cold. Even under refrigeration, a non-septic body may still continue to decompose. If the body is constricted in any way decomposition may be delayed. If the animal is overweight, has a heavy fur coat, or is wrapped in something to retain heat, putrefaction may be accelerated. Decomposition may be asymmetric occurring more rapidly in areas of injury. Decomposition may progress to skeletonization in only one part of the body due to insect feeding in areas of injury.

The sequence of decomposition in humans begins with a greenish discoloration of the abdomen. This discoloration then develops on the head, neck and shoulders along with bacterial gas formation causing bloating of the face. Marbling occurs in these areas due to hemolysis of the blood within the vessels and the hemoglobin reacting to hydrogen sulfide, developing a greenish-black discoloration along the blood vessels at the surface of the skin. The then body develops generalized bloating where the eyes may bulge and the tongue protrudes from the mouth. This is followed by development of vesicles on the skin, skin and hair slippage, and the color of the body is pale green to green-black. The weight of the internal organs actually decreases with decomposition. A red-colored decomposition fluid, known as purge fluid, will drain from the mouth and nose and may be found in the body cavities. This may be mistaken as secondary to an injury but the amount of fluid is usually small in the body cavities in contrast to the amount expected with injury. Decomposition also causes hemolyzed blood to leak out of the broken down blood vessels into the surrounding tissue (imbibition) usually within 12 to 24 hours after death. This can be mistaken for antemortem bruising so careful examination of lividity and concurrent injuries must be done to differentiate the two. Microscopically this is represented by hemolysis of erythrocytes in the blood vessels whereas the hemorrhage from antemortem bruising is represented by erythrocytes outside the vessels in the surrounding tissues.

Changes in the eyes are difficult to interpret and depend on whether the eyes are open or closed. With closed eyes, a white scummy deposit develops on the cornea making it cloudy by 24 hours postmortem. If the eye is open and exposed to the air, occasionally a brown to black band may form on the sclera or cornea due to drying called tache noire. Following the wet decomposition, the surface tissues begin to dry, collapse, and darken developing a leathery texture. The organs and tissues will become desiccated and shrink. The body may become mummified or skeletonized. The time frame for skeletonization of the body depends on environmental conditions, insect activity, and scavengers. Mummification can occur in hot, dry conditions when the body rapidly dehydrates. The skin will appear brown or black and leathery. Decomposition continues with the internal organs turning them blackish brown with a putty-like consistency. Adipocere is a grayish-white to brown, firm, wax-like material made up of the fatty acids oleic, palmitic, and stearic acids. It is found primarily in the subcutaneous tissue and other fatty deposit areas. When a body is found immersed in water or in a damp, warm environment, adipocere formation may occur. It may also be seen in bodies that have been placed in bags. In these warm moist environments, fat undergoes hydrolysis by endogenous lipases and bacterial enzymes to free fatty acids. These are then converted to hydroxyl fatty acids by bacterial enzymes, primarily Clostridium perfringens. Adipocere formation can take weeks to several months to develop and is resistant to chemical bacterial destruction. For the severely decomposed/skeletonized or burnt body the fragile body should be handled very carefully and samples taken for possible testing. The body should be photographed, measured, weighed, and radiographed. Radiographs may reveal gunshots or broken bones. Depending on the decomposition, samples of kidney may reveal ethylene glycol poisoning. Stomach contents may still test positive for poisons. Examination of bones may reveal evidence of trauma.

Livor mortis, also referred to as hypostasis or lividity, is the pooling of blood due to gravity in dependent body sites after the heart stops beating. Lividity is most useful in determining the body position at time of death and if the body was moved. It is usually visible in light-colored skin, the buccal mucosa, and the sclera. It is also found on the internal body surfaces and internal organs where it is most noticeable on the surface of the lungs. Lividity on internal organs can be mistaken for congestion. At first appearance, contusions may be grossly difficult to differentiate from postmortem lividity. When pressure is applied to the area there will not be any blanching. To differentiate between bruising and lividity, incise the area in question. A bruised area will have diffuse hemorrhage into the soft tissues whereas lividity is characterized by blood confined to within the blood vessels. A contusion involves hemorrhage into the soft tissue and when incised the blood cannot be wiped or squeezed out. This is not the case in areas of lividity. Another factor to consider is the pattern and location of the discoloration – if it is more consistent with lividity based on location and other discolorations in the body or isolated which is more characteristic of injury. Over time, decomposition can make it very difficult to differentiate antemortem bruising and lividity. Hemolysis of the red blood cells creates diffuse discoloration of the soft tissue. The blood within the vessels and the erythrocyte leakage due to the breakdown of the blood vessels from decomposition will hemolyze. The erythrocytes in the soft tissue from antemortem bruising will also hemolyze making it impossible to distinguish from an area of livor mortis.

**REFERENCES:**

1. Merck, M, ed. Veterinary Forensics: Animal Cruelty Investigations, 2nd ed. Ames: John Wiley Publishing, 2013.
2. www.veterinaryforensics.com – forms and resources

# TRUTH OR FICTION: ANALYSIS OF PATTERNED INJURIES

## INTRODUCTION

It is important that the veterinarian guard against biases and provide a clear, objective analysis of the findings. With information overload there is a tendency to use mental shortcuts, heuristics, which may or may not be subject to biases. There is a tendency to prefer information less complex instead of relying on thinking and analyzing. There may be a tendency to believe witness accounts instead of carefully considering their statements. There may be a tendency to have confirmation bias which refers to believing more positive information than negative. This can result in giving negative information less weight, possibly making it 'insignificant'. There can be the 'anchor' effect where there is a tendency to rely heavily on one piece of information, usually the first information encountered. Theory development and formation of judgements start at the beginning. Investigations done in a confirmatory manner may have the effect of making judgements to increase confidence of a theory instead of maintaining objectivity and considering all information. There are several things a veterinarian can do to guard against biases. The information from the case and photographs should be reviewed several times. Examine alternate theories and consider ways to disprove the manner of death or injury. Confirm that all negative evidence is documented. Encourage peer review and discuss theories and findings. With awareness of what can create bias on a subconscious level steps can be taken to form impartial and objective conclusions.

Opinions are developed and/or written with consideration of degrees of probabilities. The highest degree of probability is absolute certainty or certainty beyond a possible doubt where every other imaginable contingency is impossible. The next is a reasonable degree of certainty where the probability of reasonable degree far exceeds 50% and the reasonable certainty is that degree of assurance that a reasonable person relies upon. Next is the preponderance of evidence which means 'more likely than not' and permits reasonable doubts. It may also be defined as probable with a likelihood exceeding 50%. Since the medical opinions will be used in legal forums, a higher degree of certainty than probable causes is often required. This higher standard may be met by developing a larger factual database or using brevity and broadly defined terms in the medical opinions. There are two categories of probabilities of less than 50%: reasonable possibilities and speculation. Reasonable possibilities may be discussed in courtroom proceedings and have a probability of less than 50%. Speculation refers to possibilities that are so improbable that they have no basis in reason. Speculation may not be allowed in criminal proceedings.

## INTERPRETING BURN PATTERNS

The suspicion of deliberate infliction of burns on an animal is raised when the history offered by the owner does not match the presentation of the burn, the environment, or the expected animal behavior that can result in accidental burns. Some owners may blame the animal laying too close to a hot object as the cause of the burn. Although it is possible for an animal to sustain a thermal burn injury before registering the associated pain, the burn pattern may be inconsistent. Burns should be considered with the presence of any unexplained eschar.

Burns are usually a patterned injury with characteristics that reflect the cause of the injury. They are typically localized or distributed asymmetrically. Biologically abnormal patterns include unusual symmetry, drip configurations, and straight or angular borders. They typically do not progress after 5 days without repetitive injury unlike other dermatologic conditions. Proper interpretation of the burn patterns can reveal the exact nature of the incident that may support or refute the history and help direct the investigation. The multiple levels of injury present can provide valuable information. The most severe level may be indicative of where the area had initial, longer, or more intense contact with the burn causing agent. A determination of where the burn started on the body may be made when there are more severe burns confluent with more superficial burns. Burns from a liquid, such as splash or spills, typically have flow lines from the liquid impact or gravity which are usually more superficial than the initial contact area. A burn pattern that is evenly distributed with the same degree of injury is indicative of an even rate of burn such as with a flash fire or chemical agent. The location of the burn can indicate whether the burn could have been accidental versus intentional such as

protected body areas. When an animal is set on fire and the fur burns for a short period of time there may not be large areas of injury to the underlying skin. Instead, there may be a wide distribution of isolated circular burns on the skin where the fur acted as a wick for the fire to reach the skin. There may be a larger burn area on the skin where the fire was initially ignited on the body.

**Solar Thermal Necrosis**

Solar injury associated with UV rays has been well documented in animals occurring in areas of light pigmentation and sparse fur. Thermal injury due to solar radiation can also be seen in dark pigmented areas. Black skin will absorb approximately 45% more solar radiation than white skin making dark skin areas more susceptible to thermal radiation damage. Visible radiation penetrates the skin several millimeters and degrades into thermal energy increasing the thermal burden. The epidermis absorbs almost all of the UV light and therefore does not contribute to the thermal burden. The application of any topical oil-based product, such as topical flea drops, can exacerbate the thermal injury. Heat stroke, dark-colored fur, and short hair coats can also predispose the animal to these burns. Histologic findings are consistent with a full-thickness burn: epidermal, adnexal, and vascular necrosis and subepidermal vesiculation.

These cases present with burn lesions along the dorsum which may contain plaques and eschars. Multi-colored animals may have focal lesions located in the dark pigmented areas. These burns are often mistaken for signs of animal cruelty by the intentional application of a caustic agent to the dorsum but when examined closely the burn does not have a typical liquid or pour pattern with flow lines. The location is the other indicator of the cause. This solar thermal necrosis is due to prolonged exposure to direct sunlight. Animals will normally change positions and seek shade as the radiation heat increases in their skin. Solar thermal necrosis occurs when the animal is unable to escape from the direct sunlight, either through environmental circumstances or physical limitations. Depending on the circumstances, this may result in animal cruelty charges. It should be noted that the burn lesions may not appear for several days to 2 weeks after the sun exposure.

**Scalding Burns**

Scalding burns are caused by contact with a hot liquid and do not result in singeing of hair. They may be produced by immersion, spills, splashing, or exposure to superheated steam. Water heaters in houses and apartments are commonly set at 140°F (60°C) where full-thickness burns can occur in just a few seconds at this temperature. In animals, scalding can occur when the fluid temperature is 120°F (48.8°C). In humans, the time and temperature of water required to cause epidermal damage and full-thickness burns has been documented:

Water temperature and scalding burns time in humans

| Temp (°F) | Threshold for Epidermal Injury | Full-Thickness Burns |
|---|---|---|
| 120 | 290 sec | 600 sec |
| 125 | 50 sec | 120 sec |
| 130 | 15 sec | 30 sec |
| 140 | 2.6 sec | ~7 sec |
| 150 | <1 sec | 2.3 sec |

*Source*: Vincent J. Di Maio and Dominick Di Maio. 2001. Forensic Pathology, 2nd ed., p 349. Boca Raton: CRC Press.

In splash or spill burns, the fluid cools as it flows down the body. The burn is more severe where the fluid had initial contact with the skin, becoming more superficial where the fluid flowed away. Superheated steam causes severe scald-like burns. If inhaled, this steam causes airway injury including upper, lower, deeper airways. There may be massive edema in the larynx causing occlusion of the airway and asphyxia. Deliberate immersion burns are typically characterized by a straight burn line caused by the water level, depending on the body part lowered into the liquid and the struggle or resistance of the victim. In legs, this can result in a ‘stocking’ or ‘glove’ distribution with the upper margin clearly defined. The scald may be limited to the feet and pads depending on

the depth. In cats, the toes contact on contact protecting the areas between the pads. The findings in feet scald include loss of epithelium from the ventral pad surfaces with eventual weeping or darkening; normal non-erythematous areas between the pads and toes; erythematous skin with loss of hair and epidermis on the lateral and dorsal aspects of the toes or foot.

**PATTERNED BRUISING AND ABRASIONS**

Photographs, with and without a photo scale, should be taken of the bruising pattern periodically as it forms in order to capture the full representation. It is possible that early on the bruise may be more reflective of what caused the contusion and as bleeding continues, especially from the deeper tissue, the pattern may become obscured. A patterned contusion may be seen that reflects the shape and sometimes details of the object that was used to cause the bruise. Asymmetry to the bruise may be an important indicator due to the fact that bleeding follows the path of least resistance. Depending on the area of skin and gravity, it tends to flow from the center outward, forming irregular or blurred lines. Bruising may extend beyond the site of impact, obscuring the pattern created by the object. If the contusion was caused by a weapon, it may be possible to find evidence of the weapon within a bruising pattern or indentation of the skin, underlying tissue, or even bone. A linear object, depending on the width, may cause two, parallel, train track-lines, or tramlines, of bruising with the skin between uninjured. This is due to the hemorrhage under the skin being displaced laterally by the pressure of the blow. The same findings can be seen associated with blows from other type of objects such as a baseball which results in a circular bruise and a pale center. If the weapon has a rough texture, there may be parallel abrasions present with or without bruising. Blows from a weapon also can cause skin lacerations if used with enough force or if the skin is more susceptible to tearing, such as with young or geriatric animals and certain species. The imprint of a shoe or fingertips may be seen from stomping, grabbing, or holding the animal. It is important to find out if investigators have a suspected weapon that was used in the incident either seized as evidence or through interview statements. A weapon may be identified or discovered later in the investigation, so it is important to preserve any evidence that may be linked to the weapon for later comparison or confirmation. The patterns and indentation of the skin may fade or resolve very quickly, so it is important to take photographs as soon as possible, with and without a photographic scale, for a forensic specialist to analyze for weapon comparison. For any indentations or raised patterns, a cast may be taken. Mikrosil is a rubber casting material that is inexpensive and easily used for this purpose. It may be ordered from any forensic supply company noting that brown is the preferred color for tool mark examiners.

A patterned abrasion shows the imprint of the weapon or surface that caused the abrasion. This may be seen with ligature injuries that leave a patterned imprint revealing the type of ligature used. In humans, intermediary material on the body such as clothing may leave an imprint from the crushing force of the weapon used. The impact surface, such as gravel, can exhibit characteristic patterned abrasions. If the weapon has a rough texture there may be parallel abrasions present with or without bruising.

If the ligature is no longer present, the area of injury should be carefully examined for embedded trace evidence related to the ligature such as tape adhesive. There may be patterned injuries such as abrasions or contusions which may retain the ligature pattern. Evidence of ligature or patterned injury may be more evident after skin reflection during the postmortem examination. The pattern should be thoroughly photographed with a photographic scale in each photo.

**REFERENCES:**

1. Merck, Melinda. Veterinary Forensics: Animal Cruelty Investigations, 2nd ed. John Wiley Publishing, 2013.
2. www.veterinaryforensics.com – Forensic Forms

# VETERINARY ANALYSIS OF VIDEO EVIDENCE: THE IMPORTANT ROLE OF THE VETERINARIAN

## INTRODUCTION

It is important that the veterinarian guard against biases and provide a clear, objective analysis of the findings. With information overload there is a tendency to use mental shortcuts, heuristics, which may or may not be subject to biases. There is a tendency to prefer information less complex instead of relying on thinking and analyzing. There may be a tendency to believe witness accounts instead of carefully considering their statements. There may be a tendency to have confirmation bias which refers to believing more positive information than negative. This can result in giving negative information less weight, possibly making it 'insignificant'. There can be the 'anchor' effect where there is a tendency to rely heavily on one piece of information, usually the first information encountered. Theory development and formation of judgements start at the beginning. Investigations done in a confirmatory manner may have the effect of making judgements to increase confidence of a theory instead of maintaining objectivity and considering all information. There are several things a veterinarian can do to guard against biases. The information from the case and photographs should be reviewed several times. Examine alternate theories and consider ways to disprove the manner of death or injury. Confirm that all negative evidence is documented. Encourage peer review and discuss theories and findings. With awareness of what can create bias on a subconscious level steps can be taken to form impartial and objective conclusions.

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## CONSULTING EXPERT

The veterinarian's role may be a consulting expert. A consulting expert may also be a fact witness if he or she is able to make direct observations of the evidence, including the animal. The consultant may or may not testify in a case and may or may not be made known to the opposition. They have specialized knowledge, training, and experience that assists in analyzing and evaluating the evidence in a given case. Several types of situations give rise to this need. For example, a consultant may be contacted in a criminal case where the animal was not evaluated or treated by a veterinarian, and in some instances where the animal itself was not or is not available for examination. In some cruelty cases the animal may have been cremated, may have been disposed of by one of the parties, or may have run away. The consultant's expertise is also valuable in complex veterinary medical cases or those involving exotic or rare species. Some cases require expertise in unique animal features, complex events, or cases that involve unusual issues related to the cause and manner of injury or death.

In addition to video files, it is critical for the consulting expert to be provided with all reports, crime scene findings, analysis results as well as relevant information, investigation information, evidence and photographs related to the case. The consulting veterinarian must have context in order to accurately evaluate the findings. The veterinarian needs to guard against providing analysis and opinion on limited information and require all information be provided. This is important for all consultations regardless of the type of case. It will provide the needed context and help prevent questions that undermine credibility when testifying.

Whenever consulting, it is prudent to document certain information: the route of contact for the consult (email, phone call); the name of the person requesting the consult and all their contact information; the information provided with by the requesting person; any information requested by the veterinarian; and the date, time and length of discussion. It should be discussed if the attorney initially prefers a verbal report versus a written report. The consulting expert may be asked to prepare a report regarding their analysis. As a result, they may be endorsed as an expert witness in the case. In a criminal case, if the expert (retained by the prosecution) reaches an opinion that the suspect was not involved, or that no crime was committed or that the suspect should otherwise be exonerated, then the prosecuting authority is under an affirmative obligation to disclose the information to the defendant or his or her defense attorney.

The veterinarian's fee should be discussed during the initial conversation and how that payment will be made. A time estimate may be provided by the veterinarian for services requested. This should include fees for review of all materials including an estimate of 1 hour minimum for phone call discussion after initial analysis, with a written report, if requested, to be additional time and fee. Many experts offer a free initial consultation to discuss just the key issues of the case to determine if either party wants to proceed with a more in-depth consultation. It is recommended to follow up after the initial phone call with a summary of the veterinarian's understanding of services and/or or a services agreement to be signed by both the attorney and the consulting veterinarian.

**ASSESSMENT OF VIDEOS**

Animal cruelty cases may be pursued based on electronic evidence. This may include videos and photographs found on a computer, security cameras, defendant or witness interviews, social media postings or from other electronic devices. These cases may involve criminal prosecution of animal cruelty even without finding a live or deceased animal victim. Sometimes the video is potentially additional evidence in a cruelty case.

The veterinarian may be asked to review videos, related photographs and other records. It is important to discuss the entire case with the requesting prosecutor and/or detective. This discussion should include all allegations, charges and applicable statues, questions and issues in the case. All expectations of the consultation and review should be clarified.

When reviewing videos, it may be helpful to first view video without any sound and then with sound. Depending on the questions in the case, viewing the video at regular speed then at slow speed may reveal subtle animal behavior clues. Examine the video for additional evidence that could be important to the investigation such as medications or other physical evidence. Note the time on the video related to pertinent information.

**Sexual Abuse**

It is not unusual to find personal videos of the sexual abuse on the suspect's computer, phone, or CD's/videotapes. The veterinarian may be asked to review the videos, assess the animal's behavior, and comment on any pain or suffering. Sometimes the unrestrained animal does not appear on video to resist during an assault with rectal or vaginal penetration. This type of assault would be extremely painful (see above) and the lack of resistance could indicate the animal was under the effects of a drug. It may also an indicator that the animal has been 'trained' and conditioned to accept the assault, an indicator of chronic abuse. The video should be watched at a slow speed to detect subtle signs of pain or resistance. A behaviorist may be consulted to assess the animal's behavior.

**Documentation**

All the material provided and reviewed should be listed in the report. Analysis and findings of each file should be listed and then a summary of all findings, any issues, followed by conclusions. See Expert Consultation Report Template below.

**REFERENCES:**

1. Merck, Melinda. Veterinary Forensics: Animal Cruelty Investigations, 2nd ed. John Wiley Publishing, 2013.
2. www.veterinaryforensics.com – Forensic Forms

Expert Report Template:

**EXPERT CONSULTATION REPORT**
**(or VETERINARY EXPERT OPINION REPORT)**

Prepared by:

Prepared for:

Case:

Materials reviewed for the report:
Abbreviations Used:
File Analysis:
(Can list findings and individual summary by material reviewed, animal or other category)
(If review video, note time stamp when referencing observation on video)
Issues:
Summary/Conclusions:

Signature
Name Date

# ROSS H. PALMER

Ross H. Palmer, DVM, MS, DACVS
Professor – Orthopedics, Sports Medicine & Rehabilitation
Colorado State University

# Canine Joint Health, Mobility, Energy & Longevity: 5 Things a 10 year old Labrador Taught Me

**OSTEOARTHRITIS (OA) PATHOGENESIS**

The healthy joint is a highly metabolic organ comprised of cartilage, bone, synovium, neural and supportive muscle tissues whose function is critical to mobility and life quality. The healthy joint is characterized by delicately balanced anabolic and catabolic activities. In OA joints, the metabolic balance shifts toward catabolism driven by cytokine cascades and inflammatory mediators.[1] Pro-inflammatory cytokines such as interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α), produced by chondrocytes and synoviocytes, decrease anabolic activities such as collagen and proteoglycan synthesis and upregulate the production of catabolic enzymes including matrix metalloproteinases (MMP's).[1] These cytokines and other cytokines (IL-8, IL-6, etc) also upregulate the expression of pro-inflammatory enzymes cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) that lead to increased production of prostaglandin E2 (PGE2) and nitric oxide (NO).[1] Biomechanical alterations resulting from such factors as joint instability, joint mal-alignment and obesity perpetuate OA and its degradative biochemical pathways. Increasingly, chondrocyte apoptosis and premature senescence are linked to NO and other oxidative injury. It is clear that OA has characteristics of progressive, premature aging of the joint that are mechanically driven and chemically mediated. Inflammatory changes within the synovium are also characteristic of the disease process. Synovitis is typically located adjacent to diseased or damaged cartilage and bone. Regional cartilage destruction may be exacerbated by the release of proteinases and cytokines from the activated synovium.

Combined, the destructive enzymes and cytokines originating from chondrocytes and synoviocytes breakdown the extracellar matrix (ECM) of cartilage that is responsible for its mechanical resilience and toughness in its healthy state.[1] Cartilage breakdown products provoke the release of collagenase and other destructive enzymes from activated synoviocytes. Vascular hyperplasia of the synovial membrane, stimulated by pro-angiogenic factors such as vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) secreted from macrophages, fibroblasts and endothelial cells, potentiate the inflammatory process. Increased vascular permeability perpetuates the inflammation.

Inflammatory mediators act upon nociceptors to reduce the pain threshold such that simple activities that were formerly comfortable, now result in pain, stiffness, disability and avoidance behaviors. The patient loses muscle strength, cardiovascular fitness, and enthusiasm for activity while gaining weight. This process affects the pet interactions with the family and vice-versa.

**PREVALENCE & IMPACT of CANINE OA on LIFE QUALITY & LIFESPAN**

Osteoarthritis affects 1 out of 5 dogs and is the #1 cause of chronic pain in dogs. While these population statistics speak clearly of the potential impact of optimized OA management on the pet population as a whole, as clinicians our focus is often upon the well-being of our individual patients (and their families).

In Purina's Labrador Retriever Lifespan Study, a group of Labrador Retrievers (n = 48) from 7 litters was enrolled in a 'paired-feeding' study design.[2-5] Dogs in each litter were paired at 6 weeks of age based upon body weight and gender and randomly assigned to 1 of 2 feeding groups. One dog in each pair was fed ad libitum and its paired litter-mate was fed the same diet but limited to 75% of the amount consumed by its pair-mate the previous day. The housing was identical; only the quantity of food provided was different between the groups. The dogs were then studied for life and such things as onset & location of osteoarthritis, development of other degenerative diseases and lifespan were evaluated. Not surprisingly, dogs with restricted caloric intake weighed less (26% less on average) and had lower body condition scores (BCS) through life. More relevant to patient well-being, these same calorie-restricted dogs had decreased incidence of and delayed onset of osteoarthritis. For instance, radiographic evidence of osteoarthritis in multiple joints was present in only 10% of dogs at 8 years of age when caloric intake was restricted, but was exceedingly common (77%) in dogs freely fed the same diet (no caloric restriction). Also stunning was the finding that median lifespan of these Labrador Retrievers was 1.8 years longer simply by restricting caloric intake! Another shocking finding was that humane euthanasia due to OA-inflicted loss of patient well-being far outweighed any other causes of death in the study. Ineffective management or prevention of OA is no less a life-threatening risk than is cancer! The authors of the lifespan study recommended that dogs be fed to maintain a body condition score < 5 (on a 9-point scale) for the purposes of pet health, well-being and longevity.

Regardless of primary etiology, obesity is often a complicating factor that aggravates OA. Even when the underlying orthopedic disease or injury can be treated surgically (patellar luxation, cruciate ligament rupture, etc), lifelong support of joint health is indicated.

**MULTI-MODAL STRATEGIES for EFFECTIVE MANAGEMENT of CANINE OA**

Effective support of joint health requires multi-modal strategies aimed at both symptom control and long-term joint health preservation. Key strategies in this approach include pet-owner education, nutritional management of body conformation and joint health, adopting a lifestyle of regular / moderated activity, therapeutic exercise & physical rehabilitation, use of high-quality & efficacious joint protective compounds, use of non-steroidal anti-inflammatory drugs (NSAIDs) as indicated and, in some instances, the use of adjunctive analgesics, intra-articular therapies and biologic or mechanical therapies. Of course, surgical treatment should also be implemented when the underlying cause of the OA can be so benefited.

**Pet-owner education** is the foundation of effective treatment of OA because comprehensive management requires that the pet's family understands the treatment goals and actively participates in the treatment program. It is essential that pet owners understand that OA management is an ongoing, dynamic, lifelong process that is periodically updated and modified based upon response to treatment and development of new therapies, etc. As a rule, I believe that there is a HUGE potential for improved implementation of family-centered OA management in veterinary medicine and the potential market is massive.

**Attaining & maintaining a lean body conformation** through proper nutrition and feeding practices is the cornerstone of effective OA management. Unfortunately, over-feeding is the single hardest habit for most families to change. Nestle-Purina's Labrador Lifespan Study has shown the effectiveness of restricted caloric intake on weight control, delaying the onset of and decreasing the lameness associated with OA and increasing patient lifespan.[2-5] If the pet is overweight at the time of OA diagnosis, healthy weight loss is facilitated by a specifically formulated weight loss diet that ensures that the pet receives the necessary macro-nutrients while the energy content is reduced to a level that supports steady, progressive weight loss (~1-2% of body weight/week) toward the targeted weight and body conformation.[6] While the patient's estimated daily Resting Energy Requirement (RER) can be calculated and the dietary energy intake adjusted accordingly, variations in individual metabolic rates make it essential to regularly (every 2 weeks) monitor and record the patient's progress toward their weight loss goals. Effective weight loss plans typically require a thorough dietary history including feeding times, amounts, caloric content of foods, treats and supplements (such as omega-3 fatty acids), number of pets being fed, and who does the feeding. Multi-pet households and multiple family members responsible for feedings and treats are typical challenges that must be addressed for successful implementation of a weight loss plan.

**A lifestyle of regular activity** that is moderated away from intermittent extremes of exercise and activities to which the pet is not conditioned is essential. This is VERY difficult for many pet-owning families because it, by necessity, impacts their daily schedule. Interestingly, a shift to this desirable lifestyle often benefits the pet-owners simultaneously…everyone wins! Typically, the best approach is to make slow and methodical steps toward the ultimate lifestyle and activity goals. Having been a part of numerous amazing success stories, I believe that we as veterinarians frequently underestimate the lifestyle achievements that our overweight patients can realize with proper guidance and encouragement.

**Therapeutic exercise** and **physical rehabilitation** under the direction of a trained canine rehabilitation practitioner often contributes to dramatic improvement in comfort, mobility and fitness of osteoarthritic dogs. Therapeutic exercise is often a key step in slowly converting the osteoarthritic, overweight and sedentary dog to a lean, physically fit dog that is enthusiastic about activity again and the results can be quite dramatic! Such activities may include controlled swimming, underwater treadmill therapy, use of elastic therapeutic bands and other techniques. Often these activities are slowly and methodically increased in duration and/or intensity as the pet begins to

respond with weight loss, increased fitness and enthusiasm for activity. Observing such gains in fitness, mobility, and enthusiasm for active living can be very satisfying for the veterinary team and the pet-owning family!

**Nutritional management of OA with an evidence-based therapeutic diet** has a practical place in the comprehensive management of OA. Omega-3 fatty acids, key components of these diets, appear to decrease joint inflammation, improve lameness & patient activity while reducing patient reliance upon NSAIDs. Omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are most easily and safely administered within a specific therapeutic diet. Studies incorporating fish oil-derived, omega-3 fatty acids into the diet of osteoarthritic dogs showed a significant improvement in weight-bearing (peak vertical force-PVF) compared to control-group diets.[7] Improvement of weight-bearing was of similar magnitude (+5.6%) to that reported in many NSAID trials. Improved PVF was noted in 82% of osteoarthritic dogs fed the omega-3 supplemented diet as compared to 38% fed the control diet.[7] A similar study design was used to compare the effects of a test food supplemented with fish oil omega-3 fatty acids versus a control diet on serum fatty acid concentrations and owner- and veterinary-assessed severity of OA.[8] The test diet was reported to raise blood concentrations of omega-3 fatty acids and improve the owner-assessed ability for dogs to rise from a resting position, play, and walk compared with control dogs (which showed no improvement).[8] Another study showed that a diet supplemented with omega-3 fatty acids allowed for more rapid reduction in carprofen dosage in osteoarthritic dogs as compared to dogs fed a diet with a low omega-3 fatty acid content.[9] Yet another study showed that an omega-3 fatty acid enriched diet fed to dogs with naturally occurring OA increased PVF and improved locomotor disability and performance in activities of daily living as compared to a control diet.[10] The recommended dose of combined EPA and DHA is as high as 230 to 370 mg/kg of metabolic body weight (kg of BW $^{0.75}$), while doses of 90 to 110 mg/kg body weight were also effective.[7-13] Overall it is hard to elucidate the average dose received in many of the effective therapeutic food trials, but it is thought to be around 100-150 mg/kg body weight of EPA and DHA. It is easier to achieve this dose via clinically tested omega-3 fatty acid enriched diets rather than supplementing, since fish oil supplements provide approximately 9 kcal/gram and can easily unbalance the ration and promote a lower protein intake, which could be contraindicated in certain situations. When treating overweight patients, I first focus upon weight loss with a therapeutic weight loss diet until the target weight is achieved. Then, I slowly transition the pet to a clinically tested, omega-3 fatty acid enriched therapeutic diet. It is important to closely monitor the patient's weight during and after this transition as the omega-3 enriched OA diets are more calorically dense.

**Lifelong nutritional supplementation with joint protective compounds** (also called nutraceuticals) for patients with OA and postoperative joint surgery patients should promote anabolic functions while mitigating the catabolic processes. For lifelong promotion of joint health, I recommend dietary supplementation with high quality nutraceuticals including glucosamine, chondroitin sulfate, and avocado-soybean unsaponifiables (ASU). Prospective, randomized, double-blinded, placebo-controlled, parallel-group studies have shown that ASU significantly reduced pain, functional

impairment, and NSAID reliance in humans suffering from OA in the knees and hips.[14,15] Activated chondrocytes incubated with ASU showed reduced TNF-α, IL-1β, COX-2 and iNOS expression to levels similar to that of normal non-activated chondrocytes.[16] The suppression of COX-2 and iNOS expression was paralleled by a significant reduction in $PGE_2$ and nitrite.[16] These findings demonstrate the anti-inflammatory activity of ASU on both chondrocytes and synovial macrophage prototypic cells and provide a plausible explanation for the pain-reducing and anti-inflammatory effects of ASU observed in human OA patients. In a canine study, healthy young adult dogs were divided into 3 groups: (1) control, (2) 300mg ASU orally every 3 days, and (3) 300mg ASU orally once daily.[17] Knee joint fluid was analyzed prior to supplementation and then each month to measure the levels of two isoforms of transforming growth factor (TGF-β1 and TGF-β2). ASU, in both dosages, caused an increase in both TGF-β isoforms as compared to the control group. This study provides *in vivo* evidence for pro-anabolic effects of ASU since TGF-β is a stimulator of chondrocytic extracellular matrix production (type II collagen, proteoglycan).[17] Further evidence of canine *in vivo* efficacy of ASU was provided in an ACL transection study in which the ASU-supplemented group showed reduced development of early OA cartilage and subchondral bone lesions (macroscopic and microscopic lesion severity, subchondral bone loss) as compared to placebo-treated controls.[18] The therapeutic effect appeared to be mediated through inhibition of iNOS and MMP-13.[18] This observation of ASU-mediated chondroprotection is important relative to our goal of long-term preservation of joint health and goes beyond the effect of short-term symptom control. In a very small-scale study, dogs treated with a nutraceutical containing glucosamine, chondroitin sulfate, and ASU showed increased PVF similar in magnitude to that seen with various NSAIDs in a previous arm of the study (Millis DL, University of Tennessee, unpublished data, email communication 2 January 2019). Though the small study population did not permit meaningful statistical analysis, these data suggest the need for larger scale and longer term *in vivo* evaluation of high quality nutraceuticals in the restoration of function and pain relief of dogs with chronic OA. In a systematic review of human clinical trials, 53 out of 2,026 studies met the inclusion criteria.[19] Evidence of efficacy for OA treatment were classified for various nutritional supplements (glucosamine and chondroitin sulfate were excluded) as *good*, *moderate* or *limited*. Good evidence was found for ASU, moderate evidence for methylsulfonylmethane (MSM), and SKI306X (a plant extract mixture), and limited evidence for Duhuo Jisheng Wan, cetyl myristoleate, lipids from green-lipped muscles and Harpagophytum procumbens extracts.[19]

Ideally, supplementation with a high quality source of glucosamine, chondroitin sulfate and ASU should be used early in the course of OA (or following any joint injury or joint surgery) and lifelong thereafter. Pragmatically, it is important to realize that in the USA these nutraceuticals are classified as dietary supplements by the FDA and, as such, are not subject to the same stringent regulatory guidelines as pharmaceuticals. In fact, one study showed that as many as 84% of the over-the-counter nutraceutical products vary widely in their composition and fail to meet their label claims.[20] Additionally, the sources of raw chondroitin sulfate vary widely and should not necessarily be seen as equally effective.[20] This leaves the consumer in a difficult place regarding determining product value. I recommend a high-quality product that combines the glucosamine &

chondroitin sulfate ingredients with ASU and consistently meets its label claims in independent quality assurance testing (Dasuquin®, Nutramax Laboratories).

**NSAIDs** decrease inflammation and, therefore, typically improve patient comfort and mobility. Since they do not appear to significantly alter OA progression, they primarily serve the goal of symptomatic control rather than the goal of joint health preservation. Though the incidence of adverse reactions to COX-2 selective NSAID therapy is not fully known, significant adverse effects that involve gastrointestinal, liver and/or kidney function apparently occur at a very low frequency when NSAIDs are properly administered.[21,22] We recommend the medication be discontinued and immediate veterinary consultation be sought if diarrhea, vomiting, melena, lethargy or lack of appetite is noted. We recommend blood tests be performed prior to NSAID therapy and periodically throughout treatment. The general goal is to utilize multi-modal therapeutic strategies such that the minimum effective NSAID dosage can be utilized for symptomatic control. Prostaglandin Receptor Antagonists (PRA's) are designed to block the action of selected prostaglandins rather than to block their production. Galliprant® (grapiprant) is a first in class EP4 receptor antagonist that was recently introduced to the veterinary market in the US.[23] $PGE_2$ exerts its nociceptive and inflammatory effects by binding to the EP receptors including EP4. Galliprant® targets these actions of $PGE_2$ at the EP4 receptor and therefore, should not interfere with normal 'house-keeping' homeostatic functions of other prostanoids. While the safety and efficacy studies of this new medication appear promising, we are still in the early phases of clinical implementation.[23] Galliprant® should not be given concurrently with other NSAIDs or corticosteroids and it should not be used in cats.

**Adjunctive systemic medications** may decrease reliance upon NSAIDs or augment their effects. Important Note: not all the medications presented in this discussion are approved for use in dogs. Many of these drugs have not had comprehensive efficacy, pharmacokinetic or toxicity studies carried out in dogs and are being used empirically based upon extrapolation from human medicine and clinical experience. Amantadine acts via antagonism of central N-methyl-D-aspartate receptors and is often used with NSAIDs or gabapentin. Amantadine has been shown to enhance osteoarthritic canine patient mobility and the ability to perform everyday activities when used in combination with NSAIDs as compared to NSAIDs alone.[24] Gabapentin has analgesic properties though its mechanism of action is poorly understood. Sedation is its most common adverse effect. Abrupt discontinuation is discouraged. Tramadol is a synthetic, centrally-acting, mu-receptor agonist that also acts via inhibition of serotonin and norepinephrine reuptake. Side effects include sedation, vomiting, and constipation. Its use should be avoided with amitryptiline. Though commonly prescribed in many veterinary practices, a recent placebo-controlled, cross-over study design found that use of tramadol alone failed to improve pain scores or limb dysfunction in dogs with chronic OA.[25] Carprofen treated dogs, on the other hand, showed improved pain scores and limb function compared to placebo and tramadol treated groups.[25] Whether or not tramadol can augment the effectiveness of other therapies has not been determined, but seems speculative. Polysulfated glycosaminoglycan (Adequan®) acts by intra-articular inhibition of proteolytic enzymes, increased synthesis of proteoglycans, reduced prostaglandin $E_2$

concentrations and increased hyaluronate concentration. It is typically administered via IM injection twice a week for 4 weeks, then approximately once a month thereafter. Pentosan polysulfate (Cartrophen®) acts via support of chondrocytic anabolic activity and mitigation of catabolic events that lead to the loss of cartilage ECM in OA joints. Evidence supports its classification as a structure-modifying osteoarthritis drug, but its efficacy for acute symptom control is somewhat dubious. Acetaminophen (paracetamol) produces analgesia via inhibition of cyclooxygenase, but does not have significant anti-inflammatory properties. It can be prescribed in combination with codeine for added pain relief. Acetaminophen is contraindicated in cats at any dosage because of acute toxicity concerns due to their inability to properly metabolize the drug. Dogs, apparently, do not metabolize acetaminophen as well as humans so its use must be judicious. Amitryptiline has a tricycle antidepressant action and has been used to treat chronic pain, especially that of neuropathic origin. Amitryptiline's main side effects are sedation and anticholinergic properties. It should not be used concurrently with tramadol and should be used with caution in dogs with seizure disorders.

**Intra-articular (IA) injections** of corticosteroids or hyaluronic acid have been advocated for osteoarthritic joints. Obviously, aseptic technique is of paramount importance with any intra-articular injection therapy. The technique for safe collection of joint fluid or administration of intra-articular therapies in each of the major canine joints has been nicely summarized in video format (Palmer RH, Joint taps & intra-articular injections, 2011; www.videovet.org). Corticosteroid IA injection remains controversial with some studies demonstrating adverse effects on cartilage while others demonstrate symptomatic relief and chondroprotective effects. In dogs with OA induced by cranial cruciate ligament transection, triamcinolone hexacetonide, 5mg, IA reduced osteophyte size, cartilage erosions, and the histological severity of OA structural cartilage changes with no electron microscopic evidence of increased cell degeneration or death.[26] Some other corticosteroid formulations have been shown to be chondrodestructive. Corticosteroid IA administration should be avoided immediately following arthroscopy because increased risk of septic arthritis.[27] Intra-articular injection of hyaluronan has been advocated for many species including horses and humans, but its effects on naturally occurring OA in dogs has not been extensively reported. Short-term symptomatic relief has been reported in a small-scale study of dogs with naturally-occurring OA following a two injection protocol (3 weeks apart) with a high molecular weight product.[28] Its mechanisms of action and potential uses in dogs has been nicely reviewed.[29] Hyaluron's mechanisms of action may be transient improvement in joint lubrication and its longer lasting analgesic, pro-anabolic and anti-catabolic effects. Variation in molecular weight of the product, dosage, frequency of administration as well as species and OA model evaluated may account for the variation in reported outcomes. Disadvantages of its use in dogs may relate to its relatively high cost and the apparent necessity of repeated IA injections relative to its lack of robust efficacy data reported in dogs.[29,30]

**Investigational and biologic therapies** such as cytokine therapy, stem cell, and platelet rich plasma (PRP) therapy are gaining advocates, especially when more conventional therapies have failed to restore patient comfort and quality of life. Upset of the critical

balance of pro-inflammatory cytokines and anti-inflammatory cytokines is well-recognized in the pathogenesis of OA.[31] Conditioning of autologous serum from a whole blood sample has been used to stimulate the production of interleukin receptor antagonist protein (IL-Ra), IL-4 and other anti-inflammatory cytokines.[32] Intra-articular injection of this autologous conditioned serum has resulted in significant clinical and histologic improvement in OA-affected joints.[32] To circumvent the need for repeated IA injections, viral vector gene transfer technology has been employed to obtain sustained levels of IL-Ra.[33] This approach has resulted in elevated intra-articular expression of IL-Ra, significant improvement in clinical parameters of pain and disease, preservation of articular cartilage, and beneficial histologic effects on synovial membrane and articular cartilage in equine and canine osteoarthritis models. Research and development for improved viral vectors is ongoing. Stem cell therapy involves stem cell isolation from various tissues including adipose and bone marrow and, in some instances, culture expansion. Injection of these cells into osteoarthritic joints may result in clinical improvement as compared to negative controls (sham injection),[34,35] but few studies have evaluated this therapy compared to a positive control (current standard of care) therapy in the canine. While this is an exciting field of ongoing research, in the absence of robust evidence for effectiveness over the current standard of care, the expense of stem cell therapy makes it difficult to justify for the majority of canine OA patients at this time.[36] PRP is defined as an autologous concentration of platelets in a small volume of plasma. PRP contains a concentration of critical growth factors that are actively secreted by platelets to stimulate cellular proliferation, migration, differentiation and matrix synthesis. These factors can affect chondrocyte metabolism, chondrogenesis, and improve cartilage healing in vivo. Despite these purported positive influences of PRP, it is also important to know that PRP is not a singular biologic product and the many potentially critical variables include leukocyte content, erythrocyte content, fibrin content, method of platelet activation (vs. none at all), platelet concentration, and product form (gel or liquid).[37] Several human studies show favorable clinical outcomes with a PRP formulation as compared to intra-articular injection of hyaluronic acid (HA).[38,39] In humans, there appears to be an “age ceiling” (~ 55 years of age) beyond which the efficacy of PRP formulations in OA patients is diminished.[38-40] There is substantial variation in the preparation and formulation of autologous PRP, but affordable point of care preparation is certainly feasible. A recent study utilizing a PRP formulation in osteoarthritic dogs showed significant reduction in pain and lameness scores and increased peak vertical force whereas sham-treated dogs were not different than pre-treatment.[41] Recent research has explored the role of Nerve Growth Factor (NGF) for pain mediation in both human and animal OA patients. Novel anti-NGF therapies appear promising and may soon fit into the comprehensive management of OA (this will be discussed in a subsequent session).[42,43]

**Mechanical therapies** for OA include pulsed ultrasound and shockwave. There is some evidence for the efficacy of shockwave therapy in the management of osteoarthritis.[44] There is a need for more controlled studies in the canine to determine the efficacy relative to the current standard of care and recommended therapy protocols.

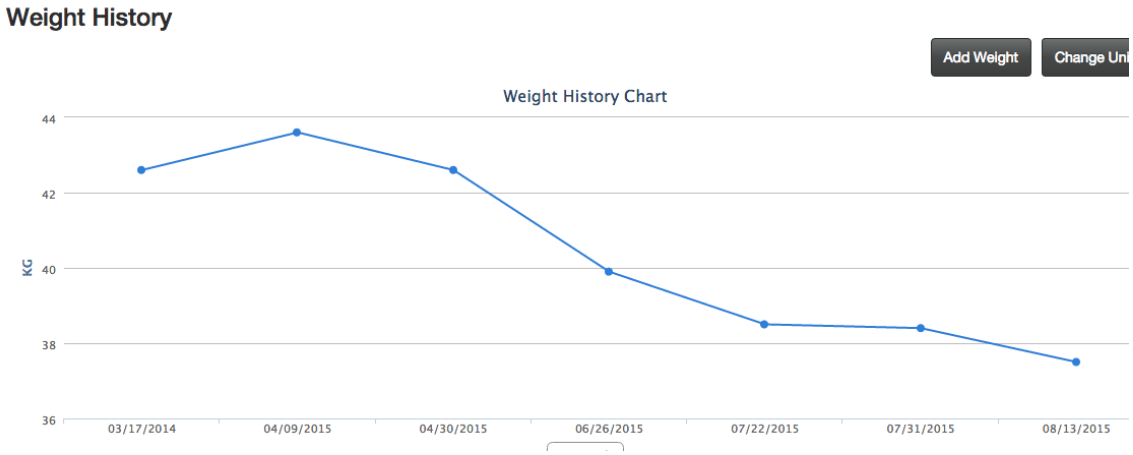
**Surgical treatment**, often required for effective management of OA, may involve joint stabilization, removal of cartilage/bony chips, or joint replacement. The relative importance and timing of surgery is variable depending upon the condition underlying the osteoarthritis.

----------CLINICAL CASE EXAMPLE----------

**"Smokey" 10 years old, M/c, Chocolate Labrador Retriever, 44kg, BCS = 8/9**
History: Failed extracapsular suture stabilization of cranial cruciate ligament-deficient stifle was revised with a TPLO. Patient is now grade 4/5 lameness due to grade 3 medial patellar luxation. Medications: He has not tolerated NSAIDs well in the past. Lifestyle: He had been a very active dog, but now receives almost no activity, Diet: 1 cup of a "senior" dry kibble diet with 1 can of Alpo® wet food and green beans. He has gained a lot of weight since this knee problem began.

Problem List:
1) Postop TPLO and lateral fascial imbrication
2) Grade 3 MPL
3) Obesity!!!
4) Historical NSAID intolerance

Assessment & Plan: We planned a revision of his patellar luxation upon complete healing of his TPLO because we were not optimistic about his grade 3 patellar luxation being responsive to physical therapy. Nonetheless, we recommended that he continue physical rehabilitation for the purposes of weight loss, resolution of his seroma, and progressive muscle strengthening while his TPLO was healing. To our surprise, his patellar tracking showed progressive improvement and we opted to "wait & watch" with regard to surgical revision. Progressive weight loss and improvements in gait continued over the ensuing 4 months. There were periodic readjustments of his caloric intake based upon his weight monitoring (see below). At 4 months following surgery, he weighed 38kg and was walking 3.5 miles per day and jogging an additional 1.5miles per day. It was at this time that his owner increased his goals for Smokey and indicated that he'd like to take him Elk hunting in the autumn/winter. These trips would require 15 miles of hiking on technical terrain to an altitude of 10,000-11,000 feet. While we were very concerned that this goal may not be attainable for a dog of his age and condition, we agreed to immediately begin to make slow and methodical steps in his training toward that goal. The duration and intensity of his endurance training was slowly and methodically increased. Once his target weight was reached, we slowly transitioned him to a prescription, omega-3 fatty enriched OA therapeutic diet. His weight was closely monitored during and after this transition.




Outcome: He was able to go Elk hunting and he performed well without any set-backs. Smokey was "a new dog" and they celebrated his 11th birthday by going deer hunting in January 2016. He remains active and enthusiastic for outdoor activities. He continues to receive his omega-3 fatty acid enriched diet (Purina ProPlan Veterinary Diets JM) and his daily Dasuquin® supplement.

5 Lessons Learned:

1) OA robs our patients of their life quality and is a 'silent killer'.
2) Obesity is a major risk factor for osteoarthritis
3) An effective weight loss plan requires detailed nutritional management that, for most pets, is best facilitated with an evidence-based, commercially formulated weight loss diet (ex. Purina ProPlan Veterinary Diets OM) that provides necessary macronutrients (such as protein) and calorie-restriction. Surveillance of the weight loss plan is key to success.
4) Use of an evidence-based, omega-3 fatty acid-enriched, commercially formulated weight loss diet (ex. Purina ProPlan Veterinary Diets JM) supports joint health & comfort once the ideal body condition score has been achieved.
5) I have underestimated what my patients are capable of achieving with proper nutritional and rehabilitation care.

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# LAMENESS EVALUATION:
# TIPS & TRICKS OF THE MEANINGFUL ORTHOPEDIC EXAM

One of the greatest challenges in small animal veterinary medicine is accurate localization of lameness in dogs. Unlike human patients, our canine patients cannot describe their discomfort or tell us where it is localized. In my career, I have had the opportunity to observe students as they learn their lameness examination skills as well as to see orthopedic examinations performed by the most skilled masters; one trait of the masters is their consistent and systematic approach to lameness evaluation. The systematic approach to the lameness exam consists of 6 basic steps (consideration of patient signalment, obtaining a careful patient history, detailed gait observation, thorough palpation examination, quality diagnostic imaging and other tests).

***Signalment.*** The signalment is a critical consideration because some conditions are more common in small breeds of dogs, while others are more common in larger breeds. Similarly, some common causes of lameness are more common in skeletally immature animals (congenital, nutritional, developmental, etc), whereas others (degenerative, neoplastic, etc) are common in mature animals. For example, Legg-Calve-Perthes disease is commonly a differential diagnosis for hip pain in a skeletally-immature dog, but need not be considered in an elderly large breed dog.

***Patient history & description of pet owners' observations.*** The purpose of obtaining the patient's history is to clearly understand and record all of the pet owner's observations regarding their dog. Too often, key pieces of information are left undiscovered in the quest for brevity and simplicity. It is not an easy task to guide the pet owner through a series of questions that will help them to recall, reveal and articulate all of their various observations, responses to therapies, etc that have caused them to schedule some of their valuable time to seek your expertise. It is worthwhile to ask them to explain their primary concern in their own words. Seeking clarification on details of their concern is very important. For example, a pet owner may state that they are concerned about the limping that they see on their pet's right front limb; however, when questioned as to why they say it is the RIGHT front limb they may quickly acknowledge that this was only their impression and that it may very well have been the LEFT front limb. Such a situation is quite common with thoracic limb lameness because the willingness of the dog to bear full weight on the normal limb causes dogs to drop their head when the comfortable limb strikes the ground, but the pet owner often interprets this "head drop" as a sign of pain in that limb. In addition to clarifying the pet owner observations (stiffness, lameness, reluctance to jump, etc), it is important to determine the nature of the onset (peracute, acute, insidious), progression (episodic, waxing/waning, progressive, improving), and duration of the identified problem. It is also helpful to identify factors that seem to exacerbate the problem (patient activity, patient cool down, rising in the morning, etc) as well as its response to any therapies (rest, prescribed medications, "over-the-counter" medications and even medications that may have been prescribed for another pet). The animal's travel history can also be

very important because some infectious disease causes of lameness are common in one geographical region, but rare in others.

**Gait Observation**

The purpose of gait observation is to identify which limb or limbs are affected and to determine if the gait abnormality appears orthopedic or neurologic in origin. It may also be possible to identify a probable source of the lameness (ie, elbow or tarsal effusion, swelling of a digit, etc), but examination will be necessary to assess the importance of that observation as well as to rule-out other possible contributors to the lameness.

I like to observe my patients as they approach the hospital, as they walk to the exam room and while I am obtaining a patient history. It is during this time that they are moving naturally because they do not know how closely that I am watching them. For example, the pet may shift weight away from one pelvic limb as evidence of discomfort. Alternatively, the patient may put his front limbs up on the counter in search of a treat…strongly suggesting that neither hip extension nor lumbar extension is uncomfortable (Fig 1). The patient may have difficulty sitting, shifting his/her weight to the thoracic limbs to do so; this finding is strongly suggestive of a bilateral pelvic limb problem such as canine hip dysplasia or bilateral cranial cruciate ligament disease (Fig 1). All of these observations are relevant and significant clues as to the source of their discomfort.

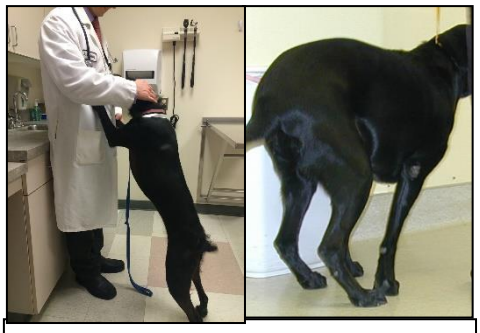


Fig 1 – The dog that is willing to voluntarily extend its lumbar spine & hips (left) likely does not have hip, lumbar or iliopsoas discomfort. The dog that shifts her weight toward her thoracic limbs in order to sit (right) is suggestive of bilateral cranial cruciate ligament disease.

In addition to watching my patient move naturally around the hospital, I like to observe him/her at a walk and trot away from me and towards me, as well as from each side. It can be very helpful to use a smartphone as a video recorder of the lameness. Many such phones come with an application for slow motion video. Slow motion video can clarify which limb is affected; this can be especially helpful in small breeds with short limbs and rapid limb movement. It can also be helpful in communicating gait observation findings to the pet owner. If you have access to stairs, pelvic limb lameness is often exacerbated while ascending stairs and thoracic limb lameness is worsened while descending stairs. The **sit test** should be a part of every gait exam; reluctance or inability to sit squarely with the stifles and tarsi in maximal flexion is highly suggestive of tarsal or stifle pathology. Frequently, a dog will be presented for unilateral pelvic limb lameness yet close scrutiny of the sit test will make me aware of bilateral disease.

***Palpation Examination***

The primary purpose of the orthopedic and neurologic examinations is to localize the lameness and, perhaps, determine its cause. Lameness can be localized via detection of instability, swelling, warmth, effusion, and/or pain. Obviously, the

orthopedic exam should not be performed at the exclusion of, nor interpreted independent of, the general physical exam. For instance, detection of a fever may have profound implications as to the cause of the lameness.

General principles of orthopedic exam including starting with examination of the normal limb in order to determine the animal's "baseline" response to non-painful stimuli. It is also generally accepted to proceed in a systematic fashion from the distal limb toward the proximal end; though there are certainly exceptions in individual patients. Since detection of pain is a valuable localizer of lameness, it is important that the animal be comfortable enough with its surroundings and the examiner, that a response to an uncomfortable stimulus can be detected. Further, it is important that the examiner perform that examination in such a way that the maneuver being performed would not be painful when performed in the healthy animal.

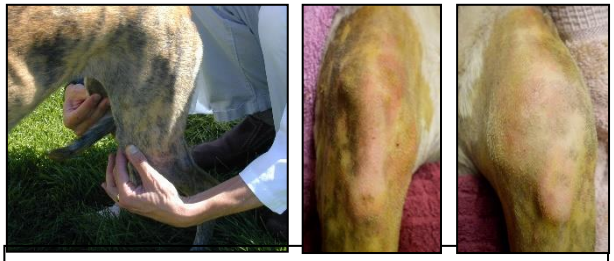


Fig 2 – (Left): Joint effusion is detected by examining both stifles simultaneously. (Center): Normal stifle has a distinctly palpable patellar tendon and flat medial joint pouch. (Right): Loss of these normal findings indicates periarticular fibrosis and /or joint effusion.

I typically start to examine the patient while it is standing. This allows me to simultaneously palpate the right and left limbs and to compare them for evidence of muscle atrophy or spasm, heat, pain, joint effusion, contracture, etc (Figure 2). Weight-bearing on the limb also makes joint effusion more evident; though effusion of the proximal joints (hip and shoulder) is seldom detectable because of the surrounding muscle mass.

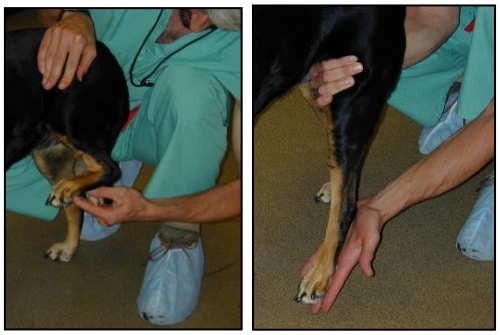


Fig 3 – Dogs with cranial cruciate ligament disease may exhibit signs of discomfort upon full flexion (left) or extension (right) of the stifle joint though veterinarians should be aware that excessively forceful joint extension may induce a pain response even from healthy joints.

Next, I perform a detailed palpation of each limb. Since a major goal of this exam is for the animal to tell me where he/she is uncomfortable, my decision to allow the animal to stand or lay in lateral recumbency for this portion of the exam depends on how the animal is most relaxed. In this exam, I typically palpate the limbs from distal to proximal starting with the lesser-affected limb; this gives me the opportunity to evaluate the dog's demeanor and typical response to my palpation maneuvers. I methodically evaluate joints, bones, muscles and tendon insertions for pain, swelling, and instability. I pay very close attention to comfort of the animal during full passive range of motion (ROM) of each joint and subtle discomfort or loss of ROM is noted. Even animals with healthy joints

may have a pain response to excessively forceful full *extension* of a joint, but a painful response to full joint *flexion* is usually indicative of pathology in that joint (Fig 3).

*Sedated Exam.* Sedation is helpful for anxious patients, but the examiner must keep in mind that heavy sedation or analgesia may mute the patient's response to otherwise painful stimuli. Any necessary imaging, arthrocentesis and/or diagnostic intra-articular analgesia can be performed under the same sedation.

*Diagnostic Intra-articular Analgesia.* It is often difficult to distinguish between shoulder and elbow causes of thoracic limb lameness. Intra-articular administration of local analgesic medication can be used in animals with obvious lameness to see if the lameness improves. Obvious improvement in lameness following intra-articular analgesia is highly suggestive that source of the lameness is within the treated joint. Conversely, the absence of significant improvement could either mean that the medication was not administered properly or that the source of the lameness is elsewhere in the limb. Aseptic preparation of the field is performed, joint fluid is collected and mepivacaine 1.5-5mg/kg is often administered intra-articular (Figure 4). The onset of action is 5-10 minutes and duration of action is 120-150 minutes. I typically video the animals gait prior to the joint block. Next, I sedate the animal with a reversible sedative, perform the joint block, and then reverse the sedation. After ~ 30 minutes I repeat the video gait evaluation.

Fig 4 – Shoulder Arthrocentesis. The technique for arthrocentesis and intra-articular injection is easy to learn. (Note: See www.videovet.org for video demonstrations of this and other surgical techniques.)

**Diagnostic Imaging**

Radiography remains the most commonly performed diagnostic imaging technique, though ultrasonography, computed tomography and magnetic resonance imaging are also used in veterinary medicine. Each imaging modality has its own advantages and disadvantages depending upon the region being evaluated. Regardless of the form of imaging used, it is best utilized to support the findings of the careful examination rather than as a substitute for it.

***Synovial Fluid Analysis.***

Septic and immune-mediated arthritis are infrequent, but important potential causes of lameness. Arthrocentesis is easily performed and video technique guides are published (Fig 4). Synovial fluid analysis can readily differentiate septic or immune causes from osteoarthritis. Nonsuppurative effusion consisting primarily of a mixture of small and large mononuclear cells is characteristic of osteoarthritis. Suppurative effusion consists of predominately polymorphonuclear white blood cells and is the hallmark of septic and immune arthritis. If micro-organisms are seen on cytologic

analysis, one can be certain of septic joint disease and a culture of the joint fluid is indicated. If micro-organisms are not seen on cytologic analysis, culture is still indicated to rule-out infectious disease because micro-organisms can be difficult to identify even in septic joints. Synovial fluid analysis from multiple joints may be indicated as immune-mediated disease commonly involves multiple joints.

## WAYS TO DESTROY A MEANINGFUL ORTHOPEDIC EXAMINATION

1. Make quick, loud or sudden movements, noises, etc
2. See the exam as only a list of specific orthopedic tests and manipulations
3. Suppress your patient's response to your stimuli
4. Lose your focus on subtle patient responses
5. Look for vocalization as the only evidence of pain
6. Over-interpret a single patient response
7. Rush to sedate your patient
8. Rush to perform radiographs
9. Forget that if the maneuver you are performing would be painful to you too, a response from your patient may not be indicative of pathology.

**Helpful Resources:**

- Canine Lameness Exam Workshop – VMX, Orlando, FL
- Canine Lameness Exam – I; VideoVet; www.videovet.org

# PATELLAR LUXATION IN SMALL BREED DOGS: SECRET TIPS for CASE SELECTION and SURGICAL TREATMENT

Anatomy

The patella is an ossification in the tendon of insertion of the quadriceps muscle group. The patella articulates with the concave femoral trochlea, bounded medially and laterally by ridges (Fig 1). The patello-femoral articulation functions as a simple pulley to alter the direction of the quadriceps muscle pull to accomplish stifle extension.

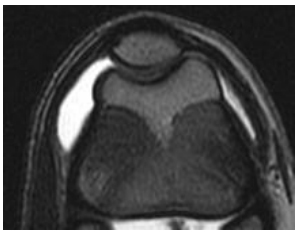


Figure 1 – MRI of normal patello-femoral joint. Note the cross-

The quadriceps group converges on the patella and continues as the patellar ligament to insert on the tibial tuberosity. Proper anatomic alignment of the quadriceps/patellar mechanism with the underlying skeleton fosters proper patellar tracking. The patella is surrounded by attachments of joint capsule, retinaculum and medial/lateral femoropatellar ligaments whose balanced tension helps maintain normal patellar position.

**Pathophysiology of medial patellar luxation (MPL)**

MPL is the result of structural abnormality and progressive degradation in the bony and soft tissues of the pelvic limb. In skeletally immature animals with MPL, the displaced quadriceps group creates a restrictive “bowstring effect” causing abnormal angular and torsional femoral growth; the femoral trochlea does not develop normally because of the absence of normal patello-femoral compression. Musculoskeletal abnormalities associated with MPL include: medialization of the tibial tuberosity, shallow/short femoral trochlea, medial displacement of the quadriceps muscle group, hypoplastic or eroded medial trochlear ridge, patellar articular surface erosion, internal rotational instability of the stifle, contracture/scarring of the medial joint capsule and muscular tissues, and tearing/stretching of lateral joint capsule and retinacular tissues. MPL is classified according to severity on a 4-point scale (Table 1).

**Table 1: PATELLAR LUXATION CLASSIFICATION**

| Grade | *Physical Findings* |
|---|---|
| 1 | Patella can be manually luxated, but returns to normal position when released |
| 2 | Patella spontaneously luxates during stifle flexion or ambulation and remains luxated until stifle extension or manual reduction. Frequency of spontaneous luxation/reduction is variable. |
| 3 | Patella is luxated most of the time. Patella can be manually reduced, but spontaneous re-luxation immediately occurs. |
| 4 | Patella is continually luxated; cannot be manually reduced. |

Clinical signs

Grade 1 MPL is primarily a veterinary examination finding in asymptomatic dogs. Dogs with grade 2 MPL often display episodic non-weight-bearing lameness. Repeated episodes of

luxation/reduction often erode the medial trochlear ridge causing progression from grade 2 to grade 3. Dogs with grade 3 or 4 MPL often have more persistent, yet less obvious lameness. Often these dogs are bowlegged and walk in a "crouched" gait due to inability to fully extend the stifles and are unwilling or unable to jump onto furniture or ascend stairs. Some dogs, especially toy breeds, with MPL are asymptomatic even with more severe grade 3 and 4 conditions. A history of mildly symptomatic MPL followed by a sudden worsening of lameness often indicates cruciate ligament rupture.

### Physical examination

Musculoskeletal exam is initially performed with the dog in a weight-bearing stance if possible and pelvic limb posture and patellar position are noted. Simultaneous hip and stifle extension may induce spontaneous MPL without overt pressure on the patella itself because this maneuver places the rectus femoris muscle under tension. Bony crepitus during patellar luxation/reduction indicate erosion of articular cartilage from the femoro-patellar joint. Indistinct transition between patellar luxation and reduction indicates severe erosion of the trochlear ridge and/or patellar articular surface. As pelvic limb conformation is evaluated, genu varum ("bowlegged") and internal rotational ("pigeon-toed") conformation is often seen with MPL. This conformation may reflect the skeletal conformation of the dog, though MPL and associated internal rotation of the stifle joint can create a similar appearance despite normal skeletal structure. In the standing dog, the alignment of the tibial crest relative to the long axis of the foot is evaluated by viewing the pelvic limbs from the dorsum toward the ground. In dogs with grade 4 MPL it may be difficult to discern the exact position of the patella since it cannot be reduced and luxated again. In such patients, it is often helpful to follow the medially displaced quadriceps muscle group distally to the medially rotated tibial tuberosity.

### Radiography - Traditional

Patellar position may be normal on radiographs of dogs with grade 1 or 2 MPL. Radiographs are also evaluated for osteoarthritis, concurrent orthopedic conditions and pelvic limb conformation. Accurate evaluation of pelvic limb conformation requires proper patient positioning and general anesthesia is usually needed. Subtle alterations in patient position dramatically alter the apparent skeletal conformation; you must confirm proper frontal plane orientation of the limb relative to the radiographic beam before you can diagnose varus/valgus mal-alignment! It is often difficult to get properly positioned radiographs of the femur and tibia in dogs with grade 4 MPL. It may helpful to segmentally position the limb for radiography (isolated femur, then isolated tibia, etc). Computed tomography (CT) scanning with 3 dimensional reconstruction, when available, is extremely helpful in obtaining accurate assessment of skeletal morphology.

### Surgical Treatment Techniques

Veterinarians are encouraged to build experience and expertise on the "simple" cases prior to pursuing treatment of more complex cases. In general, toy breeds of dogs with grade 2 and mild grade 3 MPL's are regarded as the "simple" cases. Even with these cases surgical technique or judgement error often leads to postoperative re-luxation of the patella and the need for surgical revision. Successful treatment of MPL requires detection and treatment of all skeletal and soft tissue pathology (Table 2). Surgery is typically performed with the patient in dorsal recumbency to allow accurate assessment of quadriceps/patellar alignment.

| **Table 2: MPL TREATMENT ALGORITHM** |
|---|
| **Step 1: Medial Parapatellar Release Arthrotomy** - medial release of joint capsule and quadriceps muscle group is essential before a grade 4 MPL can even be reduced to the region of the trochlea. Medial release of the capsule and quadriceps is also often indicated for grade 3 MPL. Evaluate cruciate ligaments, menisci, etc. |
| **Step 2: Evaluate trochlear depth, width and length** - If trochlear depth, width and/or length are inadequate, wedge or block recession trochleoplasty is performed. Patellar stability is tested. |

| |
|---|
| **Step 3: Evaluate tibial tuberosity position** – The stifle is locked in extension to assess the alignment of the patella, patellar ligament, tibial tuberosity and long axis of the crus and pes because this position minimizes the rotational freedom of the stifle. An imaginary line is drawn from the reduced patella to the long axis of the pes. If the tibial tuberosity is displaced medially relative to this imaginary line, then tibial crest transposition is performed (lateral transposition for MPL). A caudally positioned (deep) osteotomy of the tibial crest is recommended as the wide osteotomy surface will allow maximal lateral transposition and the large crest segment will permit solid fixation (Fig. 3). Patellar stability is tested. |
| **Step 4: Soft tissue reconstructions** – Perform capsular, retinacular imbrications and fabello-tibial crest anti-rotation sutures as needed. Grade 4 MPL patients typically require excision of redundant joint capsule lateral to the patella and the lateral retinaculum should be imbricated. The medial joint capsule may be left open if necessary or can be “loosely laced” in a non-apposed position to prevent patellar tipping. Evaluate patellar stability. |

Trochleoplasty is often required for surgical restoration of proper trochlear depth and length. I wish to see > 50% of the patellar length and > 50% of the patellar depth within the trochlea through a complete passive range of motion **(the 50/50 Rule)** and this is how I determine the need for trochleoplasty and, when necessary, the dimensions of the trochleoplasty. *Wedge* (Fig. 2) or *Block* (Fig. 3) recession trochleoplasty techniques preserve the articular cartilage of the trochlea. Poor trochleoplasty technique is, unfortunately, a common cause of recurrent postoperative patellar luxation. Veterinarians commonly perform a sufficiently deep trochleoplasty, but with little attention paid to its width or its length. If the trochleoplasty is not wide enough for the patella to fit within, you have not helped the patellar stability. Preoperatively, the patella often luxates medially when the stifle is extended and the patella is proximal to the trochlear sulcus. If the trochleoplasty does not capture the patella when the stifle is extended, luxation is likely even if it is otherwise deep enough and wide enough. After performing the trochleoplasty, the patella must be carefully re-introduced into the trochleoplasty and observed through a full passive range of motion (Fig 4). As a rule of thumb, the requirements of the 50/50 Rule should be met. In some cases, inversion of the wedge (so called, "medial ridge elevation wedge trochleoplasty") may permit improved medial ridge height (Fujii K, et al. Vet Surg 2013).

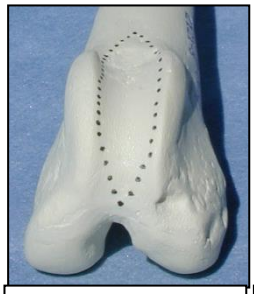


Fig 2 –Wedge trochleoplasty outline.

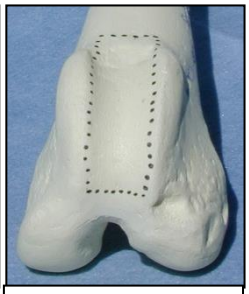


Fig 3 –Block trochleoplasty outline.

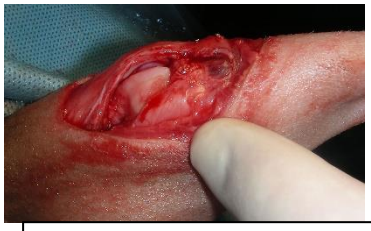


Fig 4 – View of patello-femoral joint to note position of patella in relation to sulcus through a full range of motion

Trochleoplasty begins by peeking under the margin of the joint capsule to view the patello-femoral joint through a full range of stifle extension-flexion. Pay close attention to the patellar position relative to the trochlear sulcus when the stifle is in full extension (Fig 4). The patella often rides proximal to the trochlear sulcus while the stifle is extended. The patella can now be luxated and a full stifle exploratory is performed. Pay close attention to erosive patterns on the trochlear ridge and on the patella. Most dogs with MPL will have erosion across the abaxial surface of the proximal end of the medial trochlear ridge – this indicates the importance of this portion of the trochleoplasty. Dogs will often have a reciprocal erosion on the lateral surface of the distal pole of the patella – keep this in mind because it is erroneous to believe that a trochleoplasty restores normal patello-femoral joint conformation (Fig 5).

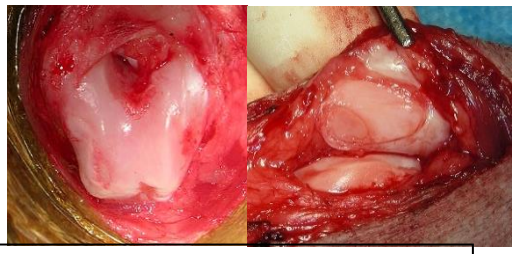


Fig 5– Note erosions on abaxial margin of medial ridge (left) and lateral margin of distal pole of the patella (right).

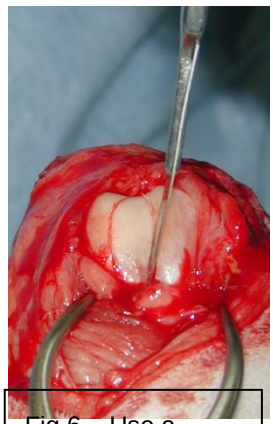


Fig 6 – Use a scalpel blade to cut through the healthy cartilage in order to outline the dimensions of the trochleoplasty

Next, I use a scalpel blade to outline the dimensions of the trochleoplasty (Fig 6). In regard to trochleoplasty width, I make it as wide as possible while still preserving the "guard rails" represented by the peaks of the trochlear ridges. That is to say, if the trochlear ridges are viewed in a skyline fashion, my trochleoplasty margins will be just 'inside' (axial to) the peaks of the medial and lateral trochlear ridges (Fig 7). Distally, the wedge comes to an apex just proximal to the intercondylar notch. Proximally the apex is at the approximate level of the proximal pole of the patella when the stifle is full extended. The purpose of these scalpel blade incisions through the cartilage is to provide a visual outline to follow and also to allow the saw blade to engage subchondral bone rather than slipping and damaging healthy hyaline cartilage. In young, small breed dogs it is often feasible to make the full trochleoplasty cuts with a scalpel, by adopting a smooth back & forth rocking motion as the cut progresses deeper and sculpting is alternately directed toward the proximal and distal apex. When a saw blade is required, it MUST be a thin blade with a fine kerf. More

aggressive kerfs will destroy the cartilage and will remove enough bone that a press-fit of the osteochondral wedge into the defect is not feasible. Trochleoplasty is more 'sculpting' than 'sawing' because the linear blade must be made to cut a diamond shaped (on its cranial surface) wedge. The rocking motion described above is essential (the video demonstration will clarify this point).

Textbooks often show making a third cut to widen the trochleoplasty such that the wedge will fit more deeply into the recipient bed – I SELDOM DO THIS! I may use a rasp or a scalpel blade to gently widen the recipient bed, but this alone is seldom enough to increase the trochlear depth as much as I'd like. It is like widening the dry-dock support for a sailboat….the sailboat will rock back and forth upon its keel, but it won't fit any deeper into the support. Instead, I use a fine rongeur to conservatively remove a small portion of the cancellous bone at the apex of the wedge (Fig 7). Don't remove too much or it will be impossible to secure the wedge into the recipient bed and expect it to heal.

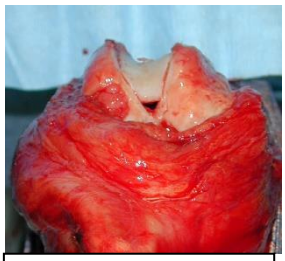


Fig 7 – Nice press fit of wedge into recipient bed as a result of slight widening of the defect and removal of the wedge apex.

Once I've widened the recipient bed slightly and removed "the keel" of the wedge itself, I will replace the wedge into the recipient bed as a trial. You can always remove more bone from the walls of the recipient defect or from the apex of the wedge, but it is hard to put it back if you've taken too much! Once I am satisfied with the depth of the trochleoplasty, I will firmly push the wedge into place. The wedge should be stable (Fig 7). Keep in mind that in some instances it is preferable to flip the wedge over such that the distal end of the wedge is in the proximal end of the recipient bed; this can be helpful in some instances of a very hypoplastic medial ridge in conjunction with MPL (Fujii K, et al. Vet Surg 2013). Once satisfied, I return to the patella to the trochleoplasty and make sure that it abides by the "50-50" rule. With regard to trochleoplasty length, pay particular attention to the proximal end of the trochlea on MPL's (Fig 8). With regard to patella-femoral joint depth, insufficient trochleoplasty depth is seldom the problem; instead, failure to make the trochleoplasty wide enough is more common. On occasion, especially in cats, parapatellar osteophytes must be removed in order to allow the patella to rest within the trochleoplasty. In order to remove these osteophytes, the stifle should be extended and the patella everted so that you have a clear view of the articular surface of the patella.

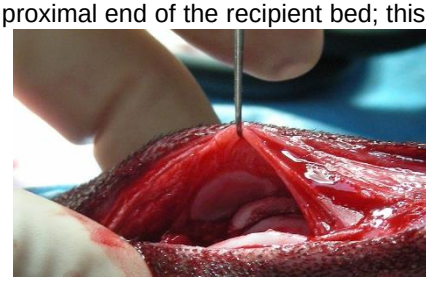


Fig 8 – Peeking under joint capsule to determine if the trochleoplasty satisfies the "50-50" rule. Note the severe patellar erosion in this patient – trochleoplasty is less able to constrain a patella that has lost its normal cross-sectional shape.

In skeletally immature patients, you should be aware that trochleoplasty disrupts the distal femoral physis. The risk of physeal dysfunction must be weighed against the benefits of restored mechanics. In small breeds, dysfunction of the cranial aspect of the distal femoral physis causes a loss of the normal femoral procurvatum when trochleoplasty is performed prior to 7 months of age, though the slight femoral recurvatum is seldom problematic. Surgery is advised in small breed puppies less than 7 months of age if they have persistent MPL (grade 3 or 4) that will cause abnormal bone development due to the persistent "bowstring effect" of the displaced quadriceps mechanism.

Fig 9 – Tibial crest osteotomy options. Harvest of a large tibial crest segment (light gray line) allows for greater lateral transposition and more secure fixation. An obliqued osteotomy (dark line) allows for cranial advancement as the tibial crest is transposed laterally. The long digital extensor (*) should be preserved.

Once satisfied with the trochleoplasty, attention is paid to the need for other corrective procedures such as tibial crest transposition, quadriceps release, capsular / retinacular imbrication, etc.

Tibial crest transposition is indicated when the tibial crest is not properly aligned along an imaginary line drawn between the reduced patella and the central axis of the hock and pes (see Table 2; Step #3). A caudally positioned osteotomy (large tibial tubercle fragment) creates a large osteotomy surface that maximizes the bony contact when marked translation is required. The tibial crest osteotomy is usually performed in the frontal plane, but can be performed in an obliqued caudo-medial to cranio-lateral direction to allow cranial advancement of the tibial tubercle as it is laterally transposed (Fig. 9). This slight cranial shift in the tibial tubercle decreases retropatellar pressure and may benefit patients with retropatellar chondromalacia. Either way, preservation of the cortex and periosteum at the distal extent of the osteotomy allows the tibial crest to pivot while reducing the need for tension band fixation. The tibial crest is aligned such that the patellar tendon insertion is aligned on an imaginary line drawn from the reduced patella to the axis of the pes with the knee locked in extension. "Temporary Door Stopper" Technique tip (Fig 10): Since it can be difficult to hold the tibial crest in proper alignment while securing it with K-wires, temporary placement of a hypodermic needle passed along side of the crest and into the osteotomy surface can hold the crest in the proper position while it is stabilized with 2 Kirschner wires. The most proximal K-wire is placed through the fibers of patellar ligament to assure purchase of the strongest portion of the tubercle. These wires are aimed so that they will exit the caudo-medial corner of the tibia immediately behind the medial collateral ligament (MCL) rather than caudally into the region of the popliteal artery. These wires can be countersunk or bent over and cut. Either way, one should be cautious not to inadvertently fracture the tibial crest segment when doing so. "Danish Twist" Technique Tip (Fig 11): If the K-wires were properly angled such that they exited immediately behind the MCL, they can be grasped at this end and withdrawn to the desired position in the tibial tubercle and bent at the level of the caudo-medial tibia; this "Danish Twist" will prevent problems with tibial tubercle fracture at surgery and soft tissue irritation postoperatively, yet makes the wires retrievable in the future if necessary. A tension band wire is placed if indicated (marked lateral transposition with little contact between the osteotomized surfaces, active dog, bilateral repairs, muscular dog, poor compliance anticipated, cats prone to jumping during convalescence, etc). Cancellous bone graft (often harvested from the trochleoplasty) can be applied to the tibial crest osteotomy if needed.

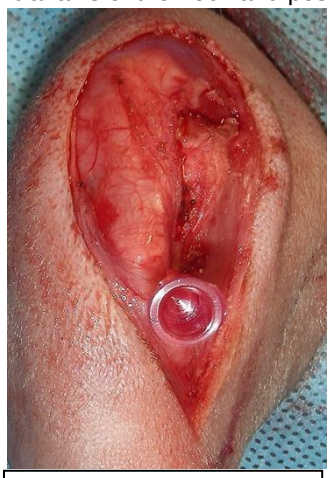
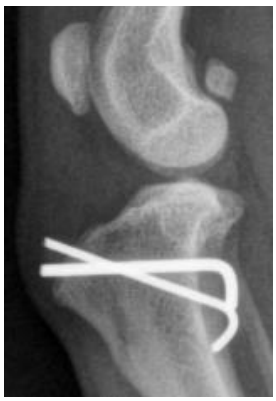


Fig 10 – The "Door Stopper" needle holds the tibial crest in the proper location for K-wire fixation. Then the needle is removed.



Soft Tissue Reconstructions include capsular/retinacular/muscular release, imbrications, and anti-rotation sutures. Soft tissue reconstructions, by themselves, will not correct bony conformational abnormalities. Soft tissue reconstructions are most commonly performed in conjunction with skeletal reconstructions. Release of thickened and contracted medial joint capsule/retinaculum is achieved by their incision from the tibial plateau to the suprapatellar recess. In most grade 4 and some grade 3 MPL cases, the quadriceps muscle group is medially displaced (Fig 12) and must be elevated from the suprapatellar region to the proximal femur, being careful to protect the descending genicular vessels. The pes anserinus muscle group (sartorius, gracilis, and semi-tendinosus muscles) can be released by elevation of their insertions on the medial aspect of the proximal tibia if their tension is causing internal rotation of the stifle. Stretched lateral joint capsule/retinaculum often need to be tightened to achieve balanced soft tension upon the patella. In grade 4 MPL cases, redundant joint capsule lateral to the patella must usually be excised. Reconstruction of the lateral joint capsule helps to properly balance the tension in the peri-patellar tissues. Extracapsular lateral fabello-tibial anti-rotation sutures can be placed to limit excessive stifle rotation and are particularly beneficial in dogs with combined MPL and cranial cruciate ligament rupture. The tibial anchor point of the extracapsular suture can either be to paired bone tunnels at the level of the extensor sulcus of the tibia (adjacent to the long digital extensor) or to a pre-formed eyelet in a tibial tension band wire.

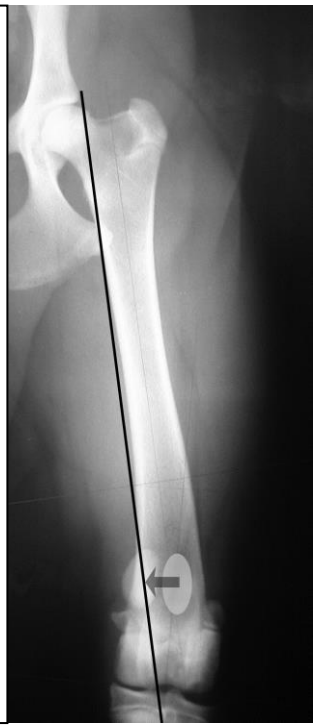


Fig 12 – In chronic grade 3 and grade 4 MPL's, the quadriceps muscle group is often scarred down in medially displaced position relative to the femur. In such instances, medial release is indicated.

Fig 11 – The "Danish Twist" technique can be used when the K-wires exit the tibia immediately behind the MCL.

***"What are the most common errors you see that lead to re-luxation?"***

Unfortunately, postoperative patellar re-luxation is a common problem. The following is a list of errors that may lead to postoperative re-luxation:

- Poor case selection (too severe for experience level of the surgeon)
- Assumed it was a medial luxation, but it was really a lateral luxation
- Patient needed a osseous procedure (trochleoplasty and/or tibial crest transposition), but only soft tissue procedures were performed (imbrication, soft tissue releases, etc)
- Trochleoplasty was too narrow and/or too short (see "50/50 Rule" below)
- Patient needed a tibial crest transposition, but didn't get one.
- The tibial crest segment was too small or the fixation inadequate.
- Patient had abnormal femoral conformation (varus/valgus, torsion) that was not identified or corrected (common in Labradors, Pit Bulls, Great Pyranees, Akitas).

**Key Points:**

- Veterinarians are encouraged to develop their surgical skills on relative simple cases before pursuing treatment of more complex cases.
- Simple cases are small breeds of dogs with grade 2 or mild grade 3 medial patellar luxation.
- Common surgical errors that lead to postoperative re-luxation and often require revision surgeries in small breeds of dogs are: inadequate trochleoplasty dimensions, failure to recognize when tibial crest transposition is indicated, poor tibial crest transposition technique, and inadequate balancing of parapatellar soft tissue tension.
- Common surgical errors that lead to postoperative re-luxation and revision surgery in large breeds of dogs are: failure to properly identify and correct associated skeletal mal-alignment, erroneous assessment of skeletal mal-alignment and surgeon error.

**Helpful Resources**

- **Practical Orthopedic Surgical Techniques Course;** NAVC Institute; Orlando, Florida; NAVC.com/Institute
- **Medial Patellar Luxation Workshop - SecurosUniversity;** www.securosuniversity.com
- **Practical Surgical Techniques of the Canine Stifle**; www.videovet.org; Ross.Palmer@me.com

# TRAUMATIC HIP LUXATION: 5 SECRETS OF EFFECTIVE TREATMENT

It has been said that we learn more from our mistakes than from our successes. To that end, I've learned 5+ ways to fail when treating traumatic hip luxation.

**HOW TO FAIL WITH CLOSED HIP REDUCTION**

1. Fail to determine the direction of the luxation
2. Fail to closely scrutinize radiographs for hip joint conformation, associated injuries, etc
3. Fail to inform clients that ~ 50% of hips may re-luxate.
4. Fail to modify Ehmer slings with an '"Abduction Roll" for cranio-dorsal luxations
5. Try to put an Ehmer sling on a chondrodystrophic breed of dog
6. Fail to keep the sling dry
7. Fail to closely monitor the sling and surrounding skin each day
8. Fail to remove a tape Ehmer sling after 2 weeks (3 weeks maximum)
9. Fail to restrict patient activity following removal of the Ehmer Sling

In short, Ehmer Slings "go bad" when they are applied to the wrong patient, when they are applied incorrectly, or when we improperly educate the pet-owner about them. I've heard many veterinarians say that they don't think that Ehmer slings are helpful, but I think that they do for many patients. I would estimate that approximately 50% of the closed reductions that fail in the hands of others, can be successfully treated via non-surgical means when properly selected and when a simple "Abduction Roll" is added to the conventional Ehmer Sling.

Once you suspect a coxofemoral luxation, radiographs are necessary to screen for concurrent injuries, to assess the conformation of the hip joint and to confirm the direction of the luxation. Ehmer slings are indicated for dorsal luxations, but are CONTRAINDICATED for ventral luxations.

**RADIOGRAPHY**

Radiographs should always be performed on patients with suspected hip luxation in order to:

1) confirm the direction of hip luxation – because closed reduction techniques and post-reduction coaptation will depend on the direction of luxation
2) evaluate the conformation of the hip joint -- because moderate to severely dysplastic hips are unlikely to stay reduced following closed or open reduction.
3) evaluate for concurrent regional orthopedic injuries – because fractures of the dorsal acetabular rim or femoral head avulsion fragment may prevent successful closed reduction. Further, other pelvic injuries may require surgical care.

**CLOSED REDUCTION CONSIDERATIONS**

Closed reduction of recent hip luxations (< 5 days?) is often indicated if there is good coxofemoral conformation, there are no associated pelvic or coxofemoral fractures and the pet owner is aware that ~ 50% of the patients will experience a re-luxation of the hip in the convalescent period. Negative prognostic factors for maintaining closed hip reduction include chronicity, poor hip conformation, obesity, elderly, weak/poor muscle tone, and multi-limb dysfunction.

General anesthesia is required for analgesia, immobilization and muscular relaxation. The technique for closed reduction of dorsal hip luxation has been described elsewhere. Reduction is confirmed via the thumb pinch test, the triangle test and, ultimately, radiography. Once reduced, it is important to evacuate all blood clot, inverted joint capsule, etc from the acetabulum by continual, deep, internal/external rotation of the hip while firm pressure is applied laterally to push the femoral head deep in the acetabulum. You've often worked > 10 minutes to get the hip reduced, don't be afraid to spend an additional 5 minutes doing your best to help it stay reduced!

**"ABDUCTION ROLL" MODIFICATION OF CONVENTIONAL EHMER SLINGS**

Though maintaining hip abduction and internal rotation is key to successful closed hip reduction, the standard Ehmer sling is minimally effective because it fails to adequately accomplish this task. Thus, I like to add a special "Abduction Roll" to the Ehmer sling to accomplish improved hip abduction and internal rotation as compared to the traditional Ehmer sling. The technique is described below:

1. Animal Position - lateral recumbency (treated leg up)

2. Apply Cast Padding to the Metatarsus – several layers

3. Apply Roll Gauze around the Cast Padding – Use caution not to apply too tightly.

4. Anchor the "Figure of 8" Sling to the Metatarsus – With the adhesive side of the tape against the medial surface of the crus, loosely apply 2" porous white tape around the metatarsus in a 'clam-shell' pattern to avoid 360° tight encircling of the limb.

5. Form the "Figure of 8" Sling – Flex the knee and tarsal joints to slightly past 90° of flexion and pass the 2" sling tape along the MEDIAL surface of the crus → over the distal end of the femur (pulling the skin distally off the femur will help retain the tape up on the thigh as the skin is released) → across the LATERAL surface of the distal thigh → around to the MEDIAL side of the metatarsus. Several layers of this Figure-of-8 encircling tape should be used to add strength to the sling. Note that the adhesive side of the tape is against the skin to resist slippage of the sling. Note also that the tape NEVER crosses the lateral side of the crus.

6. Apply a "Belly Band" using 2" white tape around the abdomen (cranial to the prepuce in male dogs).

7. Form a traditional Ehmer Sling Strap by passing 2" porous white tape from the metatarsus (distally) up around the 'belly band' (proximally).

8. Form an ABDUCTION ROLL -- Use tape to secure a clean cotton towel into a wide roll.

9. Place the ABDUCTION ROLL directly over the hip joint on top of the traditional Ehmer Sling Strap.

10. Improve the hip abduction by placing additional 'Improved' Ehmer Sling straps from the metatarsus, across the ABDUCTION ROLL and around the belly band.

11. Secure the ABDUCTION ROLL by 'sandwiching' it between the traditional Ehmer Sling and the Improved Sling straps.

**Aftercare & Precautions**

- Hip luxation may recur in ~ 50% of patients treated by closed (non-surgical) methods.

- Bandage should be monitored daily to be sure that it is clean and dry, has not slipped off the stifle, and is not cutting into the skin.

- This sling is designed for short-term application and its use is typically limited to only 2-3 weeks to avoid soft tissue contracture of the hip, knee and tarsal joints. Because soft tissue healing is incomplete after 2-3 weeks, patient activity should continue to be restricted after removal of the sling.

Prefabricated vests and slings with Velcro closures are available commercially (DogLeggs, Reston, VA) and work very nicely on most dogs and an "Abduction Roll" can easily be adapted to this device. Commercial slings have the advantages of being easily adjusted and even permitting temporary removal for physical rehabilitation. An improved Ehmer sling constructed of white tape is typically maintained for 2-3 weeks; whereas a commercial sling may be able to maintained longer if needed because of the ability to perform passive range of motion on the limb via intermittent, temporary sling removal. After sling removal, the patient is restricted from running, jumping, playing, climbing furniture or stairs for an additional 4-6 weeks. When traversing slippery surfaces, using a sling or towel under the patient's belly prevents accidental slips and falls. In addition to exercise restriction, physical rehabilitation with a trained therapist can maximize the recovery outcome via improved range of motion, muscle timing and development.

**Helpful Resources:**

Orthopedic & Wound First Aid – 1, VideoVet 2011, www.videovet.org; Ross.Palmer@me.com
Bandages, Slings, Splints & Casts – I, VideoVet 2011, www.videovet.org; Ross.Palmer@me.com

# FRACTURE MANAGEMENT: PRINCIPLES OF EXTERNAL SKELETAL FIXATION

The External Skeletal Fixation (ESF) system integrates the use of transfixation pins, an external frame, and sometimes a "tied-in" intramedullary pin for orthopedic fixation. Use of the ESF system may be in conjunction with interfragmentary fixation techniques such as cerclage wires, lag screws, and K-wires when appropriate. Bone plate and screw fixation is another example of an implant system used for similar indications including fracture management, corrective osteotomy, and arthrodesis. Neither the plate & screw system, nor the ESF system is preferred in all instances. Each system has its unique strengths and weaknesses. Both systems add significantly to the spectrum of fractures that can be effectively treated as compared to coaptation or intramedullary pin + cerclage wire techniques. The bone plate and screw system has the advantage of simplifying postoperative care, while the ESF system provides versatility and the opportunity to maximize the biologic potential for healing within the fracture zone. Biologic application of bone plates or internal fixators has been developed to overcome some of the biologic disadvantages of conventional bone plating.

**Advantages & Disadvantages of ESF**

Unique advantages of the ESF system include the following: (1) closed or minimally invasive application techniques are possible, (2) fracture alignment can be adjusted during and after surgery, (3) fixation rigidity can be changed during the fracture healing process to suit the physiologic needs of the tissues, (4) fixation devices can be removed without performing major surgery and, (4) ESF devices are relatively inexpensive and many of the components are reusable.

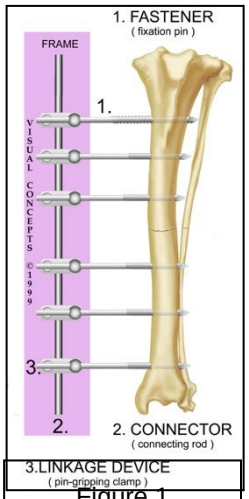


Figure 1

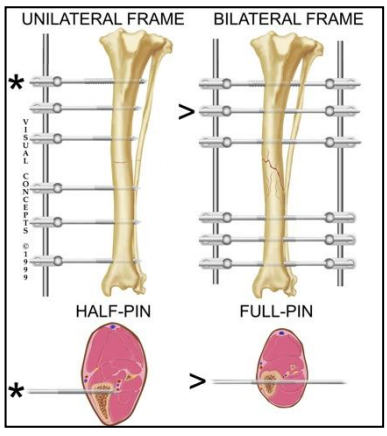
Failure to recognize and overcome the inherent disadvantages of the ESF elevates the risk of patient morbidity. Disadvantages of the ESF system that must be overcome include: (1) transfixation pins penetrate soft tissues between the skin and bone and may impair the function of neurovascular bundles and muscle tendon units, (2) closed application of the system requires intraoperative imaging or spatial awareness of the geometry of the bone, adjacent joints and fracture configuration through keen palpation skills and/or “needle mapping”, (3) soft tissue corridors for transfixation pins (pin tracts) represent an avenue of entry for contaminating bacteria, (4) unilateral ESF frames are at a mechanical disadvantage when confronted with disruptive forces acting at the fracture site because the connecting elements of the ESF are placed distant to the central axis of the bone, and (5) postoperative care is more demanding and must address such issues as pin tract hygiene and the potential for the externally placed elements to injure the patient or owner.

**ESF Nomenclature**

The ESF System is comprised of many different types of devices including linear, ring and acrylic ESF devices. Among the most popular of the current generation of linear devices is the IMEX SK™ device and it will be the device used in our discussions and laboratories. Regardless of specific manufacturer, linear devices have 3 basic elements (Fig 1):

1. Fasteners (percutaneous fixation pins)
2. Connecting rods
3. Linkage devices (clamps linking the fixation pins to the connecting rods)

Fixation pins are termed either *half-* or *full-pins* (Fig 2) based upon how they are inserted.



- Half-pins penetrate the near-skin surface and both the near- and far-cortex of bone.
- Full-pins penetrate the near-skin surface, both cortical surfaces of the bone, and exit the far-skin surface of the limb.

Figure 2

The connecting rod(s), fixation pins and clamps define an ESF frame (Figs 1 & 2). Frame configuration is described by the number of distinct sides of the limb from which it protrudes ["unilateral" or "bilateral"] as well as the number of planes it occupies ["uniplanar" or "biplanar"].

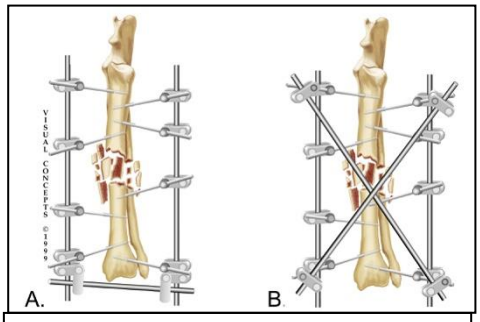



Figure 3

- Unilateral-uniplanar (Type 1a) frames protrude from just 1 side of the limb and are restricted to one plane. Type Ia frames (Fig 2 – left) are formed by connecting 1 or more half-pins of each main fracture segment.
- Bilateral-uniplanar (Type II) frames protrude from 2 distinct sides of the limb, but are restricted to just one plane (typically the medio-lateral plane). Type II frames (Fig 2, right) are formed by connecting 1 or more full-pins of each main fracture segment.
- Bilateral-biplanar (Type III) frames protrude from 2 distinct sides of the limb and occupy 2 planes. Type III frames are formed when both a Type 1a and Type II frame are applied to a bone. These are seldom used with modern ESF devices.
- Unilateral-biplanar (Type Ib) frames occupy 2 planes, but because these frames do not protrude from 2 distinct sides of the limb (180° to each other) they are thought of as "unilateral". If the frame occupies more than 1 plane, but does not connect a full-pin in the proximal segment to a full-pin in the distal segment, it is a Type 1b. Standard type Ib frames (Fig 3) are formed when two Type Ia frames are applied to a bone.

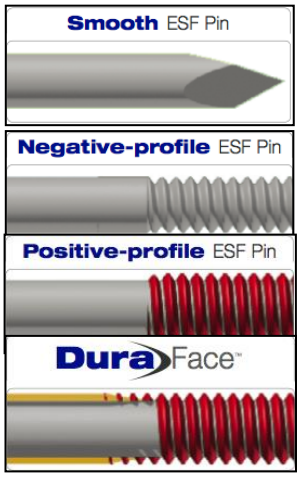
The frame classification described above fosters accurate communication between colleagues and also provides a basic sense of frame stiffness under axial loading (Type III > Type II > Type I).

Combination of 2 or more frames in different planes is sometimes referred to as a "*montage*". These multi-planar frames are typically interconnected to form a stiffer construct. These interconnections between frames can be made either as *articulations* or *diagonals*.

- Articulations do *not* span the fracture zone (Fig 3A).
- Diagonals *do* span the fracture zone (Fig 3B).

Type 1b frames are sometimes applied for the purpose of enhancing this multi-planar stiffness. Uniplanar frames are most able to resist bending forces that are applied in the plane of the frame (versus those in the plane perpendicular to the frame). As an example, a frame occupying the medio-lateral plane is less able to resist bending forces in the cranio-caudal plane. Application of multi-planar frames, therefore, imparts better multi-planar stiffness. In theory, this is best accomplished by placing the frames 90° to one another. Clinical practicality, however, dictates that frames be applied as regional soft tissue anatomy and bony cross-sectional structure warrant. As an example, Type Ib frames applied to the radius typically consist of a frame in the cranio-medial plane and a second frame in the cranio-lateral plane (Fig 3).

Type II frames are not as frequently employed as they once were. When the frames are comprised entirely of full-pins, they are called "maximal" Type II frames. A "minimal" Type II frame is comprised of one full-pin in the proximal main fracture segment and one full-pin in the distal segment, and the remaining positions are filled in with half-pins.




**ExFix Pins**

Smooth (non-threaded) Steinmann pins were originally used with ESF, however, premature pin loosening was a major problem and their use has been replaced by use of various threaded pin designs (Fig 4). Positive- versus negative-thread profile, cortical versus cancellous thread form, length of the threaded portion, and pin size must all be considered for optimal pin selection for a given bony insertion site.

Thread profile. *Negative profile threads* are cut into the pin at the expense of the core diameter. When threads are cut into the pin over its entire length, the pin loses its stiffness and is subject to bending or breakage. When threads are conventionally cut only into the end of the pin (end-threaded pin), the abrupt change in pin diameter is a *"stress-concentrator"* and these pins are predisposed to breakage at the junction of the threaded and non-threaded portions. Historically, SCAT™ pins were designed such that threads engaged only the far-cortex of bone and the breakage-prone thread-shaft junction was located within the intramedullary canal, theoretically, protecting it from cyclic bending forces. In reality, these SCAT pins are seldom used with modern devices such as the IMEX SK™ device. The weaknesses of negative profile pins were initially overcome by introduction of fixation pins with a positive thread profile. *Positive profile threads* are raised above the core diameter of the pin. This thread profile offers secure pin-to-bone fixation without having a breakage prone stress-concentrator. These pins were technically difficult to apply with older KE devices, but application is greatly simplified with the clamp design of the IMEX SK™ device. The disadvantage of these pins is their large "footprint" in available bone stock; this can be problematic in small bones or where ESF is used in combination with an intramedullary pin. Most recently, IMEX has introduced its DuraFace™ pins that have a negative thread profile with a tapered thread run-out design at the thread-nonthreaded transition zone. This design feature eliminates the stress-concentrator issue of conventional negative-thread profile pins while adding pin stiffness when compared to a positive-profile pin of equivalent thread-diameter.

Fig 4 – ExFix pin thread profiles.

Cortical versus Cancellous thread form. A cortical thread form is used in most locations. The cortical thread form has a finer thread pattern and a greater number of threads per unit of pin length when compared to cancellous pins. Cancellous pins use their relatively coarse thread pattern and few threads per unit length to maximize purchase of very soft cancellous bone in locations where there is little cortical bone for purchase (proximal tibial metaphysis, proximal humeral metaphysis, and, in some instances, distal femoral condyle, pelvis and vertebral body). The notion that all metaphyseal bone is soft is not true; cancellous pins should not be used in the humeral condyle, distal tibia or in the radius.

Regular versus Extended Length Pins**.** Extended length pins are available in end-threaded designs (for use as half-pins) and centrally-threaded designs (for use as full-pins). Extended length pins have both an increased overall pin length and increased span of threads. These pins are useful when standard thread length is insufficient to span the full diameter of bone or the soft tissue envelope is so extensive that standard length pins will not protrude sufficiently from the limb.

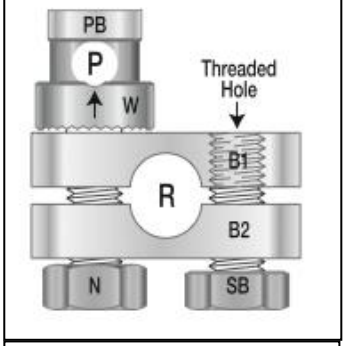



Figure 5 – Single SK™ clamp. PB = primary bolt; SB = secondary bolt; N = nut; P = pin-gripping channel; W = washer; R = rod-gripping channel; B1 = threaded half of clamp body; B2 = non-threaded half of clamp body. Arrow points to meniscus in the

**Linkage Devices (ExFix Pin Clamps)**

The SK™ clamp offers a significant improvement over the KE clamp in terms of both mechanical performance and "user-friendliness". The mechanical performance is enhanced by its adaptation to use of relatively large diameter connecting rods as compared to the old KE clamp. The connecting rods are made of carbon fiber composite or titanium instead of stainless steel to reduce their weight. The SK™ clamp design also allows simplified introduction of a variety of pin sizes and designs including positive profile pins.

SK™ clamps have a two-piece aluminum body, a pin-gripping bolt (also known as the primary bolt) with a slotted washer and tightening nut, and a secondary bolt (Fig 5). The rod-gripping channel is formed by the hemi-circular cut-out shape of each half of the aluminum body. Tightening of the primary and secondary bolts allows the SK clamp to tightly grip the connecting rod without deforming the shape of the clamp body. The clamps can either be pre-positioned on the connecting rod or can be assembled (or disassembled) on the rod at any desired location during surgical application. The gliding washer upon the primary bolt has a meniscus (slot) that enables the bolt to effectively grip a range of different pin diameters; the curvature of the meniscus corresponds to the smallest diameter pin shank that can be securely gripped by the clamp (Table 1). The back of the slotted washer has serrated teeth that engage the outer surface of the aluminum clamp body when the primary bolt is tightened. This provides a rigid lock between the fixation pin and the connecting rod. Finger tightening of the secondary bolt allows the clamp to be stabilized on the connecting rod during

pre-drilling and pin insertion, but still permits the clamp to swivel slightly as the primary bolt is tightened so that the orientation of the clamp can "self-correct" to the fixation pin.

SK™ clamps must be properly assembled to function properly. It is important to know that the two halves of the body are not the same. The B1 segment has threaded hole to receive the end of the secondary bolt whereas the B2 segment has glide holes for both the primary and secondary bolts. Proper assembly allows the threads of the secondary bolt to glide through the B2 segment and to thread into the B1 segment creating a lag effect on the clamp body. The primary bolt glides through both the B1 and B2 halves of the clamp body and is positioned such that the pin-gripping channel is opposite the head of the secondary bolt.

**Practical Techniques for ESF Application**

Basic ESF Principles:

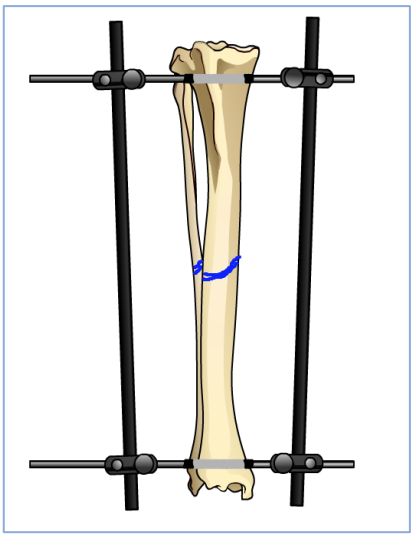
- Use threaded ESF pins
- Use of modern ESF devices such as the IMEX SK™is much more "user-friendly" than older KE-style devices and offers significant mechanical advantages.
- Soft tissue tension on ESF pins must be avoided – consider the movement of tissues against the pins during joint movement (if in doubt, a larger soft tissue corridor for pin placement is better).
- Predrilling of a pilot hole for insertion of the ESF pin is always used in dogs & cats (drill bits are available ~ 0.1mm smaller than the core diameter of the ESF pin).
    - NEVER insert ESF pin directly into the bone with a power drill or handchuck.
- Maximize cross-sectional purchase of ESF pins (use the center of cyclindral-shaped bones, but in triangular shaped bones (ie, proximal tibia) shift the pin insertion site toward the base of the triangle (shift the pin caudal to the center of the proximal tibia).
- ESF pins are seldom angulated; parallel orientation of pins is simpler and allows for more fixation pins/bone segment.
- The wise surgeon always checks that the SK® clamp has been properly assembled by his/her technical staff before using it (the soon-to-be "burned" surgeon will forget).
- Use of "clamp in" orientation (primary bolt closer to the bone) is preferable because it shortens the 'working length' of the ESF pin.
- The first 4 ESF pins are generally placed in a Far-Far-Near-Near sequence relative to the fracture zone.
- With connecting bar(s) loosely attached, the proximal- and distal-most ESF pins can be used as "handles" to adjust bone alignment. An assistant can tighten the clamps once normal alignment is attained.
- The drill sleeve is always secured to the connecting bar and primary bolt of the ESF clamp via finger-tightening when drilling ESF pilot holes (other than the proximal- and distal-most pins that establish the frame).
- Definitive tightening of ESF clamps always uses the 2-wrench technique to avoid distorting the fracture.
- Definitive tightening of ESF clamps always begins with tightening of the primary (pin gripping) bolt.

**Practical Techniques for ESF Application to the Tibia**

The tibia is the simplest bone for ESF application and is, therefore, a good place for the ESF novice to begin. While the tibia is simpler than other bones, case selection, understanding its nuances, logical preoperative decision-making, proper application technique and appropriate postoperative care are still vital to success.

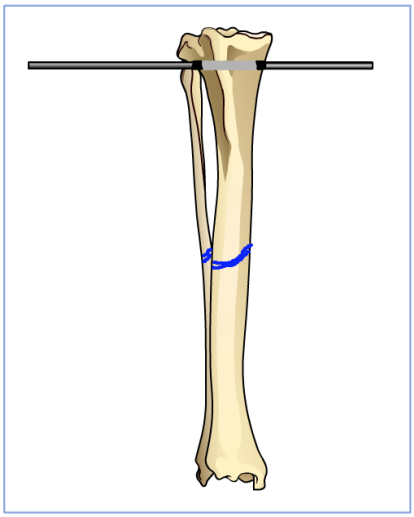
ESF application is tailored to the patient's needs as detailed elsewhere. In this exercise we will construct one of the more commonly utilized ESF frames for the tibia (minimal Type II, 4 + 3 pin frame), but it should be recognized that this frame may be "overkill" for some patients and "under-treatment" for others.

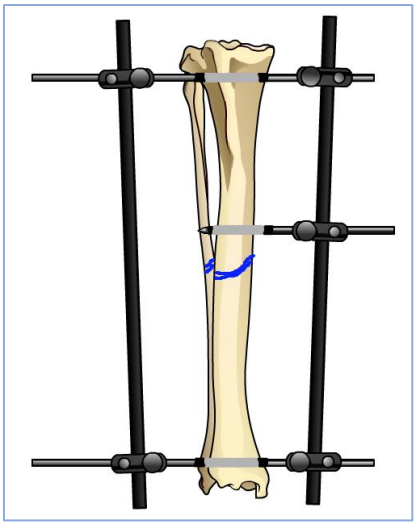
With the patient in dorsal recumbency, a hanging limb position is often used. Suspending the limb from a pointed reduction forcep in the tuber calcis or across the malleoli can reduce the tendency for recurvatum mal-alignment in the sagittal plane. A centerface® pin is inserted as a full-pin in the proximal tibia using the pre-drill method. An *extended-length* pin is sometimes indicated to be sure that the threads fully engage the bone and that there is sufficient pin length relative to the soft tissues in this region. Care is used to place the pin as parallel as possible to the joint surface. A hypodermic needle can be used to "map" the position of the articular surface. The fibular head is often palpable as a lateral side anatomic landmark. Care is also used to keep this ESF pin in the frontal plane (medial to lateral). This proximal tibial pin is typically placed from medial to lateral at the junction of the cranial 2/3 and caudal 1/3 of the tibial frontal plane (since the proximal tibia has a triangular shape in cross-section this position ensures adequate pin purchase). This ESF pin should emerge cranial to the fibular head to avoid damage to the fibular (peroneal) nerve.



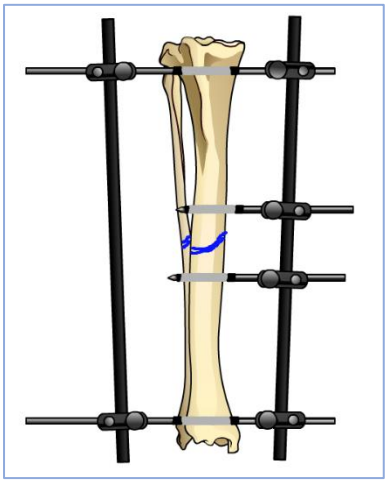
A *standard-length*, centerface® pin is inserted as a full-pin in the <u>distal</u> tibia using the pre-drill method. Care is used to place the pin parallel to the tarsal joint surface. A hypodermic needle can be used to "map" the position of the articular surface. The medial and lateral malleoli are often palpable as medial and lateral anatomic landmarks. This ESF pin is often placed at the tapered region proximal to the malleoli. Care is also used to keep this pin in the frontal plane (medial to lateral). This pin is typically placed into the center of the tibia in a medial to lateral direction and may penetrate the fibula laterally. Add clamps and connecting bars to the ends of each pin. The connecting bars can be placed on the cranial or caudal surface of the pins as desired; they are positioned so that subsequent ESF pins can be easily directed from their respective ESF clamps into the bone. At this point, the clamps are only "finger tightened" so that the proximal and distal full pins can be used for traction and to establish normal frontal (medio-lateral) and transverse plane (torsional) alignment. An assistant tightens the bolts (primary bolts first) when proper alignment is attained.

An SK® clamp is added to the medial connecting bar by temporarily removing its secondary bolt and swiveling the clamp bodies onto the bar. The pin should be oriented in the "clamp in" position (primary bolt closer to the bone) to shorten the 'working length' of the ESF pin. <u>NOW is the time to confirm proper tibial alignment in all planes</u>. Assuming frontal and transverse plane alignment, proper sagittal plane (cranio-caudal) alignment is attained before predrilling this pin. A drill sleeve is inserted into the primary bolt and soft tissue corridor to center it upon the aligned bone, adjacent to the fracture zone (~ 1 bone diameter away). The primary and secondary bolts are *finger tightened* to maintain this clamp & sleeve position. The hole is predrilled with a properly sized drill bit and the hole is marked by passing a k-wire into the hole through the sleeve. The sleeve is removed. Then, a Duraface® pin is placed in the pre-drilled pilot hole. With the tibia held in alignment, an assistant tightens the ESF clamp (primary bolt first). In this case, we hope to place 4 pins in the proximal segment; parallel pin orientation will help to achieve this goal.



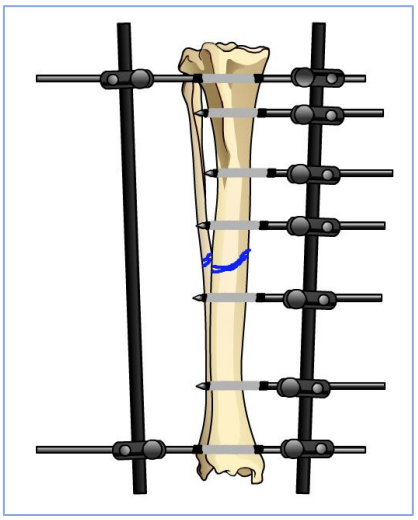


An SK® clamp is added to the medial connecting bar in the "clamp in" orientation as described above. Proper sagittal plane (cranio-caudal) alignment of the distal bone segment is confirmed before predrilling the pilot hole for this pin. Hypodermic needles and regional palpable anatomic landmarks can be used to locate the fracture zone. The drill sleeve, drill bit and k-wire are used as described above to predrill and mark the pilot hole adjacent to the fracture zone (~ 1 bone diameter away). A Duraface® pin is placed in the predrilled pilot hole. With the tibia held in alignment, an assistant tightens the ESF clamp (primary bolt first). Placement of subsequent ESF pins in the "middle clamp" positions of each bone segment is relatively easy; before doing so, now is a good to time to be sure that you are satisfied with the frontal, transverse and sagittal alignment of the tibia (it should have been aligned before you placed a 2nd pin in each segment, but it is better to identify a problem now than after you've got 3-4 pins in each segment).



**NOTE:** The first 4 ESF pins of most frames are generally placed in Far-Far, then Near-Near position relative to the fracture zone. After the "far" and "near" pins are placed in each segment, the desired number of pins can be placed in the "middle clamp" positions of each segment. Since pins in the proximal tibia are predisposed to premature loosening, we hope to place 4 pins in the proximal segment in this exercise. This will distribute pin-bone interface stress over 4 pins; additionally, it will allow us to pursue removal of any prematurely loosening pins as a strategy of staged disassembly during fracture healing (see later discussion).

Insert Duraface® pins into the "middle clamp" positions within each main fracture segment. As always, be sure to make an adequate soft tissue corridor for each pin. To be certain that the predrilled hole is properly oriented relative to the connecting bar and ESF clamp you should always use a drill sleeve that is *finger tightened* into the primary bolt of the ESF clamp upon the connecting bar.



NOTE: All half-pins must fully engage the far-cortex such that the entire trocar point is emerging from the bone. Pin insertion depth can be adjusted postoperatively if radiographs show incorrect pin insertion depth (it is preferable to have to insert a pin deeper than it is to need to "back out" the pin because the latter can contribute to premature loosening).

NOTE: This minimal type II frame is designed to minimize disruption of the lateral musculature of the tibia (thus, all of the half-pins are placed from the medial side). It is also designed with the "pre-plan" to perform 'staged disassembly' by converting from a type II frame to a type Ia frame (concepts of staged disassembly will be discussed in Postoperative Care). This conversion can be either by simple removal of the lateral connecting bar (leaving full-pins in place) or removal of one or both of the full-pins if they are causing patient morbidity.

TIP: In a clinical case, run the limb through a complete range of motion and relieve all soft tissue tension upon the pins before un-draping your patient!

**Postoperative ESF Care & Staged ESF Disassembly**

The need for attentive postoperative care is often regarded as the most significant disadvantage of ESF use. Conversely, the need for this level of care may be beneficial as it prevents the pet owner from slipping into an "out of sight, out of mind" mentality with regard to convalescent care. Recommended postoperative care is usually comprised of patient activity restriction, pin tract cleansing and bandaging. Most pet owners can be trained to properly perform these functions at home. The goals of this care are to encourage early restoration of limb use, promote bone healing, to maintain pin-bone interface stability, and to minimize pin tract drainage and discomfort.

Slow, controlled walking on a very short leash is instituted the day following surgery as a means to encourage early use of the limb. Usually it is helpful if the "dog walker" walks on the side opposite the injury in order to lean into the pet to encourage weight-bearing. Walking deliberately slowly is recommended as excessive gait speed commonly results in a non-weight-bearing gait.

Pin tract care begins immediately following ESF application with the goals of minimizing pin tract contamination and impingement/motion of the soft tissues upon the fixation pins. Prior to anesthetic recovery, the limb is passed through a full range of motion and a #11 blade is used to relieve all detected soft tissue tension/motion upon fixation elements. Several sterile gauze squares are incised half-way across and the "split" dressing is applied around each fixation pin. Packing of gauze squares or laundered and sterilized foam scrub sponges can be placed between the connecting bar and the sterile gauze dressing to immobilize the soft tissue zone around each fixation pin. In the immediate postoperative period, a Robert Jones Bandage is often applied from the toes to the mid-thigh or brachium region for fractures of the tibia and radius/ulna, respectively. This Robert Jones Bandage is placed directly over the frame and associated gauze dressings of the pin tracts. After the first or second bandage change, the Robert Jones bandage can be weaned to a bandage of the pins tracts and ESF frame only. For this style of bandage, once the pin tracts have been cleansed and bandaged, "bumper" padding can be applied over the tops of fixation pins and bars and outer elastic wrap is applied around the frame to keep all of the bandaging material in place. Whether using a Robert Jones Bandage or an ESF Frame bandage, the sterile gauze pin tract dressing is typically changed 2-3 times in the first 5-10 postoperative days depending upon the amount of drainage, regional soft tissue health, etc. Patient sedation is often necessary for the first few bandage changes/pin tract cleansings and the pet owner can be trained how to perform the pin tract care and bandage change by ~ 10 days postoperative. Once the pin tracts are filling with granulation tissue, the frequency of the bandage changes can be reduced to every 3 to 5 days. The owner is instructed to use gauze soaked in an antiseptic solution in a "shoe shine" fashion to remove any accumulated crusts and scabs from around each pin in order to promote free drainage of any pin tract exudate. Pet owners are cautioned that excessive limb use and/or infrequent pin tract care are common contributors to increased pin tract drainage, lameness and pain that may be encountered 4 to 8 weeks after surgery as the owner's attention to ESF care begins to wane. They are encouraged to remain vigilant in their aftercare as premature pin tract irritation and pin loosening may necessitate revision surgical procedures that can add significantly to the overall treatment cost.

General Strategies for Staged ESF Disassembly

- In the early stages of bone healing, rigid fixation is important to minimize patient morbidity. If the construct is not rigid enough in the early postoperative period, a progressive cycle of pin tract loosening and drainage, pain and lameness, and delayed bone healing is likely. However, during the later stages of bone healing, less ESF rigidity may be advantageous so that the healing bone can be "challenged". If the ESF remains rigid, bone healing may progress toward a slower process of primary bone healing or even delayed union that leaves the bone at risk for fracture when the ESF is removed. Research suggests that the best opportunity to consider staged disassembly is approximately 6-8 weeks after ESF application in the adult dog (and 8-10 weeks in the adult cat). In skeletally immature patients, assessment may be as early as 3 to 4 weeks after surgery.

Assessment for disassembly is as follows:

1. **Examine the patient** for any pin tract morbidity (active wound around pin, pin tract drainage, sensitivity to manipulation of pin tract or fixation pin).

2. **Heavy sedation**
   - Radiographs – examine for early callus formation in the fracture zone as well as lucency (indicative of pin loosening) around any pins. Patients with complex, multi-connecting bar frames may require oblique radiographic views or temporary removal of a connecting bar to

allow assessment of fracture zone healing (radiographic ease is an advantage of composite carbon fiber connecting bars).
- Palpation of fracture zone – if mineralized callus formation is not evident radiographically, the connecting bars are temporarily removed and the fracture zone is palpated for 'relative stability' imparted by early soft callus formation.

**3. Decision-making**
- If neither radiographs nor fracture zone palpation reveals early callus formation → re-apply connecting rods and consider interventions that may accelerate healing.
- If radiographs and/or palpation reveal early callus formation → begin staged disassembly strategies

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- Specific Strategies for Staged Disassembly of IMEX SK® ESF

1. Base disassembly strategy upon removal of any pins that are causing patient morbidity
   - 
2. Removal of a frame is preferable to removal of isolated pins when feasible.
   a. Type III frames → Type II, Type Ib or even a Type Ia depending on the amount of fracture zone callus.
   b. Type II → Type Ia
   c. Type Ib → disassemble to Type Ia or remove articulations/diagonals (if frame removal is too aggressive)
   d. Type Ia → removal of pins closest to fracture to reduce construct stiffness (increased working length of connecting rod)
   e. IM pin 'Tie-in" → progressive removal of fixation frames (modified Type Ib frames) or removal of fixation pins (Type Ia frames) until the intramedullary (IM) pin and its "tie-in" are the last elements to be removed (the IM pin provides excellent protection against disruptive bending forces). If, however, there is significant morbidity involved with the IM pin site, the IM pin is removed and the ESF is left in place.
      - 
3. Decrease the size of the connecting rods where feasible. Some of the fixation pin sizes are compatible with two different sizes of fixation clamps (and connecting rods). When such pins are used, the ESF construct is initially often built with the larger size of clamps and connecting rods for greater rigidity. At the time of staged disassembly, the larger size of clamps and rods are removed and they are replaced with smaller clamps and rods.
   - 
4. Changing from a metallic connecting rod to a carbon fiber rod will decrease construct stiffness, especially with the small SK® device.

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**Helpful Resources**
- Principles & Techniques of External Skeletal Fixation; VideoVet; www.videovet.org (Ross.Palmer@me.com)

# FRACTURE MANAGEMENT: IM PIN & CERCLAGE WIRE FIXATION PRINCIPLES

Intramedullary pins and cerclage are available in most primary care veterinary practices and can be used successfully to treat selected fractures in dogs and cats. Unfortunately, when used improperly or in contraindicated scenarios, these fixation methods frequently cause severe complications including fracture disease, quadriceps contracture, mal-union, delayed or non-union, and/or infection; any of which can lead to limb amputation or euthanasia. Unexpected complications can negate their apparent affordability and, thus, lead to client dissatisfaction. Therefore, the key to successful treatment using these fixation modalities is a thorough knowledge of their indications, proper application and limitations.

**Intramedullary (IM) Pin Fixation**
As with external coaptation, one must consider the ability of any internal fixation method to resist the disruptive forces acting upon the fracture to be treated. We will consider each of these disruptive forces individually.

*Control of Bending with an IM Pin*
Intramedullary pins, because they are placed in the central axis of the bone, are very good at resisting bending forces in all planes. An IM pin's ability to resist disruptive bending forces is related to the pin's radius raised to the 4$^{th}$ power; thus, small changes in pin radius have a profound effect on its stiffness. In theory, a pin that completely fills the intramedullary canal would impart the greatest bending stiffness; in reality, it is not feasible or advisable to completely fill the IM canal because of the irregular shape of the bone (bones are not uniform cylinders) and the relatively thin cortical bone typically has many grossly invisible "micro-cracks" that can easily propagate into fissures or fractures if the pin is too large. As a rule of thumb, we typically select an IM pin that fills 60-75% of the IM canal at it's narrowest portion (even smaller pins, ~ 30-50% canal fill, are used when combined with external skeletal fixation or bone plating). When deciding between two sizes of IM pins, it is typically better to initially choose the smaller pin; one can always "step up" in pin size if desired, but it is not possible to "drop down" to a smaller diameter pin if the first pin was too large. As we look at other disruptive forces, you will quickly note that an IM pin is a "one trick pony" that is only capable of resisting bending forces.

*Control of Rotation with an IM Pin*
An IM Steinmann pin has no ability to control rotation whatsoever. Because most, if not all, long bone fractures are subjected to significant rotational forces, supplemental fixation (cerclage wire, ESF, and/or bone plate) is nearly always required with an IM pin.

*Control of Axial Compression (Axial Collapse) with an IM Pin*
An IM pin has little/no ability to resist axial collapse. Therefore, an IM pin either requires bony architecture (ie, an intact adjacent bone, an incomplete fracture or a properly reduced transverse fracture configuration) or appropriate supplemental fixation to resist axial collapse.

*Control of Tension with an IM Pin*
IM pins have minimal ability to resist the pure tensile forces of muscle tendon unit insertions. Thus, whenever you see a patient with a fracture of a traction apophysis, either a figure of 8 tension band or a tension band plate will be required for adequate treatment of these fractures in most instances.

*Other Relevant Factors for IM Pin Fixation*
IM pin fixation is only beneficial when the pin can be inserted without disruption to articular surfaces and other important structures such as ligaments, nerves, etc. The radius is not amenable to IM pin fixation because there are no extra-articular prominences for safe pin entry/exit; in addition, the IM canal of the radius is so small that an appropriately sized IM pin imparts very little bending stability. The tibia must be pinned using a normograde technique from the proximal end with pin entry in the extra-articular margin of bone between the medial collateral ligament and the tibial tuberosity (retrograde pinning disrupts the proximal articular surface and cruciate ligaments). The femur can be pinned using the normograde technique from the proximal end or retrograde pinning in the proximal direction though caution must be applied with the latter method. In normograde pinning, the pin is typically introduced into the lateral-most margin of the trochanteric fossa. In the retrograde technique, care must be used to direct the pin cranially and laterally as it is advanced proximally to try to achieve an exit point within the lateral-most margin of the trochanteric fossa; the ability to direct the retrograde

pin's exit point is progressively less controllable by the surgeon in progressively more distal fracture locations. During retrograde pin insertion into the proximal femur, it is also important to position the hip in extension, neutral abduction/adduction and neutral rotation so that the proximal pin tip is directed away from the sciatic nerve as it exits the trochanteric fossa. The humerus can pinned normograde from the either the proximal or distal end of the bone or retrograde in either direction depending upon the fracture location and the desired position for pin seating in the distal segment.

*IM Pin Summary*
Intramedullary pins are uniquely capable of resisting bending forces in all planes, but this is the extent of their abilities. Therefore, IM pinning typically requires some form of appropriate supplemental secondary or primary fixation.

**Cerclage Wire Fixation**
To understand the ability of cerclage wire to resist these disruptive forces, the principles of proper cerclage wire application must first be discussed.

*Only for Perfectly Reduced Long Oblique or Spiral Fracture Configurations*
Full-cerclage wire fixation is an encircling wire that is capable of generating significant interfragmentary compression between the 2 bone segments, but only when properly applied to LONG oblique or spiral fracture configurations. The length of the fracture line must be at least twice the bone diameter; fracture lines that are 3 times the bone diameter permit greater interfragmentary compression (ie, improved fracture stability). Sufficient interfragmentary compression is only achieved when the long oblique or spiral fracture configuration can be perfectly reduced (in this instance, "close" doesn't count!). After closely studying your high quality, orthogonal view radiographs, one simple rule kept in mind can save you a lot of problems: *if you see multiple cortical fragments (especially small ones), "put down the wire and nobody gets hurt!"*.

*One Cerclage Wire is Never Enough for Fracture Stabilization*
A single cerclage wire is never sufficient to stabilize 2 main fracture segments because it concentrates all of the disruptive forces into this single site. When properly used to stabilize a long oblique or spiral fracture configuration, each cerclage wire adds to the interfragmentary compression achieved. When proper wire spacing is used (discussed below), insufficient room for a 2nd cerclage wire indicates that the fracture line is not sufficiently oblique for effective use of cerclage wiring.

*Proper Cerclage Wire Spacing is a Must!*
Proper wire spacing is required to permit vascular inflow and outflow from the cortical bone while achieving the needed interfragmentary compression. Adjacent cerclage wires are to be spaced 1 bone diameter apart from one another. Cerclage wires placed adjacent to the tips of long oblique/spiral fracture lines should be at least ½ bone diameter from the tip of the segment. Note that if a fracture line is less than 2 bone diameters in length, it would only be possible to place a single cerclage wire when the rules of proper wire spacing are applied. A fracture line that is 2 bone diameters in length will permit proper application of 2 cerclage wires and a fracture line that is 3 bone diameters in length will permit application of 3 cerclage wires.

*Use the Correct Size of Wire*
In small animal orthopedic surgery, 18gauge wire is used for medium and large breed dogs, 20gauge wire is used for medium and small breeds of dogs, and 22gauge is used for most cats and toy breed dogs. Braided wire is not used because it is not possible to generate sufficient wire tension with conventional tensioning and knotting techniques.

*Cerclage Wire Knots*
The twist knot is the most frequently used method to tighten and secure cerclage wires. In this technique, it is important that tension be applied as the wire is twisted in order to twist the wire ends uniformly around one another like a barber pole. On occasion, one end of the wire while twist upon the other like a snake on stick; this twist knot is not secure and the wire should be replaced. When an adjacent cerclage wire is placed, the additional interfragmentary compression that is produced often causes subtle, but relevant, loosening of the first wire. For this reason, when using twist knots, do not cut the twisted wire until all cerclage wires have been applied because additional tightening cannot be achieved once the wire is cut. Twist knots are usually cut between the 3rd and 4th twist. Bending the twist knot after the wire has been cut loosens the wire, so the twisted tip is usually left protruding into the soft tissues where a fibrous capsule will form around it. If there are critical neurovascular structures adjacent to the twist, the knot can be twisted as the wire is bent toward the cortical surface in attempt

to minimize the loss of tension associated with bending. Single- and double-loop knots can also be used and have their own distinct advantages and disadvantages. While there are mechanical advantages (especially for double-loop knots), one of the key disadvantages is the requirement for purpose-specific instrumentation. Practically speaking, any these forms of cerclage wire fixation can be used effectively in most instances provided the principles of proper use are strictly adhered to.

*Preventing Cerclage Wire Loosening*
Loose cerclage wires do not impart interfragmentary compression and, worse yet, they interfere with bone healing because they disrupt blood flow in/out of the bone. In short, "loose wires kill". In order to minimize the risk of loosening, full cerclage wires should oriented perpendicular to the bony long axis. As previously mentioned, application of an adjacent cerclage wire can loosen a wire that was previously tight; therefore, it is vital that all wires be checked for tightness prior to surgical closure. For my pre-closure "wire-looseness" check, I like to use a periosteal elevator to try to shift each wire up or down the bone. Any loose wires are re-tightened (if possible) or replaced; a little extra work here can save hours of work and agonizing in the weeks to come. In conical segments of bone, cerclage wires are prone to migration toward the narrower region. A small diameter transfixing k-wire can be placed adjacent to the cerclage wire on the narrower side, but this k-wire may encroach upon the IM pin in doing so. Alternatively, a triangular file can be used to etch a very subtle notch in the bone into which the cerclage wire can be tightened; this notch does not need to pass around the entire circumference of the bone and should not be deep into the cortex as this could increase the risk of fracture at this site; instead, the subtle notch need only accept a small portion (~ 5-10%) of the cerclage wire's thickness at 1 or 2 sites around the bone's circumference.

*Control of Bending with Cerclage Wire Fixation*
Cerclage wire is able to contribute to the control of disruptive bending forces assuming perfect anatomic reconstruction of a long oblique or spiral fracture with properly placed wires. Cerclage wire should never be used without supplemental fixation because its application is, by definition, restricted to the region the of the fracture rather than distributed along the entire length of the bone.

*Control of Rotation with Cerclage Wire Fixation*
Properly placed cerclage wires provide good rotational stability, at least in the short term. When a long bone is subjected to repeated cycles of complex loading forces that include concurrent rotation, bending, and compression, the wires will tend to loosen especially when supplementing an IM pin (remember, IM pins really only contribute to bending stability so the cerclage wire is heavily challenged in IM pin + cerclage scenarios). Thus, IM pin + cerclage wire fixation is typically reserved for cases in which rapid bone healing is anticipated (young patients, good soft tissue health, good systemic patient health, etc), the number of cycles of load can be controlled (good patient / pet owner compliance) and the magnitude of the load cycles are not extreme (smaller patients, good compliance, 3 other healthy limbs, etc).

*Control of Axial Compression (Axial Collapse) with Cerclage Wire Fixation*
Properly placed cerclage wires provide good resistance to axial collapse, at least in the short term. Once again, cerclage wires tend to loosen somewhat rapidly if subjected to repeated cycles of complex loading, especially if they are of larger magnitude (ie, running, jumping, playing, stairs, falling, etc). This tendency to loosen is particularly profound when cerclage wires are used in combination with IM pin fixation because IM pins have no ability resist rotation and compression; thus, the cerclage wires are heavily relied upon with IM pin + wire fixations. Thus, it only makes sense to restrict IM pin + wire fixation to rapidly healing scenarios with a controlled number and magnitude of cyclical loads as described in the paragraph above.

CHECKLIST FOR EFFECTIVE USE OF IM PIN & CERCLAGE WIRE FIXATION

- ☐ Rapid bone healing anticipated (young healthy patient, healthy fracture zone, etc)
- ☐ Limb will not be excessively loaded (3 other functional limbs, compliant patient, etc)
- ☐ Long, oblique / spiral fracture configuration
- ☐ Perfect, anatomic reconstruction can be achieved
- ☐ Femur, tibia, humerus (not radius)
- ☐ Proper equipment & implant sizes are functional, sterile and available

**Helpful Resources:**

- Practical Surgical Techniques of IM Pin & Cerclage Wire Fixation – I; VideoVet; www.videovet.org (Ross.Palmer@me.com)

# TERRY MARIE CURTIS

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# BEHAVIOR BASICS LEARNING AND COMMUNICATION: SPEAKING DOG & CAT WHY IT'S SO IMPORTANT

As veterinarians, we are tasked with having to communicate – on a daily basis – with individuals that don't speak our language. Our patients are talking to us – it's up to us to learn what they're saying! Dogs and cats learn using the same basics we do – classical conditioning [learning by association] and operant conditioning [goal-directed learning]. It's important that we know how to implement the learning techniques that our patients actually understand and use to get the resultant behaviors that we're all looking for.

# INTER-CAT AGGRESSION

# GETTING CATS TO GET ALONG: IT'S POSSIBLE!

Cats ARE social animals and exhibit this sociality towards their conspecifics. However, feline societies are insular and strangers are not accepted readily. This fact needs to be taken into account when introducing cats to one another – especially as adults. Many people adopt single cats and keep them as single cats for most of their lives. This form of living doesn't allow the cat to hone any of its feline social skills, so it may have limited ability to get along with a new-comer. Treatment for inter-cat aggression typically involves environmental and behavioral modification, and may require the use of anxiolytic medication – especially for the "victim". Actual cases will be discussed to illustrate.

# INTER-CAT AGGRESSION

# GETTING CATS TO GET ALONG: IT'S POSSIBLE!

The number one reason that dogs show aggressive behavior towards humans [growling, snarling, lunging, biting] is FEAR – **not** [the over-diagnosed] dominance. In dogs, their aggressive behaviors "ensure the outcome" – to make the scary individual to go away. Numerous considerations are involved in the diagnosis and treatment of human-directed behavior in dogs such as the human-animal bond, public safety, and euthanasia. With the treatment of any aggression, it is important to caution owners of the unpredictability of any attempt to treat. NO TREATMENT IS 100% EFFECTIVE**. Any dog may bite**, whether they have done so previously or not. The various manifestations of human-directed aggression will be discussed as well as treatment options.

# INTER-CAT AGGRESSION

# GETTING CATS TO GET ALONG: IT'S POSSIBLE!

It's important that our clients – and YOU – understand WHY their dog is ripping up the carpet and chewing on the door frames. Dogs may experience distress and engage in problem behaviors related to the absence of family members. Common behaviors seen in dogs with Separation Anxiety are destruction, vocalization, and elimination, and tend to occur within the first 30 minutes after departure. Dogs with Departure Anxiety are okay if they find themselves alone – but don't see their human[s] leave! Dogs with Barrier Anxiety can't be crated. Period. A diagnosis is imperative for proper treatment – which typically involves behavioral modification, environmental modification, and often the use of anxiolytic medication. Actual cases will be discussed.

# INTERDOG AGGRESSION

# WHY DO DOGS FIGHT AND WHAT CAN BE DONE ABOUT IT?

Inter-Dog Aggression can be status-related, fear-motivated, arousal-related, possessive, protective, territorial, redirected, and/or predatory. The most common presentation is fighting between household dogs and is typically, the result of some "communication breakdown". In those cases it is important to determine what each dog is saying to each other and work on repairing the relationship. There are also dogs that have "issues" with non-household dogs, which may be secondary to an aversive event (e.g. attacked by a dog as a puppy). Some cases are clearly territorial – where the aggressive dog is fine with other dogs when it is off its property. Often, the cases are more subtle – especially when there's a medical and/or cognitive component involved. All of these will be discussed and treatment options presented.

# INTERDOG AGGRESSION

# WHY DO DOGS FIGHT AND WHAT CAN BE DONE ABOUT IT?

Medications can be a very helpful tool when addressing various behavioral issues. Most of the medications used by veterinarians to help modify behavior target anxiety and reactivity. The more common medication classes include selective serotonin reuptake inhibitors [SSRIs], tri-cyclic antidepressants [TCAs], benzodiazepines, and azapirones. But there are other less common medications at our disposal as well. Knowing what "tools" are available, how to use them correctly and which of them to use when is the focus of this lecture.

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# EL EXAMEN NEUROLOGICO: COMPRENDIENDO EL CABLEADO BASICO

INTRODUCCION:

*This is the "prerequisite course" and will be a refresher of neuroanatomy only as it relates to the neurological exam. Don't let the neuroanatomy scare you away. This lecture is presented by a clinician for clinicians. Understanding the basic wiring schematic will help tell you why the lights went out. It is what you need to survive neurology in practice, because if you can't localize the lesion then you can't formulate the differential list and plan.*

**The neurological examination, the start to any neurological patient.**

There is great variability in the neurological exam. Not only does patient size necessitate change in technique but also patient temperament, however with all patients much information may be gleaned by the casual observation of the patient.

**Overall mentation and awareness** should be noted. Pacing, circling, head pressing, disorientation, seizures and aggression may all be signs of forebrain disease. If the patient circles left the lesion should be on that side. A short observed walk may help in giving clues on what to look for prior to the detailed exam. A short flight of stairs is also very helpful in bringing out subtle deficits.

**The cranial nerves** are next evaluated with some of them rarely having any abnormalities while other cranial nerves should become very familiar to the practitioner. Loss of smell is very rare.

Loss of vision may be from many different etiologies some of which are based in pathology that is not neurological. The menace reflex (CN II and CN VII) is easily tested using an open hand with fingers spread to prevent the fanning of air against the face. If the patient were to feel the air flow against the skin then it would be CN V and CN VII that would be tested. Field of view (peripheral vision) is tested with the dropping or throwing of cotton balls.

CN III, Oculomotor; The oculomotor is motor to the iris allowing for pupil constriction and it is functional together with CN IV and CN VI in controlling the extraocular musculature. By moving the patients head from side to side a oculo-cephalic reflex or "Dolls eye" is elicited. Signals from the vestibular nuclei travel up the medial longitudinal fasciculus and influence the nuclei of CN III, CN IV and CN VI which then control the extra-ocular muscles.

Vestibular dysfunction, brainstem involvement or periocular pathology may all cause an abnormal or lack of normal oculo-cephalic nystagmus. It is these same connections that drive the spontaneous nystagmus seen with diseases of the vestibular apparatus.

CN V or the Trigeminal nerve is sensory to the face and motor to the muscles of mastication. Deficiencies in this nerve may show loss of sensation in any of or all three of the branches/areas supplied by the nerve, mandibular, maxillary and ophthalmic.

The Trigeminal is also sensory to the cornea. Common enough in general practice is the patient presenting with an inability to close the mouth. The mouth hangs limply with a passive manipulation to close the mouth resulting in a jaw that just falls open. This loss of motor CN V must be differentiated from a patient that presents with an inability to *open* the mouth. In evaluating the cranial nerves remember that the cranial nerves, save for CN IV do not cross the midline but exit ipsilateral.

CN VII is tested in concert with the trigeminal when doing the palpebral reflex (the examiner lightly touches the canthus of the eye then the patient blinks) or as part of the menace reflex (sees the menacing gesture then blinks). Facial symmetry is important to look for as a clue to a CN VII deficit.

CN VIII has two parts, cochlear and vestibular. The cochlear half may be tested with a very crude "Clap Test" i.e. stand behind the patient then clap your hands and see if the patient alerts. As a definitive test Brainstem Auditory Evoke Responses (BAER) may be done at referral centers. BAER testing is a very objective way to evaluate hearing and is sensitive even in patients under anesthesia. The vestibular component of CN VIII, if affected, will shows signs of a head tilt (not head turn), circling, leaning, rolling and/or spontaneous nystagmus. The nystagmus may be of differing types, horizontal, rotatory or vertical. Peripheral vestibular lesions may have horizontal or rotatory nystagmus and the fast phase of the nystagmus will be in the direction away from the lesion. Central vestibular disease may have either horizontal or rotatory but pathognomonic for central vestibular disease would be vertical or positional nystagmus. In positional nystagmus the character may change with the position of the patient, *this is why it is important to evaluate the eyes in each different position in which the patient is placed*.

CN IX, CN X and CN XI are usually examined together. If the patient can eat and swallow normally then it may be presumed that their function is intact. In the exam room a squeezing of the larynx will often elicit a swallow thus preventing the examiner from having to stick his/her fingers down the animal's mouth. Included in the history should be the question about any change in the animal's voice since the vagus (CN X) innervates the vocal folds. CN XI is mentioned but of very little clinical significance. It is added here since the three nerves, IX, X, XI, exit the skull in close proximity through the tympanoccipital fissure. A lesion at this site would involve all three. CN XII the hypoglossal nerve is motor to the tongue and if damaged will cause deviation of the tongue with resultant muscle atrophy. This is a rare occurrence.

**Postural Responses**

These are called responses versus reflexes because to get the desired response the stimulus must travel to the brain, be interpreted then acted upon with the resultant physical movement. Most of these pathways consist of large well myelinated fibers with very fast transmission times. Anatomically they are situated on the periphery of the spinal cord so as to make them susceptible to the first effects of compressive lesions. Conscious proprioception is that function that allows us to be cognizant of the spatial position of the body and extremities. Information from distal receptors travels up the peripheral nerve then up the spinal cord via the dorsal funiculi. These tracts are ipsilateral until they decussate at the level of the pons before radiating to the cortex. Because of their location and fiber size, deficiencies in conscious proprioception (CP), is often the first abnormality seen with disease of the spinal cord. A test for CP is the knuckling of the paw *while supporting the patient's weight*. The normal animal will quickly replace the paw to the normal position. As with so many neurological

deficiencies there may be only a partial loss, in this case one may turn over just two of the four toes thereby giving less stimulus to the patient. If the patient leaves the two toes the examiner may gently sway the animal's body back and forth to accentuate the stimulus.

Hopping is an excellent way to elucidate subtle deficits. Holding the patient in front of you and having them face away from you. Holding up the rear end and holding up one fore limb move the patient in a lateral motion, **patients do not hop medially!** Now hold up the other forelimb as you move them in the other lateral direction. Spinning the patient around so they now face you this test may be repeated with the rear limbs. By altering the speed of lateral movement and by watching the character and strength of the patient's placement a good evaluation can be made for laterality of lesions and severity of lesion. In really large dogs you may only be able to do hemi-hopping or hemi-walking but you can still evaluate for laterality and overall strength. Unconscious proprioception is that which allows us to walk and talk at the same time and is transmitted by the four spinocerebellar tracts. We evaluated these when the patient was walked down the hall and we looked for ataxia/dysmetria and also by hopping the patient.

**Segmental Reflexes, Upper motor versus Lower motor neuron disease.**

With the patient in lateral recumbence and before even striking the first tendon or muscle belly, lightly grab the distal end of the limb. This should elicit a mild withdrawal reflex. By pulling on the limb the strength and overall tone of the limb may be assessed and the possibility of a lower motor neuron disease evaluated. The main reason we evaluate the segmental reflexes is for lesion localization. The segmental reflex is graded on a scale of 0 to 4. Zero is no reflex, 1 is a depressed reflex, 2 is normal. 3 is exaggerated/brisk and 4 is exaggerated/brisk with clonus. To simplify, answer if the reflex is there or not? If there is a loss of or decrease in the reflex then we must put a lesion in the reflex arc (ventral horn cell, peripheral nerve, neuromuscular junction, muscle, sensory nerve and dorsal nerve root). Knowing from which cord segment each reflex arises we may then track back to that location, if the reflex is brisk or exaggerated then we call that an upper motor neuron sign and look rostral for the lesion. A paradox would be the "False localizing sign" where the lesion is caudal to the spinal cord segment. This is easily explained if you think about the quadriceps (patellar reflex) and the biceps femoris (sciatic reflex). Place a lesion in the sciatic and you effectively remove the antagonistic muscle to the patellar reflex, no antagonist gives a faster reflex. In the more common situation if the reflex appears brisk it is because it has lost the inhibition from the upper motor neuron. The lesion is rostral to the spinal cord segment of that reflex. Other reflexes that are evaluated and classed as upper motor are the Babinski and the Crossed Extensor. A positive or abnormal Babinski response would be when the examiner strokes the lateral plantar/palmar surface of the paw in a proximal to distal direction and the toes dorsiflex. The normal response would be no reaction.

The crossed extensor is a reflex that is normally present however with loss of communication with the upper motor neuron the reflex becomes exaggerated. With the patient in lateral recumbence one rear toe is pinched giving a nociceptive stimulus, the contra lateral limb will reflexively increase in tone with a slight extension evident. With upper motor disease the contra lateral limb will have an obvious exaggerated extension.

Fore limb reflexes are the biceps, which is the musculocutaneous nerve from C 6, 7 and 8.and triceps, radial from C 7, 8 and T 1.Remember that anatomically there are 8 cervical spinal cord segments while there are only 7 cervical vertebrae.

The rear limb has the patellar reflex which is the quadriceps muscle innervated by the femoral nerve cord segments L 4-5 and the sciatic L 6, 7, S 1. The sciatic is evaluated by tapping the belly of the cranial tibialis (peroneal nerve) and the gastrocnemious (tibial nerve). Both the peroneal and tibial are branches of the sciatic. The sciatic is also evaluated when at first you elicit the withdrawal reflex in the rear limb. The tail and anus are looked at together. Lightly stroking or pinching the perineal area should cause a reflexive contracture of the anus. Pinching either the prepuce or the vulva should elicit a reflexive contracture of the anus. These maneuvers check the pudendal nerve, S 1-3. When in doubt of rectal tone a gloved finger and rectal examination can give more information.

**Pain Sensation**

Saving this till last there are two levels of pain to be evaluated. First is superficial pain and this may be evaluated at the same time as the panniculus AKA lateral cutaneous trunci reflex. Giving a light pin prick to the skin first at the level of lumbo-sacral then slowly moving cranially. The sensation is felt in the skin ascends the spinal cord then exits around T-2 to cause a perceptible contracture in the lateral cutaneous trunci muscle. This is especially helpful in delineating the level of a spinal cord lesion. The reflex will be absent if the stimulus to the skin is being given caudal to the lesion site.

Deep pain is that sensation we experience as deep throbbing unrelenting pain. It is transmitted by small non-myelinated fibers that are most resistant to compression hence they are usually the last to lose function. Deep pain is evaluated by using a strong instrument i.e. carmalt, and squeezing the bone of a toe. To have a positive response the patient must turn toward the stimulus demonstrating cerebral recognition. Remember that with a severed spinal cord the leg will still pull back because of the withdrawal reflex.

Once finished with the exam the examiner must **“Place the lesion”**.

# INCLINACION DE CABEZA: SIMPLE INFECCION DE OIDO O TUMOR DEL TALLO CEREBRAL?

**INTRODUCTION:**

*From otitis media, benign idiopathic senile vestibular syndrome, nasopharyngeal polyps in cats, to central vestibular syndrome and its paradoxical head tilt, when your head's not on straight it can mean a number of differentials. How is the clinician to tell, and what should he/she do about it? After this hour it will all be clearer.*

From an evolutionary aspect it was necessary for man/animal to be able to right himself before he was even able to stand upright; hence the vestibular component of the brain is contained within the oldest parts of the CNS. Although the cerebral cortex receives balance projections via the medial geniculate body it does not maintain balance; balance is maintained by the rhombencephalon/hind brain. The neurons of the vestibular ganglion receive impulses from 5 sites: the crista of the ampulla of each of the three semicircular canals and the macula of the utricle and macula of the saccule. The crista record movement of the head while the macula record the static position of the head. These neurons synapse in the vestibular nuclei (there are 4 main nuclei) in the medulla. Neurons from the vestibular nuclei ascend ipsilaterally while others decussate then ascend. They project to the medial geniculate body and on the way give off multiple branches to the nuclei of cranial nerves III, IV and VI thereby giving a strong influence to eye movement. These ascending tracts are predominantly in the medial longitudinal fasciculus. There are also numerous projections into the ascending and descending reticular formation. Some of these descending reticular projections are involved in the vomiting and cardiovascular reactions which may occur in vestibular disturbances.

Clinical signs to differentiate central versus peripheral vestibular disease.

| **Signs** | **central** | **peripheral** |
|---|---|---|
| Loss of balance | yes | yes |
| Head tilt | yes | yes |
| Falling/rolling | yes, greater tendency to | yes |
| Nystagmus | yes | yes |
| Horizontal | yes | yes |
| Rotatory | yes | yes |
| Vertical | yes | no |
| Positional | yes | no |
| Strabismus (ventral) | yes | yes |
| Cranial nerve deficits | Possible V, VI, VII. | possible VII |
| Horner's syndrome | no | possible |
| Cerebellar signs | possible | possible |
| Mental depression | possible | no |
| Hemiparesis, ipsilateral CP deficits | possible | no |

Pendular nystagmus is a nystagmus that has equal moment in each direction. This is a "normal" in certain breeds of cats i.e. Siamese.

**Idiopathic Vestibular Syndrome**, aka Senile Vestibular Syndrome or Blue Tailed Lizard poisoning in the south. Typical signalment is a patient, 12.5 years of age with an acute onset of unilateral

peripheral vestibular signs; head tilt, rolling/leaning, eye drop/ventral strabismus and/nystagmus. There is no histological pathology. Diagnosis is based on the rule out of other causes of the vestibular syndrome; otitis media, otitis interna, trauma, etc. A minimum data base is important to rule out underlying disease such as compensated renal failure which may be exacerbated when due to nausea the patient is unable to take liquids orally. In the rare case serology may reveal RMSF, Lyme, E. Canis or Toxoplasmosis. Treatment is often symptomatic with O. T. C. Meclazine (Antivert) 25 mg P.O. daily and often protective cage/padding, or tranquilizers are indicated. In the older debilitated patient fluid support may be needed. There is no place for steroids. The prognosis is good with
improvement coming in stages. The nystagmus is the first sign to wane and with it goes the vertigo and nausea. This happens in the first 48 hours with the patient becoming ambulatory. After complete recovery the patient may be left with a permanent slight head tilt.

**Infections** are a common cause of vestibular symptoms. Otitis media-interna gives symptoms of peripheral
vestibular syndrome e.g. head tilt, nystagmus, leaning or falling against walls, ataxia and occasionally vomiting. If severe enough there may be a Horner's' syndrome. Route of infection is usually by ascending
the eustachian tube to the middle ear with secondary inflammation affecting the endolymph of the semicircular canals, utricle and saccule. Penetration of the tympanic membrane may also be a source. Common organisms are Staph., Strep. and Pseudomonas. Diagnosis may be aided by visualization of a cloudy or darkened bulging tympanic membrane. Minimum Data Base (MDB) should include thoracic radiographs.

Skull radiographs, if taken, should be as an open mouth view. Only 70% of the cases will have radiographic changes. C. T. or MRI are very useful since they give much better visualization of soft tissue and fluids. The treatment depends on the severity. Given a first time presentation clean the external ear canal (be sure to avoid oily compounds and medications) then put the patient on 4 to 6 weeks of antibiotics. First choice is Enrofloxacin or Marbofloxacin. Good second choice antibiotic is a cephalosporin. For the chronic case take skull radiographs and while anesthetized perform a needle myringotomy to obtain a culture and sensitivity from the middle ear then flush and clean the ear. For the extremely chronic case with radiographic changes of the bullae a bulla osteotomy or total ear ablation
may be required. In all cases a residual head tilt may persist.

**Central Vestibular diseases** differ from peripheral vestibular syndromes by having a greater tendency to
roll. Vertical nystagmus or a nystagmus that changes with head position may also be seen. There may be
cerebellar signs, depression, long tract signs, i.e. loss of proprioception. Other cranial nerves may be involved as well. Etiology may vary; i.e. congenital in the Doberman, distemper(predilection for cerebellar peduncles), GME and to a lesser extent neoplasia (neurofibroma of the 8$^{th}$ cranial nerve). Central vestibular disease is diagnosed by physical and neurological exam, MDB (CBC, Chemistries), thyroid, serology, thoracic and abdominal radiographs, abdominal ultrasound, CSF and special imaging
i.e. CT and MRI. A paradoxical head tilt may be seen with lesions in or about the cerebellar peduncles or flocculonodular lobe of the cerebellum.

One article[1.] describes adult canines, predominantly Labradors, presenting with an acute onset of central
vestibular syndrome. MRI was performed on a few of the patients and lesions compatible with vascular
infarct was identified. All patients improved with thyroid supplementation. It was presumed that the elevated triglycerides caused the cerebrovascular disease. Thyroid screening should be a part of any vestibular patient's data base.

**Medical Treatment options for vertigo/motion sickness**

Phenothiazines , (Alpha 2 antagonist for use in cats), Diazepam, Antihistamines (H1-histaminergic antagonist for dogs), Cerenia (NK1 receptor antagonist) and

Metoclopramide (D2-dopaminergic antagonist)

- Protective padding, Fluid support and Steroids? (**No**)

**Deafness** may be evaluated by performing brainstem auditory evoked responses (BAER). An audible click is delivered to the external ear and the nerve transmission picked up by electrodes placed in the scalp. Because of all the back-ground noise/transmissions, the signal must be averaged.Peaks are generated by I the cochlear nerve, II the intracranial portion of the nerve plus or minus the nuclei, III the dorsal nucleus of the Trapezoid, IV rostral pons and lateral lemniscus and V the caudal colliculus. Both amplitudes and latencies may be evaluated. BAER is used frequently to evaluate hearing in puppies. Testing is done at the age of 6 weeks or older. Normal hearing patterns are in place by 30 to 40 days of age. Congenital deafness is associated with lack of migration of melanoblasts to the area. Embryological precursors of melanocytes migrate from the neural crest and share a capability of tyrosine metabolism with other CNS cells. This lack of melanocytes is associated with a degeneration of the organ of Corti, its associated hair cells and a collapse of the sacculus.
In evaluating hearing in puppies it has been shown that 25% of Dalmatians may be deaf in one ear and 7% deaf in both.

[1.] Higgins, MA, Rossmeisl JH, Panciera DL, Hypothyroid associated central vestibular disease in 10
Dogs 1999-2005 J Vet Int Med 20; 2006; 20: 1363-1369

# CONVULSIONES: PORQUE OCURREN Y QUE HACER CON ELLAS?

**INTRODUCTION:** *Seizures are exceptionally frightening to the client. The causes, diagnostic approach to seizures and their treatment will be discussed as per the recommendations of the 2015 published report of the International Veterinary Epilepsy Task Force. Status epilepticus will be addressed separately toward the end of the hour.*

Seizures are a common part of general practice with 0.5 to 5.7% of all dogs and 0.5 to 1.0% of all cats having seizures. One author lists a high 7.0% of cats with seizures. **True epilepsy/Idiopathic epilepsy/epilepsy** is defined as seizures of a nonprogressive, intracranial disorder; this may be inherited, acquired or idiopathic. **Symptomatic/structural epilepsy** is seizures of a progressive intracranial disorder e.g. neoplasia/infection. **Reactive seizures** are those in response to or reacting to a change in the system i.e. hypoglycemia or toxin.
Seizures may be of different complexities, the simplest being partial or focal. These are without impairment of consciousness. **Complex Partial**, aka psychomotor seizures (running fits) have serial complex movements and may have some impairment of consciousness. The most common seizure seen is the generalized seizure. It is typically of a tonic/clonic nature. Other forms of seizures are absence, myoclonic, tonic and atonic. Generalized account for about 60% of all seizures in cats and 80% of those seen in dogs. Typically a seizure has four phases; prodromal, aura, ictus (active seizure) and postictal. Most patients have a normal interictal period with some demonstrating distinct calendar rhythms. **Status epilepticus** is repeat seizures without interruption or with very short interictal periods. **Cluster seizures** are multiple seizures spaced over a day or two. Causes of seizures are many and varied.

| | | | |
|---|---|---|---|
| **DAMNIIITTV** | Degenerative | Neoplastic | Trauma |
| | Anomalous | Infection | Toxic |
| | Metabolic | Inflammatory | Trauma |
| | Vascular | | |

**True Epilepsy** usually begins at 6 months to 5 years of age and the breeds most commonly affected are Tervuren, Beagle, German shepherd, Keeshunden, Collie, Golden Retriever, Irish Setter, Saint Bernard, Cocker Spaniel and miniature Poodle. There is no gender preference. In the history taking there are specific questions to ask the client; previous illnesses or trauma, family history, vaccination status, travel history and environmental. Ask the owner to describe what the seizure looks like, is it symmetrical? Also ask about frequency and duration. When did the patient have the first seizure? Are the seizures progressive or nonprogressive; is there a certain time of day? How long do the seizures last and what is the length of each phase of the seizure. Often seizures will cycle on 4 or 6-week intervals. Are there triggers that precipitated the seizure, i.e. the doorbell, parties, excitement? On the physical examination do not neglect the ophthalmoscopic exam since it may give clues of chorioretinitis due to distemper, FIP or retinal hemorrhages etc. Cardiac auscultation may aid in the defining of syncope which may be confused with a seizure. Abnormal bumps and lumps need to be explored whether it is a hemagiosarcoma of the spleen or a palpable mass on the calvarium. Given the patient with seizures the findings of the physical and neurological exam may be consistent with the Cerebral Syndrome or may be totally normal. Minimum Data Base: Complete blood count, Serum chemistries with preferably a fasting blood glucose. MDB should also include urine analysis, radiographs of chest

and abdomen and abdominal ultrasound, heartworm and fecal exam. Additional Diagnostics depend on the preliminary findings and the compliance of the owner. Tick titers and fungal titers may change with geography. Electroencephalography (EEG) is done rarely anymore however C.T., MRI, and CSF analysis are the mainstay. MRI is far better than CT for evaluation of the brain.

When is the need for an **anticonvulsant?** Based on variables such as the owner, seizure frequency, character of the seizures, cost, time, and monitoring capabilities the time to start anticonvulsant medication may vary greatly.

***Remember that a proportion of animals will not be controlled despite medical therapy. This may be as high as 20 to 30%*** Selection of an anticonvulsant is not dictated by strict rules. Some use Bromide more with those patients who tend to cluster while starting with Phenobarbital is certainly acceptable and will achieve therapeutic blood levels sooner. In the canine my preference is Phenobarbital, bromide and then Keppra (Levetiracetam) in that order. In the feline I use Phenobarbital and then add Keppra [1.] Always consider ½ lives when starting and/or stopping anticonvulsants. With Phenobarbital 60 to 80% of epileptic dogs may be controlled effectively at 2 to 4 mg/kg/day. The ½ life of Phenobarbital is 70 hours so steady state will not be reached until 10 to 15 days ***(steady states of drugs are usually achieved in 5 times the ½ life)*** Monitoring of drug levels is only a guide—ask your patient if it's working. If the patient is still having seizures then they need more drug, take the drug to the toxic level before adding another anticonvulsant. The time of day that blood levels are measured is not critical what is important is not to use serum separator tubes when measuring Phenobarbital levels. A simple way to adjust the dose is use the equation;

***Desired concentration/Observed concentration X current amount being taken = new dose to administer***

While on Phenobarbital the patients will have some expected alterations in their chemistries, T4 may be reduced by 50%, free T4 a 50% reduction, TSH a 50% increase and total T3 will have minimal reduction. Liver enzymes will also be affected; ALT may triple, ALP may increase 7 fold, GGT has a minor change, Albumin is unchanged but Cholesterol may increase by 50%**.** All these changes are seen hematologically and when the liver is then evaluated histopathologically there are few pathological changes observable.

**Bromide** has been used from the mid 1800's. 40mg/kg/day for KBr, KBr = 67% bromide and NaBr = 78% bromide. Eliminated through the kidneys Bromide has no effect on the liver. The half-life of bromide in the canine is 21 days so steady state will be achieved in 3 ½ months. Bromides' ½ life in cats is 12 days so steady state is achieved in 2 months. You may use analytical grade KBr mixed with distilled water to give 250mg/ml (60 grams KBr in 8 oz. of $H_2O$) **If** you compound this yourself there may be liability issues. When using Bromide you want to obtain blood levels of at least 1mg/ml. Bromide is a salt so side effects are a salty taste, possible pancreatitis, megaesophagus and skin eruptions. In the cat the most troublesome side effect is an asthmatic like condition presenting as a cough, this necessitates discontinuation of the Bromide. In the diagnostic lab Bromide may falsely elevate Chloride determination since many analytical machines see the Br as Cl.

Loading with Sodium Bromide i.v. may be done however I find it easier to do either oral loading via stomach tube or rectally at 400 to 600 mg/Kg bid for two days.

For **Feline Anticonvulsants** I use Phenobarbital at 3 to 5 mg/kg/day with monitoring levels the same as for dogs. **I no longer use Bromide** in cats because of the side effect of pneumonitis. **Diazepam** at 0.5 to 2.0 mg/kg divided tid may be used. The ½ life of Diazepam in cats is approx. 15 to 20 hours with up to 20% of cats not responding to diazepam therapy*. Fatal hepatic necrosis* has been seen in some cats with diazepam therapy. When starting Diazepam therapy in cats it is advisable to check liver enzymes over the first few days.

**Keppra** in cats at 20mg/kg bid as a single drug or in combination with Phenobarbital at

a reduced dose of 10 mg/kg bid. Dogs dose 20mg/kg tid

**Levetiracetam (Keppra)** in both dogs and cats has proven to be exceptionally safe and well tolerated. Levetiracetam has a totally different method of action than either of the other anticonvulsants by its effect on the synaptic proteins in the nerve axon terminal thus inhibiting release of neurotransmitter. Because it is excreted mainly by the kidney it is very safe to use in patients with potential liver problems. Its main drawback is the short half-life in dogs of only 4 hours (3 hours in cats) necessitating tid dosing. You may use the sustained release form and get by with bid dosing. An injectable form is now being used to aid in loading patients and as the longer term therapy in status epilepticus patients after the initial Diazepam is given. At the University we completed a study showing the effective levels of Levetiracetam being reached quickly after rectal administration. Dosing at 40 – 60 mg/kg therapeutic levels were reached and maintained for up to 9 hours. Cost of the drug is coming down.

**Zonisamide** is a sulfonamide derived antiepileptic approved in 2000. It has a long half-life in dogs (15 hours) which allows for bid dosing at 5 to 10 mg/kg. With minimal hepatic metabolism 80% is excreted unchanged in the urine. Appearing to be very safe in dogs side effects may be transient sedation, ataxia and inappetence. One study had 58% of poorly responding epileptics having good control when Zonisamide was added to the regime. Zonisamide may be used as a tertiary drug.

**Topiramate** Recently reported as a possible 5$^{th}$ line anticonvulsant it is started at 5mg/kg BID it seems to have minimal side effects and no changes to lab work. [2.]

**Rectal Diazepam** An alternative or home therapy that may be of benefit rectal Diazepam will help avoid trips to the E-clinic. Injectable Diazepam is placed rectally with the aid of a plastic teat cannula while dosing at 1mg/kg. Rectally Diazepam is almost as effective as an i.v. Another alternative therapy is vagal stimulation. The client may achieve this by pressing on the eyeballs, this stimulates the vagal nerve. This has been shown to have some effect especially if done in the prodromal period. There was one series of patients with uncontrollable epilepsy in which vagal nerve stimulators were placed. These were generators with coils placed around the cervical area of the vagus. In these patients there was a 50% reduction in seizures however the stimulators cost over $10,000 and that that does not include the surgery to place them.

**Acupuncture** using straight needles or gold bead implants has been shown to be of a benefit, again resulting in about a 50% reduction. Because of gold bead's potential interference with repeat MRIs we have used beads made of a slowly absorbable material that gives chronic focal stimulation and no MRI metal artifact. The previous alternative therapies are all examples of small case series in the literature, none of which have been tested by large blinded case studies.

***Status epilepticus*** is repeated seizure activity that without intermission can lead to hyperthermia hypoxia, and acidosis. This is a medical emergency. 60% of epileptics will experience status at some time. Increased body weight has been shown to predispose to status. Where epilepsy will not normally shorten life span an episode of status statistically will.

In treating Status Epilepticus of the patient that comes in the door all of the following take place almost simultaneously. Establish an I.V. and start fluids and obtain blood samples (especially for glucose). Get a history to rule out exposure to toxins etc. Do a physical exam for wounds about the head, blood from the nose or ears and be sure to smell the patient. Is there an odor of uremia on the breath or an odor of insecticide on the fur? Take the temperature because seizure activity readily makes the body temperature go up. Often these patients are hyperthermic and are in need of cooling. If suspect administer i.v. glucose 50% 2 to 4 ml/kg diluted 1:2 with sterile water, this is done as a test to help rule out hypoglycemia. If the seizure is not stopping then give Diazepam—0.5 to 1.0 mg/kg i.v. Diazepam is a first pass metabolite so blood levels remain for only 20 minutes. If there is no response to Diazepam proceed to Propofol to effect then establishing a CRI of Propofol. An alternative to Propofol would be

Pentobarbital, 3 to 15 mg/kg or to effect. This move will necessitate intratrachael intubation and constant monitoring with oxygen being supplied at the same time. You now have a critical care patient that may not be left when the clock hits five and everyone wants to head home! ***It is next to impossible to stop status with only i.v. Phenobarbital***

If toxicity is suspect now is the time to perform gastric lavage with copious amounts of warm water with the instillation of activated charcoal. If there was an initial response to the Diazepam then seizure control may be continued with just Phenobarbital. Phenobarbital given at 2 to 4 mg/kg I.V. repeat in 20 to 40 minutes as needed or a simple guide is stop each seizure with Diazepam then follow with 4mg/kg iv of Phenobarbital. Using this protocol we have not had to give more than 4 doses of Phenobarbital. If barbiturates are to be avoided (patient history of hepatic dysfunction) Levetiracetam given rectally (40-60mg/kg)will give rapid therapeutic blood levels that will last 9 hours. Bromide is another alternative. Oral loading with Bromide will induce more side effects such as pancreatitis so ***now is a good time for rectal loading!***

If 24-hour care is not available at your clinic then the client should be advised to transfer the patient to a 24-hour care facility where the patient may be monitored throughout the night. If the client declines this level of care then make note in the medical record.

When possible seizure patients should not be left in the hospital unattended.

One published report stated that status epilepticus was associated with a shortened life span, the article did not say exactly how much shorter. Quoting another article which looked at 62 dogs with cryptogenic epilepsy and compared their life span with a population of 3000 in the general population "The median age at death of dogs was 7.0 years". The life span of dogs in which euthanasia or death was directly caused by their epileptic condition was significantly shorter as compared with epileptic dogs that were euthanized because of other causes. The median number of years that a dog lived with epilepsy was 2.3 years. Females lived longer with epilepsy than males. Seizure type (primary generalized versus focal seizures) was not significantly associated with survival time. The remission rate of epilepsy (spontaneous remission and remission with treatment) was 15%.

The diagnosis of epilepsy implies an increased risk of premature death. The prognosis for dogs with epilepsy is dependent on a combination of veterinary expertise, therapeutic success, and the owner's motivation.

**Little White Shakers** (not always white)

This disease is a possible immune reaction aimed at tyrosine-producing cells. Tyrosine is a precursor to melanin and some neurotransmitters. Histopathologically there is a very mild diffuse, nonsuppurative encephalomyelitis. Aside from the tremors the neurological exam is normal. Treatment is with immunosuppressive doses of Prednisone and Diazepam to help control the tremors. The prognosis is good with most patients responding within a week of starting therapy. Relapses are possible.

1. International veterinary epilepsy task force consensus report on epilepsy definition, classification and terminology in companion animals BMC Veterinary Research (2015) 11:182 DOI 10.1186/s12917-015-0461-2 Berendt et al.

2. J Small Anim Pract. 2013 Oct;54(10):512-20. Topiramate as an add-on antiepileptic drug in treating refractory canine idiopathic epilepsy. . J Small Anim Pract. 2013 Oct;54(10):512-20. Kiviranta AM1, Laitinen-Vapaavuori O, Hielm-Björkman A, Jokinen T.

# CAIDO ATRAS: COMO DIAGNOSTICAR Y QUE HACER CON LAS PARAPARESIA/PARAPLEGIA

**INTRODUCTION:** *Armed with the lesion's location, and patient signalment, specific syndromes will be explored and their method of diagnosis elucidated. Although MRI and CT are helpful, you will learn that not all cases require their use. Discospondylitis, lumbosacral stenosis, FCE and intervertebral disc disease will be discussed. The drug Polyethylene glycol (PEG) will be covered as well as the use of laser in the treatment of paralysis.*

Paraparesis (weakness in the rear limbs) and paraplegia (paralysis of the rear limbs) unaccompanied by signs of additional CNS disturbance suggests that the disease is located caudal to T2. If the rear limb reflexes are intact, the lesion is between T2 and L3. If the rear leg reflexes are diminished to absent, the lesion is between L4 and S2. This can be refined further in that lesions between L4 and L5 result in loss of femoral nerve function, manifested as a decrease in the patellar tendon reflex and inability to support weight in the rear legs. Lesions between L6 and S2 result in sciatic nerve dysfunction, reducing rear leg withdrawal, cranial tibialis muscle, gastrocnemius muscle and sciatic nerve reflexes.

The differential diagnosis of paraparesis and paraplegia include a number of congenital diseases, including vertebral malformations, various spinal cord malformations, multiple cartilaginous exostoses, lysosomal storage diseases, and breed-specific disorders. Other disorders are similar to those which affect the cervical spinal cord including meningomyelitis (from various causes), degenerative disc disease, spinal cord trauma, fibrocartilaginous infarction, and neoplasia. In some breeds, the differential also includes degenerative myelopathy.

Diagnostic Approach:

The neurologic assessment of patients with rear leg problems helps to confirm that the disease is neurologic in nature and the its location. Weakness can indicate neurologic disease, muscle disease or systemic illness. Reproducible deficits in proprioception usually is indicative of neurologic disease, whether knuckling, stumbling, conscious proprioceptive deficits or dysmetria. When deciding whether rear leg lameness is secondary to orthopedic or neurologic disease, examination of proprioceptive function can help make the differentiation.

Unlike cervical disease, there are several neurologic tests which can assist in lesion localization with Thoraco-lumbar disease. If the lesion is between T3 and L3 and severe enough, Schiff-Sherrington syndrome may be seen. Also, between T2 and L6 is the panniculus reflex, where superficial stimulation of the skin over the back results in stimulation of intraspinal pain pathways with the resultant contraction of the cutaneous trunci muscle. Due to the overlap of sensory dermatomes, the panniculus response will be absent 1-2 segments caudal to the lesion

Thoraco-lumbar Intervertebral Disc Disease: (IVD)

IVD disease can occur as a protrusion of the IVD (Hansen's Type 2 IVD) with the dorsal annulus still retaining the disc material or as a herniation/extrusion of the nucleus pulposus into the neural canal (Hansen's Type 1 IVD). The former (type II) is most common in non-chondrodystrophoid animals (straight-legged dogs) and occurs as a result of age-related changes in the IVD. As animals age, the water content of the IVD diminishes and the collagen content increases. This results in a decrease in the IVD elasticity, leading to degeneration of the annulus fibrosis and protrusion of the IVD. Depending upon the location, this can result in spinal cord or nerve root compression and development of neurologic signs. The onset of signs increases with age, peaking around 8-10 years of age. This type of IVD protrusion (Type II) is uncommon before 5-6 years of age.

On the other hand, chondrodystrophic breeds of dogs are prone to the development of IVD (type I) herniation early in life. In these breeds (including dachshunds, beagles, Pekinese, miniature poodles, cocker spaniels, Pomeranians and basset hounds), there is a metaplasia of the nucleus pulposus whereby the normal collagen fibers of the nucleus are replaced by hyaline fibers. The hyaline fibers are less elastic than collagen fibers leading to degeneration of the annulus fibrosis. The hyaline fibers during this degenerative process calcify, creating further inelasticity. Due to the fact that the annulus fibrosis is thinnest dorsally toward the spinal cord, the least line of resistance for the degeneration and breakdown of the annulus is toward the spinal cord. Ultimately, the annulus ruptures allowing the herniation of the degenerative nucleus into the neural canal, compressing the spinal cord. Not only does the IVD material compress the spinal cord, but the degenerative material is irritating in nature. The presence of the herniated material in the epidural space causes inflammation, furthering the swelling associated with the herniation.

Almost all chondrodystrophic dogs will show some degree of IVD degeneration within a year of age. Usually the onset is between 2-3 years of age with the peak incidence being between 4-6 years of age. IVD herniation is less common in the upper thoracic region due to the intercapital ligament which connects the rib heads and reinforces the dorsal annulus in that area. Of the remaining spinal column regions, 20% of IVD herniations occur in the cervical region (C2-C7) with 80% of these at C2-3. 80% of the IVD herniations occur in the thoraco-lumbar region with 67-75% of these occurring at T12-13 or T13-L1. The incidence rapidly dissipates cranially and caudally from the TL junction. From L4 caudally, each disc has an incidence of around 2.5%. Cervical IVD herniation will cause quadriparesis (or quadriplegia) while TL IVD herniations result in paraparesis to paraplegia.

In addition to location, the dynamic factor dictates the severity of clinical signs. The amount of traumatic force imparted by a small amount of material traveling rapidly is greater than a larger amount going slowly. In most cases of IVD disease, definitive treatment must be started before 24 hours in order to achieve the greatest success. In some cases, this time is shorter. Unfortunately, delaying treatment to see the outcome may preclude success. We treat severe IVD disease as a medical and surgical emergency.

Spinal trauma from a disc extrusion has two components, primary and secondary. The specific therapy depends on the grade of spinal injury.

Grade 1. The patients' only sign is pain. This is the earliest stage since only the meninges has pain nerve endings and at this point only the meninges is being involved.

Grade 2. The patient is paretic (weak and ataxic) but still walking. The compressive nature of the protruding disc is starting to affect the outer white matter of the cord. These white matter tracts carry proprioceptive information in large very sensitive fibers that are very susceptible to compression.

Grade 3. The patient is no longer walking but still has voluntary control of urination and if supported will have very weak voluntary motor movements (non-ambulatory paretic). The patient may act uncomfortable and whine to go out or drag themselves to the door to urinate. Once outside they can voluntarily initiate urination. The cord compression is now affecting the motor fiber tracts found deeper in the cord parenchyma.

Grade 4. The patient is not walking has no voluntary motor movement (paraplegic) nor does he have control of urination. In both, the patient is not walking but does retain the ability to sense deep pain.

Grade 5. The patient is paralyzed and has no sensation of deep pain below the level of the lesion. Deep pain is evaluated by seeing the patient not only pull the limb back when the toe is pinched but also the patient must turn and look at the limb and or try to bite. There must be cerebral recognition! Once deep pain is lost the cord has suffered such compressive forces as to render ineffective those very small non-myelinated fibers which are most resistant to crush.

On the premise that the injury is of an intervertebral disc protrusion the following treatment plans are to be followed.

Grade 1. This requires only confinement. DO NOT reach for the steroids! If you want to relieve the discomfort then use an NSAID only. Be absolutely sure to strictly confine (crate or cage) for 3 weeks. Steroid use has been repeatedly shown to cause complications, create polypharmacy and increase the cost of hospital stays. In one study of dachshunds given steroids for CNS injury there was a higher incidence of GI complications, higher hospital costs but their hospital stay was no longer and neurologically they were better than the non steroid group 24 hours post op but no different at time of suture removal.

Grade 1 patients generally will have a 100% recovery in 3 weeks. They are an outpatient unless there is a question as to possible progression in which case it is advisable to hospitalize and do serial neurological exams.

Grade 2. The same as for grade 1, absolute confinement if the process is not progressing. This therapy gives a prognosis of 84% recovery within 6 weeks. Steroids may be used with caution at a one-time anti-inflammatory dose if the patient is seen soon after the initial insult otherwise steroids should be avoided. PEG (polyethelene glycol), a 30% solution given IV at 1 ml/pound twice over 24 hours may be used. PEG has not undergone large double blinded studies, however, extrapolating from its use in human medicine it may be of veterinary benefit. If it is longer than 72 hours since injury the benefit of PEG is doubtful.

In those patients presented as grade 2 and having decompressive surgery versus conservative care only, the recovery rate improves to 95% and the recovery time is shortened to less than 2 weeks. Cost versus benefit is to be weighed.

Grade 3. Same as grade 2. The recovery percentages and time to recovery are the same as for grade 2. However if cost is not an issue surgery would be advised because of the extra nursing care required to maintain a non-ambulatory patient over a 6 week rehabilitation time versus a less than two week time.

Grade 4. Immediate surgery. Even at this grade conservative care will result in an ambulatory patient 81% of the time. Recovery time without surgery may take 9 to 12 weeks while with surgery it will be only 1 to 4 weeks. For many on fixed incomes or retired clients they may have the time but not the money. Conservative care is a viable option.

Grade 5. Immediate surgery. Conservative care gives only a 7% chance of recovery while surgery within the first 24 hours will increase that percentage to 64% chance of recovery. After 24 hours it drops to 50% and keeps dropping after that. The longer the compressive force stays on the cord the more permanent the deficit.

A recent article states that 56% of grade five patients will recover after having surgery (even if greater than 48 hours) unless they develop myelomalacia. 1.

Remember:

- When we say confinement it is confinement not just locked in the bathroom.
- Minimal steroids! I know this will be hard for many but unless you see the patient soon post injury refrain from steroid use. Reach for NSAIDS and PEG instead.
- Try PEG, it's not expensive; it can't hurt and may soon be proven to help.
- If money is an issue many will recover with conservative care alone. Grades 1 through 4 have an approximate recovery rate of 81% with conservative care alone; they just take time and nursing.
- If surgery is indicated don't delay, the deficits will only become more permanent.

In some patients that have suffered a severe disc protrusion with a loss of deep pain sensation there is a subset who will present with fever and spinal hyperesthesia. These are classical signs of myelomalacia a progressive ascending and descending deterioration of the spinal cord. These patients will progress to apnea as the liquefaction of the cord reaches the level of C-5. The presence of myelomalacia may be seen with MRI or if it is suspected a durotomy at the time of surgery will result in the affected cord oozing out of the durotomy site. These patients should be euthanized.

*PEG Polyethylene glycol

Fibrocartilaginous Infarction:

Even though animals do not suffer from to the same degree of vascular disease as human beings, infarction of the spinal cord with fibrocartilaginous material is not uncommon. It occurs in any breed of dogs, but is most common in large breeds, such as Great Danes, Labrador retrievers and German Shepherds. It is believed that herniation of the nucleus pulposus takes place either into the vertebral body or the venous sinuses within the spinal column. Since the vertebral body represents a vascular space communicating with the spinal venous system, the material gains access to the spinal veins. These veins do not have valves, allowing the fibrocartilaginous material to flow up and down the spinal column. The pattern of infarction usually affects a quadrant of the spinal cord, although initial signs may affect more of the spinal pathways from inflammation and spinal cord swelling. The infarction can occur

anywhere along the spinal cord, but the cervical and mid- to lower lumbar spinal cord segments appear to be most frequently involved.

The presence of spinal cord infarction should be suspected whenever a patient presents with acute onset of paresis or paralysis which is markedly asymmetrical and there is no evidence of hyperpathia. Vascular disease is generally acute and non-progressive. In addition, the spinal cord contains pain pathways, but no pain receptors. As such, strict diseases within the spinal cord without meningeal involvement are usually not painful. Most of the other diagnostic tests will be within normal limits. Occasionally, there will be evidence of hemorrhage on CSF analysis. Spinal radiographs, do not demonstrate the disease, but may reveal other evidence of spinal column degeneration. Myelography will be normal or demonstrate mild intramedullary swelling.

The treatment of spinal cord infarction is that for acute spinal cord injury, using methylprednisolone initially. I dose at 10 to 15 mg/kg. We also use PEG 30% 1ml/pound IV repeated in 24 hours. Many cases will improve dramatically within the first week, although they will still improve over several months. If there has been no improvement in the first week, re-examination and additional tests may be indicated. Since usually only a quadrant of the spinal cord is affected, the patient will improve most on the unaffected side. Reorganization will usually allow these patients to function adequately. Spinal cord infarction from fibrocartilaginous material is a sporadic problem and, usually, does not reoccur.

Degenerative myelopathy (DM)

DM is a degenerative disease of unknown etiology. Most often in German Shepherds but other large breeds affected. Generally over 5 years of age. Corgis have recently been described as having a specific homozygous allele predisposing to the disease. DNA testing is available via U of Missouri. Multiple etiologies have been implicated but none proven. Work done in the German shepherd breed is suggestive of an immune mediated disease. Some association with low serum levels of vitamin B12 and E however when these vitamins were supplemented no change in condition was noted.

Histologically most lesions are in the white matter of the thoracic cord with axonal and myelin loss. The clinical picture is of normal to hyper segmental reflexes in the rear with 10 to 15% of patients showing decreased to absent patellar reflexes. This is due to involvement of the dorsal root in that motor unit segment. Slowly progressive and non-painful there is a loss of proprioception and motor movement in the rear limbs. Urinary and fecal control is maintained. Eventually the fore limbs start to exhibit symptoms with progression to quadriplegia. Diagnosis is a diagnosis of exclusion. EMG will be normal; Cord Dorsum Potentials may have reduction of amplitude. Myelography and MRI will be normal.

Treatment with ethylaminocaproic acid 500mg tid is costly and controversial. Vitamin E and B have also been advocated without any solid proof of effect.

Exercise has been shown to be the most beneficial. Prognosis is poor with a slow progression over 6 to 12 months, fortunately bowel and bladder control remains.

University of Missouri www.caninegeneticdiseases.net/DM/testDM.htm

Anomolous vertebral malformation

Hemivertebra, wedge vertebra, block vertebra and spina bifida result from improper or lack of normal closure of vertebral body ossification centers. Depending on which centers affected will give differing shapes of vertebra i.e. butterfly, hemi. The breeds affected are mostly screw-tailed, i.e. Boston, Pug and Bulldog* These deformities may be asymptomatic or they may result in scoliosis, kyphosis or lordosis which may be so severe as to cause spinal cord compression and neurological deficits compatible with lesion location. Diagnosis is often coincidental but is based on radiography and CT with CT 3-D reconstruction a very valuable tool. Unless there are neurological deficits there is no treatment needed, if there are deficits or if the condition is worsening then surgery is indicated. A warning is that surgery may result in disastrous circumstances because of resultant instabilities and collapse of the vertebral body.

1. Factors associated with recovery from paraplegia in dogs with loss of pain perception in the pelvic limbs following intervertebral disk herniation N. Jeffery JAVMA Feb 15 2016 Vol 248;No.4

# CAIDO Y NO SE PUEDE LEVANTAR: LAS CAUSAS Y TRATAMIENTO DE CUADRIPLEGIA/CUADRIPARESIA

INTRODUCCIÓN:

*Diseases of the cervical region such as "Wobblers", and cervical disc disease will be discussed and their treatment reviewed. Not to be left out are the diffuse neuromuscular diseases. Unless you can tell an upper motor lesion from a lower motor lesion you won't be able to diagnose coral snake, Myasthenia Gravis or tick paralysis.*

**Quadriparesis** (weakness and ataxia of all 4 limbs) and quadriplegia (paralysis of all 4 limbs) are common problems in all animals. Faced with an animal having neurologic disease affecting all 4 limbs and knowing that the mentation and cranial nerves are normal then you may deduce that the lesion is below the foramen magnum (meaning a spinal cord or peripheral disease). This gives 4 possible anatomic locations for the disease process: 1) if there is UMN (upper motor neuron) dysfunction in all 4 legs, the lesion is most likely to be in the spinal cord between C1-C5; 2) if there is LMN (lower motor neuron) dysfunction in the fore legs and UMN dysfunction to the rear legs, the lesion is severe and involves spinal cord segments C6-T2; 3) if there is UMN dysfunction to the rear legs and "root signature" (lameness due to nerve root involvement) in the forelegs, the lesion is mild and affecting spinal cord segments C6-T2; or, 4) if there is LMN dysfunction in all 4 limbs, the lesion is due to a diffuse LMN disease.

In developing the differential diagnosis for quadriparesis, the basic mechanisms of disease must be considered along with the signalment and history. Congenital diseases are not uncommon in the cervical spinal column of dogs. These include agenesis of the dens (with resultant atlantoaxial subluxation), blocked vertebra, multiple cartilaginous exostoses, leukoencephalomyelopathy of Rottweilers, and hereditary ataxia of Jack Russell and Smooth-haired Fox terriers. In older animals, degenerative intervertebral disc (IVD) disease, inflammatory meningomyelitis and neoplasia are not uncommon. If the signs are symmetrical, then nutritional, metabolic and toxic diseases must be considered. On the other hand, most asymmetrical diseases can be separated into their most likely causes, which must be included in the differential. These causes are discospondylitis, meningomyelitis, IVD disease and neoplasia.

**Diagnostic Approach:**

Like the rest of the nervous system, the neurologic examination is the single most important diagnostic method to localize diseases of the cervical spine, providing an indication from which to make a tentative differential diagnostic list. Localizing diseases in the cervical spinal column to a specific spinal segment can be difficult, since tests like the panniculus response cannot be performed there. Segment specific hyperpathia can be difficult to elicit and hyperesthesia is not easily mapped. Often it is just lumped as "neck pain".

The ancillary diagnostic tests for spinal cord disease are similar regardless of the cause and include the minimum data base, spinal radiographs, EMG, CSF tap and analysis, myelography and/or MRI. The minimum data base will often be normal or may need to be expanded based upon the physical and neurologic examinations. In older patients, routine chest and abdominal radiographs and abdominal ultrasound may help make a diagnosis of the cervical disease or assist in making the prognosis. Spinal radiographs may show signs of degenerative disc disease, congenital malformation, spinal arthritis or discospondylitis. Diagnosis of discospondylitis may be made on plain spinal radiographs alone. The other diseases will need additional imaging techniques to confirm that they are the source of the problem. The CSF tap can help determine the presence of inflammation or infection in cervical diseases. The problem of inflammatory myelitis is increasing, making CSF tap and analysis critical in assessing cervical neurologic disease. Even when other neurologic conditions are identified, myelitis may be present. Unfortunately, many patients are treated with corticosteroids before being adequately worked-up for cervical disease with the steroids altering CSF results. The work-up performed in the face of the steroids may be erroneous. As such, surgical intervention may be performed, only later to discover the cause of neck pain was inflammatory meningomyelitis.

MRI can add diagnostic detail. MRI may be important is assessing neoplastic disease processes, including nerve root tumors. The sequence of diagnostic tests logically follows the pattern of minimum data base, spinal radiographs, CSF tap, EMG and, finally, MRI. If an accurate diagnosis is made along the way, the remaining tests may not be needed.

**Cervical Vertebral Malformation Complex:**

Wobblers' disease occurs in young and old animals. In young animals, it appears to be secondary to inherited malformation and mal-articulation of the cervical vertebrae, in older animals it appears to be secondary to chronic degenerative disc disease. Although other large breeds can be affected, it is said to be a disease of young Great Danes and old Doberman pinchers. When a Doberman pincher presents with signs of rear leg ataxia with "root signature" in the forelegs, there is a high probability that the dog has Wobbler's disease.

The onset of clinical signs can be acute or slow and insidious. There is evidence of ataxia in all four limbs with the pelvic limbs being more affected. There will be both conscious and unconscious proprioceptive dysfunction with a wide-based stance in the rear legs. The forelegs may show a stiff and stilted gait while the rear limbs are wide, swaying and ataxic, this is the classic "Two Engine Gait". The diagnosis can be suspicioned on survey radiographs of the neck, looking for narrowed IVD spaces and sclerosis of the demi-facets. CSF analysis is usually within normal limits, although a small number of cases will show a mild increase in cells (4-10 cells/microl) and protein (25-35 mg/dl). EMG can help confirm the location and the denervation of the muscles with fasciculations. The diagnosis is confirmed on MRI, which shows evidence of IVD protrusion and the presence of ligamentous or bony intrusion into the neural canal. *Since* CVM represents a dynamic lesion, MRI or myelography with an extended view is the diagnostic technique of choice. The treatment of CVM is surgery. In cases where surgery is not possible (patient has complications or is elderly), medical management with prednisolone and diazepam may provide temporary relief. However, in the absence of compelling reasons not to perform surgery, surgical decompression is needed. There are several surgical techniques available to treat Wobblers' disease including dorsal

laminectomy, ventral slot and ventral slot with distraction (by various means). In cases of multiple lesions, dorsal laminectomy is one method of choice. Dorsal laminectomy has risks and the success rate is the lowest of methods for correcting CVM. In qualified hands, it is still a good technique. The overall success is around 75% with 20-25% morbidity and 5-10% mortality. Large breeds do not tolerate dorsal laminectomy well. Ventral slot is excellent for IVD protrusion, but increases compression from ligamentous hypertrophy. In simple IVD protrusion, ventral slot has a 90-95% success rate with a 5% morbidity and <1% mortality. The morbidity and mortality increase for ventral slots when ligamentous hypertrophy is present. When ligamentous hypertrophy is present, ventral slot alone is generally inadequate to correct the problem. A number of techniques have been described to perform a ventral slot and maintain distraction across the IVD space. Distraction fusion surgeries with bone cement and titanium screws is one method utilized because Titanium does not interfere with MRI so that if MRI is needed in the future we may utilize that imaging modality.

Following surgery, the patient should be kept quiet for 30 days. After the first month, the activity level is gradually returned to normal. Depending upon the severity of the initial damage, most patients will improve, reaching 80% of their recovery in the first 3 months. There is a potential for the "domino" effect, whereby the IVD on either side of the fusion surgery site will develop problems in 6 months to 2 years following the initial correction. This may occur 25% of the time.

**Caudal Occipital Malformation Syndrome (COMS)**

COMS is common in Cavalier King Charles spaniels and may also be seen in other small breeds. COMS is a developmental abnormality of the occipital bone that leads to compression of the caudal fossa and herniation of the cerebellum out the foramen magnum. There is the boney malformation and there may also be meningeal hypertrophy. This combination causes altered CSF flow dynamics with resultant changes of pressure gradients of the CSF. This action and combination of malformations result in syringohydromyelia. This disease is very prevalent in the UK and is now being diagnosed more often in the USA. The mode of inheritance of this abnormality appears to be separate from that which codes for epilepsy in the breed. Selection for coat color has been shown to affect the prevalence of epilepsy and heart disease in the breed but as yet not linked with the COMS malformation.

Age on presentation has ranged from 4.5 months to 13 years. There is no sex predilection.

Clinical presentation may be an asymptomatic patient but the most common symptoms are thoracic limb weakness (thoracic limbs worse than the pelvic), cervical spinal hyperesthesia and "air scratching". This is persistent scratching at the neck and shoulder area often without touching the skin. There may be torticollis and vestibular signs. Treatment is either medical or surgical. Medical may be by any of three methods; treat pain, reduce CSF production or with steroids, steroids will put 67% of patients into remission but the side effects may be intolerable. Treating pain is with NSAIDS, gabapentin or Tramadol or all three. Reduction of CSF is with Omeprazole, a proton pump inhibitor (10mg/day), acetazolamide, or furosemide. Surgery for some is the best option. The surgery involves a sub- occipital craniectomy with partial laminectomy of C 1, the meninges is also resected at this time. Prognosis is variable; in one early survey by Dewey those patients that underwent surgery approximately 50% improved, however, many remained unchanged or worsened. Utilizing the newer techniques pioneered by Dewey success rates are now closer to 90%.

**Diffuse Lower Motor Neuron Diseases**

**Tick Paralysis**

Reacting to a neurotoxin in the tick's saliva, dogs present with an ascending, flaccid (LMN) paralysis. Cats seem to be fairly resistant. The species *Dermacentor variabilis* is the most common cause in the USA.

A tick must be attached for approx. 5 days before the toxin results in clinical signs with weakness as the first sign progressing to quadriparesis/plegia within 1 to 3 days. Treatment is by removal of the tick which results in return of ambulation within 8 to 24 hours. Some cases may last a few days especially if the offending tick is of the *Ixodes* species.

**Polyneuropathy (polyradiculoneuritis)**

The most common polyneuropathy seen in dogs is acute polyradiculopathy. This disorder is also referred to as "coonhound paralysis" since a great number of hounds developed an ascending flaccid paralysis following contact with raccoons. This suggests that there are a number of inciting causes of polyradiculopathy in dogs, including something present in the bite of the raccoon. Other patients experience similar syndromes following rabies vaccination. It is probable that the inciting cause initiates a cross-reactivity with the neural antigens in the nerve roots, leading to demyelination and the clinical signs.

This disorder can affect any age, breed or sex of dog or cat, although the condition is rare before the age of 6 months. The onset of signs begins as rear leg weakness which rapidly ascends over 24-48 hours until the animal is quadriplegic. Occasionally, the condition can start in the fore legs and then progress to quadriplegia. Physical examination is usually within normal limits (an old raccoon bite might be apparent in hounds). Usually, there are no cranial nerve signs; however, in severe cases, the bark may be altered, swallowing impaired and facial nerve signs evident. In some cases, respiration is impaired necessitating respiratory support.

The diagnosis is supported by finding mild elevation of CSF protein, particularly from lumbar spinal tap. The EMG reveals denervation potentials (fibrillation potentials and positive sharp waves). The motor conduction velocity is usually slower (< 50 M/sec), particularly later in the course of the disease.

There is no specific treatment for polyradiculopathy. Corticosteroid therapy has not been shown to be of benefit. The clinical course is variable and may last from a few days to several weeks. In some cases, there are permanent neurologic deficits. Recovered animals may have the condition reoccur. Recurrences are often more severe than the initial incident.

**Episodic weakness**

**Polymyositis**

Idiopathic polymyositis is a diffuse inflammation of the skeletal muscles. An autoimmune process is suspected in most cases. Hypergammaglobulinemia, positive titers for serum antinuclear antibody (ANA), and elevations of circulating anti-muscle antibodies (also demonstrable by indirect immunohistochemistry) have been found in many cases. There is generalized weakness which worsens on exercise. These patients also have a stiff stilted gait, lameness and pain on muscle palpation.

Occasionally, generalized loss of skeletal muscle mass is evident. Megaesophagus may be present with regurgitation and aspiration pneumonia.

The main features on examination are the stiff, stilted gait. Neurologic examination (in a quiet room) is often within normal limits, except for possible muscle pain on palpation. Other signs relate to the presence of aspiration pneumonia, including fever and listlessness. During the acute phase, muscle enzymes (CPK) will be elevated. The diagnosis is supported by the findings of an abnormal needle EMG with normal nerve conduction velocities. There is occasionally a decremental response on repetitive nerve stimulation. Muscle biopsy will confirm the diagnosis.

The treatment of polymyositis is with immunosuppressive doses of corticosteroids. Cases with aspiration pneumonia have a poor prognosis, since treatment with immunosuppressive drugs cannot be initiated. In those cases where corticosteroids are effective, monitoring the CPK may be useful in determining the course of therapy. If the CPK declines to normal for 1 month, the steroid medication can be stopped. The prognosis is generally good if esophageal, pharyngeal and laryngeal muscles are not severely affected. The megaesophagus may resolve with therapy or be permanent.

Recently, (probably due to a more aggressive approach to muscle disease including biopsy and special staining procedures) many additional muscle diseases which present similarly to polymyositis have been uncovered. Lipid-storage myopathy is one of these. These patients present with stiff, stilted painful gaits with tremendous pain on muscle palpation and histopathology reveals increases in mitochondrial lipids on special (oil red O) stains. These patients may respond dramatically to coenzyme Q-10 and l-carnitine supplementation.

**Myasthenia Gravis**

A motor unit disease, specifically a junctionopathy. There are two forms of myasthenia, congenital and acquired. Congenital is a congenital lack of acetylcholine (Ach) receptors and this is seen in the Jack Russell terrier, Springer Spaniel, Smooth haired fox terrier. Acquired is an immune mediated destruction of Ach receptors with a breed preference for German shepherds, labs and Golden Retrievers. The acquired form may be associated with a thymoma. The antigenicity of the thymus cells may mimic those of Ach receptors. It is also reported with carcinomas. The physical exam may show a generalized weakness on exercise and mega esophagus or may be a focal weakness of just the eyelids. There is also an acute fulminating form of myasthenia with total collapse. 25 to 40% of dogs with mega esophagus have MG. Often the neurological exam is normal.

Diagnosis is based on EMG, repetitive nerve stimulation with a demonstrated decremental response or a Tensilon (edrophonium 0.1-2.0 mg i.v.) challenge. If edrophonium availability is an issue neostigmine 0.05mg/kg i.m. may be used as a challenge. Response to i.v.Tensilon is within a couple minutes while clinical signs resolve in 15 to 20 minutes with i.m. neostigmine. A return to ambulation gives a presumptive diagnosis of myasthenia. Atropine should always be available in the event of a cholinergic crisis (vomiting, diarrhea, excessive salivation, lacrimation and bronchospasm).with the gold standard for diagnosis being the Acetylcholine receptor antibody test (acquired form only). The clinician must not forget the minimum data base and Chest X-rays, thyroid, and ACTH response test..

The treatment of myasthenia is to suppress the production of antibodies and to increase acetylcholinergic function. The former is usually done by the administration of prednisolone at 1-2 mg/kg/ day. The dose is reduced while monitoring the serum anti-Ach receptor antibody levels. Increasing acetylcholine function is done by giving pyridostigmine (Mestinon) at 10-60 mg twice a day (depending upon the size of the patient) or 0.5-3mg/kg bid to tid. Pyridostigmine inhibits the hydrolysis of acetylcholine (ACH), this allows ACH to buildup in the synapse keeping ACH in contact with the receptor for a longer time. Adverse effects of Pyridostigmine are nausea, vomiting, diarrhea, excess salivation and difficulty breathing.

During a myasthenic crisis, intramuscular injections of neostigmine (0.5-2.5 mg) may be given in cats and dogs.

Azathioprine (1mg/kg bid) may be used in concert with a lower dose of prednisolone (0.5mg/kg bid). This therapy has shown to be of very good effect in humans, however, bone marrow suppression is the major drawback and must be monitored closely.

Prognosis is poor because of complications from megaesophagus and pneumonia, or the patient being refractive to medications. Only 40-60% live beyond a year. There are however some spontaneous remissions, some authors quote up to 85%.

The Bailey Chair has helped many patients monitor their megaesophagus. Visit

http://www.caninemegaesophagus.org/dogs/roxanne.htm for more videos and information on the Bailey Chair.

Myasthenia gravis has been considered a rare disease; however, the adult-onset form seems to be on the rise. Whether this represents improvements in diagnostic criteria and methodology or a real increase in the condition remains unsure. This may represent an increase, similar to that for other immune-related diseases.

# COJERA O DEBILIDAD ORTOPEDICO O NEUROLOGICO: COMO DIFERENCIARLOS?

**INTRODUCTION:** *Attendees will be challenged with video cases and will need to decide if the case is an orthopedic or neurological problem. We will explore cruciate rupture, hip dysplasia, luxating patellae, malignant nerve root tumors, disc disease, discospondylitis, and a few "tricks". Are you up to the challenge?*

Osteochondritis Dissecans (OCD)

Osteochondritis Dissecans an inflammatory condition that occurs when the diseased cartilage separates from the underlying bone. Normal joint stresses, focal trauma (excessive weight), or some other unknown mechanism causes cracks and fissures to develop in the zone of chondrocytes of the epiphyseal cartilage layer. Ultimate extension of these fissures into the joint results in the release of cartilaginous breakdown products into the joint fluid with a resultant synovitis, inflammation of subchondral bone and cartilage (osteochondritis), and creation of a flap of cartilage that dissects away from its underlying subchondral attachments (dissecans). The cartilaginous flap may initiate superficial erosions of the cartilage of the opposing joint surface contributing further to the inflammatory arthritis. The dissection of synovial fluid into subchondral bone results in a focal necrosis of the bone and bone marrow under the flap. If the flap is extensive and the dog is of sufficient weight a large area of avascular necrosis of the bone and bone marrow results, followed by entrapment of synovial fluid and subsequent cyst formation. Generally large breed dogs between 6 and 9 months of age are most commonly affected, and it may occur more often in male dogs. OCD most commonly affects the shoulder joint, the elbow may also be seen at a lesser frequency and also on the lateral aspect of the femoral condyle and medial trochlear ridge of the hock.

Studies have shown that limiting dietary intake of energy and calcium reduces the incidence of this condition,

At first treatment may entail rest, short leash walks, anti-inflammatories and passive range of motion exercises to maintain the joint flexibility if however the flap persists or detaches to become a joint mouse surgery is indicated. Surgery involves arthrotomy with flap excision and curettage.

Prognosis for OCD of the hock is worse than the other sites with the role of surgery at that site less clear with permanent lameness the usual result. Surgeries in the other locations are usually more rewarding.

Hip Dysplasia is the abnormal development of the CF joint that may result in varying degrees of subluxation leading to progressive degenerative joint disease. Seen commonly in large breed dogs there are those breeds that are over represented. Radiographs may diagnose hip dysplasia in 10 to 48% of dogs with some breeds (Golden Retrievers, Rottweilers) showing 50

to 70% with hip dysplasia. The cause of hip dysplasia may be the result of many factors, genetics, nutrition, growth rate and exercise access. The factors that influence the biomechanics of the coxofemoral joint and a causative for Hip Dysplasia are; the degree of joint laxity, amount of joint fluid, abnormal pelvic muscle development, abnormal conformation of the acetabulum and femoral head and neck and the dog's rate of growth. The clinical presentation will vary with patient age with young animals less than 12 months of age having pain, difficulty rising, a Bunny Hopping gait or Marilyn Monroe walk and joint laxity with minimal radiographic degeneration. Mature animals may present with the above clinical signs and also with degenerative joint disease with bony remodeling.

Examination of either may show lameness, painful palpation on extension or abduction of the hip and decreased range of motion. There may be varying degrees of laxity as demonstrated by the Ortolani sign (best if done under sedation).In longer standing cases with more degenerative joint disease there may be crepitus and a greater decreased range of motion.

There are two primary Radiographic Registries; OFA (Orthopedic Foundation for Animals) and PennHip®. PennHip allows an objective measurement of laxity in the CF joint which is expressed as distraction index (DI). PennHip has a greater predictive value than OFA and is valid in animals > 16 weeks of age.

Surgical Treatment in the young patient may entail a femoral head and neck ostectomy (FHO), this is reserved for severe cases or in those where cost is a consideration. There is no specific window of opportunity since the FHO may be done anytime. The goal is to eliminate bone to bone contact. If done successfully there is a false joint or pseudoarthrosis established in the gluteal muscle. Another option in young animals is the Triple pelvic osteotomy (TPO). In this surgery the acetabulum is rotated dorsally and laterally while performing ilial, pubic, and ischial osteotomies. The ilial plate is angled: 20o, 30o, or 40o allowing the head of the femur to seat deeper and more securely in the acetabulum. For this to be successful there must be minimal pre-existing osteoarthritis. Age for a successful TPO is 6 to 11 months. TPO will slow the development of osteoarthritis.

Total Hip Replacement is thought to be the gold standard in those patients with moderate to severe osteoarthritis secondary to hip dysplasia. Much of the pain is due to joint capsule distension and inflammation and the effect of bone on bone contact within the joint.

Success rates are close to 95% with a result of pain free function.

Cranial Cruciate Ligament Rupture

Cranial Cruciate Ligament Rupture is a complete or partial rupture of the cranial cruciate ligament. This is usually secondary to a degenerative process, occasionally traumatic and rarely resulting in avulsion fractures.

The function of the cranial cruciate ligament is that it prevents cranial drawer, (cranial tibial displacement relative to the femur). It also limits internal tibial rotation and limits stifle hyperextension.

Etiology of this degenerative process is unknown with the main theories being autoimmune, genetic or conformational. Degenerative changes may precede complete rupture and this degeneration is accelerated with instability. Because of the possible genetic predisposition when one cruciate rupture is diagnosed often the contralateral limb is soon to follow.

On palpation of the limb there may be medial buttressing of the stifle but diagnosis is generally straight forward by checking for the cranial drawer sign. The cranial drawer sign demonstrates cranial tibial displacement and is best done by standing or kneeling behind the patient and placing the thumb and index finger on the femur and a thumb and index finger on the tibia, then forcing the tibia cranially relative to the femur. Another test is the tibial compression test. While holding the limb in partial flexion one hand is placed on the cranial aspect of the stifle. With the other hand flexing the hock and compressing the tibia in its lengthwise dimension the head of the tibia will be felt to move cranially if there is a cruciate rupture. The result is subtle and may not be as dramatic as the drawer.

Treatment Conservative care may help some especially if the tear is not complete; weight loss, exercise limitation and anti-inflammatories are all indicated until the stifle may self-imbricate by hypertrophy of surrounding tissues.

There are many surgical techniques at the surgeon's disposal when it comes to repair of the cruciate patient. There are intracapsular repairs, extracapsular repairs and corrective osteotomies. Results are comparable regardless of technique with most resulting in an 85 to 90% success rate. In the intracapsular techniques an autogenous, allograft, or synthetic ligament replacement is utilized to attempt to mimic the normal cruciate course through the joint. This technique may be augmented with an extracapsular technique. The extracapsular may be only a non-absorbable fabellar to tibial suture. The most common corrective osteotomy is the tibial plateau leveling osteotomy (TPLO). A circular cut of the bone is made caudal to the tibial crest. After rotating the proximal tibia and using internal fixation the result is a reduced caudal angulation of the tibial plateau.

Malignant Nerve Sheath Tumors arise from the Schwann cell (Schwannoma) or the connective tissue surrounding the nerve (neurofibroma). Locations are usually the caudal cervical area (brachial plexus) and the sciatic nerve. On physical there may be marked muscle atrophy in the distribution of the nerve and typically a monoparesis of a Lower Motor Neuron (LMN) character. A LMN symptom is a "flaccid" paralysis versus the Upper Motor Neuron (UMN) of spastic paralysis. If the nerve root tumor extends into the spinal canal there may be symptoms demonstrable in the caudal limb on the ipsilateral side and radiographically there may be enlargement of the intervertebral foramen otherwise there are no radiographic changes. Treatment is surgical resection with the caveat that most return with time. Chemotherapy is not beneficial with fractionated radiation therapy being of some benefit.

Fibrotic gracilis or semitendinosis is chronic progressive scarring and contracture of these two muscles. Most common is the semitendinosis. Typical symptom is a shortening of the stride in the rear limb which produces a goose stepping gait. The cause is unknown with theories of repetitive trauma, immune mediated or secondary to a neuropathy. There is a breed predisposition for German Shepherds and Belgian shepherds. Diagnosis is done with EMG and digital palpation of the firm fibrotic band of muscle on the caudal aspect of the gracilis/semitendinosis. Surgical removal of the effected muscle has been tried however surgery usually results in re-contracture/fibrosis of the muscle.

Infraspinatus contracture usually occurs in hunting and working dogs. The exact cause unknown however it appears to be more of a primary myopathy with histology compatible with degeneration and fibrosis as would be seen with a severe strain. Trauma is not needed to instigate the injury. Acute pain in the shoulder with resultant lameness develops and persists over the next 2 to 4 weeks. Diagnosis is by palpation and observance of gait. The walk has

been described as a dog scrubbing the floor as he walks. There is restricted range of motion to the Scapulo-humeral joint with the elbow adducted

Treatment of infraspinatus contracture is a surgical tendonotomy of the infraspinatus with immediate return to normal.

Scotty Cramp is a recessively inherited neurotransmitter deficiency of serotonin. The lack of Serotonin results in a hypertonic myopathy. The patient is normal at rest with signs associated with exercise, excitement or stress. The disease is non-progressive. There is some improvement with Acepromazine (0.1-0.75mg/kg bid) or Diazepam (0.5mg/kg tid) and recently the use of Serotonin re-uptake inhibitors (SSRIs) has been used with success.

Dancing Doberman Disease is a breed specific gastrocnemius myopathy that occurs in Doberman Pinchers from 1 to 10 years of age. The patient will have a normal gait with normal strength but while standing intermittently raise and lower one rear limb. As Dancing Doberman disease progresses the patient will start to exhibit signs in both rear limbs. EMG is beneficial in diagnosis as is muscle biopsy. There is no known treatment and some dogs have been known to have spontaneous remissions or merely continue with symptoms still being acceptable pets.

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# CLINICAL APPROACH TO ANEMIA

Anemia is not a diagnosis in itself but is a common clinical sign and laboratory test abnormality in companion animals. Thus, anemia may indicate a specific erythrocyte problem or can be associated with other organ disorders. Because anemia and other hematological abnormalities occur so frequently, a complete blood cell count is generally requested in the diagnostic assessment of any seriously ill patient. Anemia is defined as a decrease in the red blood cell (RBC) mass as expressed by a reduction in number of circulating RBCs, hematocrit, and hemoglobin. Clinical signs of anemia result from decreased oxygen-carrying capacity, reduced blood volume, underlying disease, and the adjustments made to increase the efficiency of the erythron. The severity of clinical signs depends on the rapidity of onset, the degree and cause of anemia, and the extent of physical activity.

Anemias are differentiated into regenerative and non-regenerative anemias depending on the response of the bone marrow to anemia. Regenerative anemias are associated with hemolysis and blood loss. Non-regenerative anemias refer to reduced or ineffective erythropoiesis for the degree of anemia. All forms of anemia start of as being non-regenerative for the first few days until the bone marrow had time to react with the release of reticulocytes, but some remain non-regenerative. Hemolytic and blood loss anemias are often only mildly regenerative in cats. Anemias due to reduced or ineffective erythropoiesis develop generally slowly because of the long half-life of erythrocytes. Patients can adapt to the lower hematocrit, and therefore the clinical signs are often less severe and only noticed with severe anemia. Pallor is the typical clinical sign of non-regenerative anemias due to reduced or ineffective erythropoiesis often without any other helpful clinical features.

Erythropoietic response and diagnostic approach

The number of erythrocytes present in the circulation is a dynamic equilibrium between the production and delivery of erythrocytes into the blood circulation and their destruction or loss from circulation. The erythroid bone marrow response is mostly regulated by erythropoietin, a lineage-specific hematopoietic growth factor. Erythropoietin synthesis in the renal cortex is induced by anemia, although the actual sensor measures oxygen tension and recognizes only renal hypoxia. This hormone acts predominantly on erythroid precursor cells of the bone marrow known as burst-forming units-erythroid (BFU-E) and particularly colony-forming units-erythroid (CFU-E). At maximal stimulation, the bone marrow is capable of producing erythrocytes at 10- to 50-fold the normal rate. Erythropoietin also contributes to the maturation from the early committed erythroid precursors to fully hemoglobinized erythrocytes, which takes normally approximately 1 week. There is an inverse relationship between serum erythropoietin and hematocrit and only in anemia of chronic renal failure is there an absolute erythropoietin deficiency.

Reticulocyte counts

The most useful marker of accelerated erythropoiesis continues to be an increased number of reticulocytes in circulation. Because they contain residual RNA, which can be precipitated into a reticulum network and stained by certain supravital dyes such as new methylene blue or brilliant cresyl blue, reticulocytes can be readily enumerated. The latter stain is particularly suitable as it is relatively free of precipitates. On a vital stained blood smear, the number of reticulocytes is counted per 500 to 1000 erythrocytes and the reticulocyte result is reported as a percentage of cells examined (number per 100 cells). Few of the new in-house hematology instruments can also enumerate reticulocytes. Because canine reticulocytes contain strong aggregates, they are relatively easy to count. In contrast, cats produce two types of reticulocytes, namely aggregate and punctate reticulocytes. The aggregate reticulocytes correspond to the reticulocytes seen in dogs and indicate an active regenerative response.

The upper limit of a normal reticulocyte count is often stated as 1%; however, healthy small animals generally have <0.6 per cent reticulocytes per 100 erythrocytes. This number is not only increased by enhanced hematopoiesis, but also affected by anemia, as it depends on the number of circulating erythrocytes, and the duration of reticulocyte maturation in circulation. Therefore, various adjustments to the reticulocyte count are being used. If the erythrocyte count is available, the absolute reticulocyte count can be calculated and is less than 60,000/µL in a healthy animal:

The absolute reticulocyte count has now been adopted as the preferred expression of erythroid regeneration. Several automated hematology analyzers have incorporated staining to detect reticulocytes and provide the absolute reticulocyte count; it should be noted that some automated counts may be falsely increased in the presence of Heinz's bodies and Howell-Jolly bodies as well as punctate reticulocytes (cats). However, if the absolute erythrocyte count is not known, the correction for anemia can also be made on the basis of the patient's hematocrit compared with the average normal packed cell volume (PCV) value (dogs 45%; cats 37%) and is normally less than 0.4%.

A low absolute reticulocyte count or corrected reticulocyte percentage provides the best evidence for a lack of a bone marrow response. Although not as accurate, other hematologic manifestations may be used to indicate increased erythropoiesis, when a reticulocyte count is not available. On a regularly (Wright; Diff-Quik) stained blood smear, polychromatophilic cells represent erythrocytes recently released from the bone marrow and are equal to reticulocytes. As their blue-grey tint color is due to the presence of RNA, their numbers correlate well with the

reticulocyte count. When more than one polychromatophilic cell is recognized per microscopic oil immersion field, accelerated erythropoiesis is suggested. Polychromatophilic erythrocytes are often macrocytic, which indicates that these cells are released prematurely from the marrow, thereby contributing greatly to the high mean cell volume (MCV) and red cell distribution width (RDW) as well as anisocytosis of regenerative anemias and low MCHC (still need to be hemoglobinized). It should be noted that a macrocytic anemia is not always regenerative, but may indicate a maturation problem such as myelodysplasia, feline leukemia virus (FeLV) infection or folate deficiency in cats.

Normoblasts or nucleated RBCs

Nucleated erythrocytes also known as normoblasts or metarubrocytes with variably shrunken nuclei are rarely found in blood of healthy animals (less than 1 per 100 white blood cells). Depending on the hematology instrument they may be not counted or under the white blood cells (WIC vs WOC). Large numbers may accompany a marked regenerative response in anemic patients. However, nucleated RBCs may also be seen in patients without reticulocytosis and regenerative response because of a breakdown of the barrier between marrow and vasculature. In fact, the highest numbers of normoblasts are observed in acute lead poisoning in the absence of anemia. Mild to moderate normoblastosis with nonregenerative anemia may be seen with myeloproliferative disorders, dyshematopoiesis, extramedullary hematopoiesis, hemangiosarcoma, and sepsis. Thus, normoblastosis should not be equated with a regenerative marrow response without confirmation by a reticulocyte count.

Bone marrow examination

If the anemia is characterized as non-regenerative on the basis of an absence of reticulocytosis, bone marrow examination is indicated. In non-regenerative anemia, the bone marrow cellularity can be decreased, normal or even increased. However, the ratio of myeloid to erythroid elements in the bone marrow is generally below one. Although the erythropoietin response is lineage specific, independent stimulation of thrombopoiesis or granulopoiesis or lack thereof may also be present. Bone marrow examination may provide helpful information about an underlying cause (cancer, infection) or marrow iron deposition in patients with non-regenerative anemia that would otherwise remain undetected. Bone marrow examination from humerus and even ribs has become more standard.

Degree of anemia

The degree of the anemia can be simply defined by the determination of a packed cell volume (PCV) by microcentrifugation or hematocrit as part of a complete blood cell count (CBC). The PCV or microhematocrit is directly measured, whereas the hematocrit is calculated from the mean cell volume times the erythrocyte number. Typically, these two values should be equal,

although in vitro crenation, swelling, or lysis of erythrocytes and inadequate sedimentation by the microcentrifuge could cause erroneous results. An EDTA-anticoagulated sample is ideal for most hematologic tests. It is important to assure prompt mixing of blood with anticoagulant in the correct proportion; therefore, for small sample sizes, pediatric or microtubes should be used.

Blood hemoglobin values are generally used in human medicine rather than a PCV or hematocrit to define the degree of the anemia. The point-of-care HemoCue and other instruments have been validated and can be applied in any species to assess blood hemoglobin concentrations, whereas hemoglobin measurements by some of the laboratory CBC instruments may be affected by lipemia and leukocytosis. There is a good correlation between PCV and hemoglobin concentration in that the PCV is roughly three times the hemoglobin. The HemoCue has proven invaluable when using Oxyglobin as a transient oxygen carrier in the treatment of anemia because it allows for accurate total blood and plasma hemoglobin determinations in practice. The hemoglobin in erythrocytes (times 3 will give the PCV) is obtained by subtracting the plasma hemoglobin from the blood hemoglobin. Mild degrees of hemoglobinemia may also be caused by intravascular hemolysis or could be blood collection or storage artifacts; a second blood sample and urinalysis including examination of the urine sediment will discover the difference.

Testing for anemias

One of the most important but simple blood tests for an anemic patient is the microscopic evaluation of a fresh EDTA blood sample. For instance, the presence of polychromasia and anisocytosis on a blood smear suggests a regenerative anemia. The finding of various morphologic erythrocyte abnormalities may determine a cause of the anemia, such as hypochromasia with iron deficiency anemia or agglutination, and spherocytosis with immune-mediated hemolytic anemia, schistocytes with disseminated intravascular coagulation, Heinz bodies with oxidative insults, and erythrocyte parasites seen with infectious anemias. Note that parasitemias are often transient and quickly disappear after treatment.

Current standards in small animal medicine also demand a CBC by a hematology instrument in order to better characterize the anemia and other associated hematologic abnormalities. Each of these hematology tools has to be validated for small animals, as instruments in human laboratories are not set to accurately assess canine and feline blood cells. The small size of feline red blood cells and large size of feline platelets present a particular challenge. Impedance instruments were the first ones to provide more details regarding red cell indices and white blood cell (WBC) differentials. However, these instruments continue to have problems in counting and differentiating accurately blood cells; for instance, nucleated red blood cells may not be separately assessed. Furthermore, some instruments may perform well with blood from healthy animals but are inaccurate when abnormalities are encountered. In the past, validated instruments for CBCs were only available in large reference laboratories and teaching hospitals because of the expense and expertise required to run the instrument.

Several smaller hematology instruments have become available for use in practice, which can now provide immediate and in some cases similarly accurate results as the large laboratory instruments. The QBC was the first of its kind attempting to further differentiate the buffy coat to provide some estimation of a WBC differential and reticulocytes but was, unfortunately, inaccurate. The most recent advances in laser technology utilized in novel in-practice hematology instruments appear particularly promising in providing small animal clinicians not only accurate red cell parameters, including reticulocytes, but also better WBC differentials and platelet counts and cell volumes. Although these instruments can be used in practice, they will not replace the clinical pathologist who can provide a careful and better review of all hematologic data ill patients, including the cytologic evaluation of blood smears and bone marrow aspirates.

Bone Marrow Evaluation

In the case of nonregenerative anemias, bone marrow evaluation often becomes crucial. Although overall cellularity and the presence of megakaryocytes can be readily determined, the various cell lineages and degree of maturation in the bone marrow is left to the experienced eye. Similarly, special stains for the presence of iron stores (healthy cats generally do not have stainable iron in their marrow) and immunohistochemistry for differentiation of the various hematopoietic precursor cells, as well as the recent application of flow cytometry of blood or marrow cells, is only done in reference clinical pathology laboratories.

Iron, Vitamins, Erythropietin

In addition to this general assessment of anemia, several other tests have become available for the clinical characterization of anemias. Instead of simply determining serum iron, there are now opportunities to define the iron saturation and serum ferritin. Serum iron and ferritin concentrations are expected to be low in iron deficiency; ferritin is an acute-phase protein and therefore its concentrations vary significantly in small animal patients and are increased with inflammation. Furthermore, as cobalamin (vitamin B12) and folate deficiencies contribute to nutritional anemias, serum cobalamin and folate concentrations may need to be measured in cases of nonregenerative megaloblastic anemias. Acquired and inherited forms of cobalamin malabsorption have been recognized. Serum erythropoietin assays have been validated to discover relative and absolute erythropoietin deficiencies in non- or poorly regenerative anemias, and absolute and relative erythropoietin deficiencies have been documented with chronic renal failure and cancer, respectively, leading to anemia. It should be noted that antierythropoietin assays for pure red cell aplasias following recombinant human erythropoietin therapy are not generally available.

Blood Chemistry and Toxicology

Along with the CBC, a serum chemistry screen is often requested to suggest renal and hepatic failures or endocrinopathies, but it may also reveal a secondary hypophosphatemia responsible for intravascular hemolysis. Toxicology laboratories now offer identification of a large variety of substances including heavy metals such as zinc, lead, and copper, causing various forms of anemias and anticoagulant rodenticides, as well as drug levels in blood. Many drugs have been implicated to cause various forms of anemia and other cytopenias by immune and bone marrow suppressive processes.

Hemostatic Tests

Standard hemostatic evaluation includes determination of platelet count and morphology, plasma von Willebrand factor, and coagulation parameters. Simple in-practice tests to assess hemostasis include platelet estimates on blood smears, a buccal mucosal bleeding time, and an activated clotting time. Microscopically, >15 platelets per high-power oil emersion field are normally found, and macroplatelets may suggest regeneration or myelodysplasia. In case of reduced platelet numbers, aggregates may be detected on the margins of the blood smear, as particularly feline platelets are readily activated, which leads to pseudothrombocytopenia. The buccal mucosal bleeding time (normal <3.5 minutes) is performed only if platelet numbers are adequate and drugs known to interfere with platelet functions have been excluded. The buccal mucosal bleeding time assesses exclusively primary hemostasis and is prolonged with hereditary and acquired thrombopathias and von Willebrand's disease. The tube activated coagulation time is a simple and inexpensive way to evaluate overall coagulation (secondary hemostasis) as it is expected to be prolonged with any coagulopathy, except isolated factor VII deficiency (seen in beagles).

The classic coagulation tests, partial thromboplastin time and prothrombin time (PT), were only offered in clinical pathology laboratories on fresh citrated plasma, which had to be immediately separated from red cells and shipped frozen or on ice for analysis. However, partial thromboplastin time and PT can now also be done with a simple point-of-care instrument on fresh citrated whole blood in practice allowing for immediate identification of any coagulopathy. The protein induced by vitamin K antagonism or absence (PIVKA-) test is a PT offering no advantage over the regularly performed PT and a prolongation is not specific for rodenticide poisoning. The PIVKA test has long been replaced in human medicine by the standardized PT. Special coagulation tests are available to determine a specific factor deficiency at Cornell's Comparative Hemostasis Laboratory and PCR-based tests are also available for von Willebrand's disease in a few breeds including Doberman pinschers, Scotties, Shelties, Kookier, and German short and wirehair pointers through commercial laboratories. However, von Willebrand's disease, a primary hemostatic disorder, is best diagnosed with a plasma von Willebrand factor analysis (ELISA test utilizing citrated or EDTA anticoagulated blood).

Immunological Assays

A diagnosis of immune-mediated hemolytic anemia requires the identification of persistent autoagglutination after saline washing (3 times with physiological saline), marked spherocytosis, and a positive direct Coombs' test (antiglobulin test), whereas agglutination on the slide and response to immunosuppressive therapy are insufficient evidence for an immune process. True autoagglutination that does not break up after saline washing precludes the performance of both Coombs' test and blood typing as the endpoints of these tests is agglutination. Coombs' tests have to be done with species-specific reagents and proper techniques in special laboratories in order to minimize false-positive and false-negative results. Dogs with active immune-mediated hemolytic anemia (IMHA) should have a positive Coombs' test result, even when treated for a couple of days with steroids. Whereas dogs often have a primary/idiopathic form of IMHA, cats rarely have IMHA and the hemolytic anemia is generally due to an underlying disease or trigger. Thus, even when documenting an immune destruction of erythrocytes, it is important to rule out other underlying disease processes as cause. Similarly, platelet-associated antibody tests are offered on a limited basis for the confirmation of immune-mediated thrombocytopenia, due to the small number of platelets flow cytometric methods appear preferable.

Furthermore, as anemic patients may be in need of a transfusion, each patient should also be blood typed, and if previously transfused, cross-matched to assure the administration of safe and effective transfusions. There are simple in-practice kits available to type dogs for DEA 1.1 and cats for type A, type B, and type AB. There are also protocols available for performing a cross-match in practice to assure compatible blood transfusions.

Infectious Disease Screening

Although microscopic and serologic screening tests for infectious and parasitic diseases have been available for many years, the diagnosis of many blood-borne diseases remains challenging. For instance, there is no serologic test for hemobartonellosis and serologic tests for babesiosis are cross-reacting between species of Babesia. However, the recent introduction of polymerase chain reaction (PCR)-based methods allows a more sensitive and precise diagnosis of different forms of infectious diseases such as babesiosis, including Babesia canis subtypes and Babesia gibsoni. PCR tests can also distinguish between feline hemobartonellosis caused by Mycoplasma haemofelis or less likely M. haemominutum. Serology and PCR tests are also available for aiding in the diagnosis of ehrlichiosis and leishmaniasis. In addition, infections with Leptospira spp have reemerged as an important cause of acute systemic illness and hemolysis. Simple SNAP tests are available to determine exposure to Ehrlichia canis, Bartonella burgdorferi, Anaplasma sp. and Dirofilaria immitis.

Genetic Disease Testing

Finally, several hereditary erythrocyte disorders have been discovered that may mimic acquired hemolytic anemias such as IMHA, and biochemical and molecular genetic tests for some of these disorders have become available (www.vet.upenn.edu/penngen). In particular, PCR tests are offered for phosphofructokinase deficiency in English springer and few other breeds (albeit this can also occur in mixed breed dogs). PFK deficiency can cause severe intermittent anemia and myopathy. PCR testing is also available for pyruvate kinase (PK) deficiency in basenjis, beagles, West Highland white and cairn terriers, dachshunds, and Abyssinian and Somali cats. Interestingly, PK deficiency in any canine breed is associated with severe chronic anemia and osteosclerosis, whereas this enzyme deficiency in cats results in an intermittent anemia without osteosclerosis. Similarly, PCR tests are available for canine leukocyte adhesion deficiency in Irish setters and red and white setters, a disorder associated with a massive leukocytosis and anemia. With respect to hereditary hemostatic defects, several PCR-based tests (besides the ones for mutations in the von Willebrand gene) have emerged, including coagulopathies FVII, VIII, IX XI and XII, macroplateletes, and Glanzman thrombasthenia.

Non-regenerative anemias / ineffective or reduced erythropoiesis

These non- or poorly regenerative anemias are usually normocytic-normochromic. Exceptions include microcytic-hypochromic anemia due to iron deficiency, anemia associated with hepatic shunt as well as very rarely anemia of chronic disease and macrocytic anemias with FeLV infection and folate deficiency in cats and some forms of myelodysplastic anemias. Clinically the following classifications are being made which may also reflect a continuum.

- Refractory anemias are non-regenerative, usually mild to moderate, with normal to increased leukocyte and platelet counts, suggesting a failure of erythropoiesis due to an extra-marrow disorder such as anemia of chronic/inflammatory disease, chronic renal disease, cancer and endocrine disorders.

- Aplastic anemias are characterized by pancytopenia (anemia, leukopenia and thrombocytopenia) and aplastic or hypoplastic bone marrow suggesting an intra-marrow disorder caused by irradiation, chemicals, infection or lympho- and myeloproliferative disorders.

- Myelodysplastic syndromes are a group of related bone marrow disorders characterized by cytopenias and normal or hypercellular bone marrow with a relative excess of blast cells that may rarely progress to overt leukemia.

- Nutritional deficiency anemias
- Iron deficiency (usually still regenerative)
- chronic blood loss
- chronic malabsorption
- Vitamin deficiencies
- Cobalamin (vitamin B12) deficiency (receptor defect)

- Dietary folate deficiency
- Gastrointestinal malabsorption with folate or/and cobalamin deficiency

- Chemical-induced aplastic anemias
- Idiosyncratic drug and other reactions
- Chemotherapeutic and immunosuppressive agents
- Irradiation
- Exogenous and endogenous estrogens (only in dogs)

- Anemia associated with infection
- Ehrlichiosis
- FeLV and FIV – infection
- Parvovirosis (more leukopenia)
- Other infectious diseases

- Anemia of chronic disease
- Anemia of inflammatory disease
- Associated with many organ disorders

- Anemia associated with bone marrow infiltration
- Osteopetrosis (congenital, hereditary pyruvate kinase deficiency only in dogs)
- Myelofibrosis/osteosclerosis (secondary)
- Lympho-/myeloproliferative diseases (leukemias, multiple myeloma)
- Rarely metastatic neoplasia

- Anemias associated with organ disorders
- Renal disease (erythropoietin deficiency)
- Liver disease
- Endocrine diseases (hypothyroidism, hypoadrenocorticism)

Other laboratory tests

Routine laboratory tests are required in the diagnostic approach of non-regenerative anemia patient, including a chemistry screen and urinalysis, in order to define other organ disorders. Infectious disease screens for tick and flea transmitted and other infections depending on the geographic area may be very important. Other specific tests may help in further defining the cause of the anemia. Serum iron concentrations are low in iron deficiency anemias due to blood loss (which generally remain somewhat regenerative), can also be slightly low with renal insufficiency (gastrointestinal ulcers), but are normal along with adequate bone marrow iron stores in many other diseases with non-regenerative anemia. Serum iron levels may be low in anemia of chronic disease, but bone marrow iron stores should be adequate. Bone marrow from cats generally contains low iron accumulation. Other nutritional elements such as vitamin B12 and folate may need to be determined as they may result in cytopenias.

Therapeutic principals for non-regenerative anemias

Animals with non-regenerative anemia due to reduced or ineffective erythropoiesis have a guarded prognosis, but can benefit from specific and symptomatic therapy. Ideally, the cause of the anemia is corrected by treating the underlying disease or removing the triggering agent, such as an infectious organism or drug. Blood transfusion can provide immediate support for the critically ill patient. Except for animals with true iron or erythropoietin deficiency, no effective bone marrow stimulants are currently clinically available Except human recombinant erythropoietin).

As non-regenerative anemias are often relatively mild and develop slowly, animals usually tolerate the anemia well. However, it may progress to severe anemia, because of a complete lack of a bone marrow response or because another type of anemia is complicating the picture (blood loss and hemolysis). Severely anemic animals will benefit from blood type (and crossmatch) compatible transfusions, ideally in the form of stored packed red blood cells or fresh whole blood. Transfused erythrocytes will generally exhibit a normal survival, but because of the lack of regeneration, these animals may require repeated transfusions. During subsequent transfusions the red cell survival may be shortened because of the development of alloantibodies, thus it is imperative to assess compatibility by typing and crossmatching. The transfusion rate should be slow (< 10 ml/kg/hour), because these patients are generally volume expanded and are at risk of developing pulmonary edema and heart failure.

With the exception of anemic animals with chronic renal failure, the serum erythropoietin concentration is exponentially increased; in fact the highest serum erythropoietin concentrations are observed in animals with red cell aplasia and therefore additional erythropoietin administration would not be helpful. Recombinant human erythropoietin

(Darbepoietin) weekly has been used in anemic animals with chronic renal failure. The dose is reduced and the interval extended as soon as the hematocrit reaches 25 to 30%. In addition iron is being supplemented orally and any hypertension is corrected. Erythropoietin supplementation improves the overall well-being of these patients, but does not correct the renal failure. Furthermore, animals may develop neutralizing antibodies against human erythropoietin. Recombinant human erythropoietin has also been used with some success in patients with anemia of chronic disease due to cancer in the hope that additional erythropoietin could override the inhibitory effects of the cancer on the bone marrow.

Other hematopoietic growth factors have also been tried in combination with erythropoietin for various forms of anemia, but currently there is insufficient data on their efficacy and safety. For decades androgens have been proposed for the stimulation of the bone marrow, but there is no good experimental or clinical evidence of its efficacy. Because idiopathic aplastic anemias are assumed to be due to immune mediated processes against precursor cells, a trial with immunosuppressive agents is often initiated, including prednisone, cyclosporine, and intravenous human immunoglobulin, but none have been documented to be effective beyond anecdotal reports.

In case of iron deficiencies long-term supplementation of iron in the form of iron sulfate/gluconate or intramuscular iron dextran can be highly effective. It is important that ferrous rather than ferric iron is administered and that parenteral routes are only used in case of malabsorption. Initially a red cell transfusion will also add quickly bioavailable iron for erythropoiesis. However, most other anemic patients do not experience iron deficiency, and thus the general use of iron supplementation is not recommended and can even be harmful to some animals. Furthermore, animals with vitamin deficiencies may benefit from parenteral supplementation of folate or cobalamin; this has proven highly effective in dogs with hereditary cobalamin malabsorption.

In conclusion, the diagnostic approach to anemias in small animals has been assisted greatly by new tools and tests. Their appropriate use will permit a more precise and rapid diagnosis and thereby effective therapy.

# IMMUNE-MEDIATED HEMOLYTIC ANEMIAS

Immune-mediated hemolytic anemia (IMHA) in dogs has been recognized to cause major morbidity and mortality in dogs for half a century. However, there are no generally accepted guidelines and standard tests to diagnose IMHA in dogs. The assessment of published studies on IMHA disease course, complications, prognosis and therapies are hampered by the varied diagnostic criteria used and dearth of diagnostic studies. Supported by a comparative study of different diagnostic tests for IMHA in dogs by the author's laboratory (Caviezel et al., 2014), this is personal perspective on the diagnostic approach applied.

## Introduction

Hemolytic anemias are characterized by an accelerated erythrocyte destruction which occurs commonly extravascularly and rarely also intravascularly. While IMHA is commonly suspected, when presented with an anemic dog, there are many other causes of anemia and hemolysis. It is critical to search for evidence of hemolysis such as hyperbilirubinuria/-emia, icterus, hemoglobinuria/emia, and regenerative erythroid response. In case of a documented hemolytic anemia, infections (e.g. babesiosis, caval syndrome, malignant histiocytosis and bacterial sepsis), cancer (e.g. malignant histiocytosis, hemangiosarcoma), toxins (onions, zinc) and inherited erythrocyte defects (e.g. PK and PFK deficiency) should be considered. For those diseases, specific diagnostics are available to guide the most specific therapeutic approach.

Immune-mediated hemolytic anemia is one of the most common and serious hemolytic anemias in dogs, but occurs rarely in cats and other animal species. In IMHA, immune responses, including anti-erythrocytic antibodies, complement, and macrophages, target directly or indirectly erythrocytes and a hemolytic anemia ensues. There are likely many triggers for IMHA, such as infections, drugs and other agents, and cancer leading to secondary IMHA, but in many dogs no cause is identified (so-called idiopathic, autoimmune or primary IMHA). There are also genetic predisposition to IMHA (e.g. Cocker spaniels). Furthermore, alloimmune hemolytic anemias, such as acute hemolytic transfusion reactions in previously transfused dogs (e.g. DEA 1, DEA 4, Dal) and, experimentally, neonatal isoerythrolysis (only litters from previously transfused bitches), are caused by specific anti-erythrocytic alloantibodies (e.g. anti-DEA 1, anti-DEA 4, anti-Dal). In contrast to other species, dogs with IMHA also develop often overwhelming inflammatory responses resulting in thrombosis and necrosis of various organs. And while the anemia can be corrected with transfusions, the inflammatory, necrotic, and thrombotic tendencies in dogs are causing severe morbidity and mortality, despite aggressive immunosuppression and antithrombotic interventions.

## Immune Destruction of Erythrocytes

Regardless of the underlying cause, IMHA results from a breakdown in immune self-tolerance or from a deficit in the control mechanisms that regulate B and T lymphocyte activity as well as macrophage reactivity. Immune destruction of erythrocytes is initiated by the binding of IgG or IgM antibodies to the surface of erythrocytes; the actual red cell antigens for IMHA in dogs even in the case of an alloimmune reaction have not been well defined in dogs. Under most clinical circumstances, immune destruction is an extravascular process that depends on recognition of erythrocytes opsonized with IgG, IgM, and/or complement by specific receptors on reticuloendothelial cells. Macrophages with engulfed erythrocytes may be noted on cytological examination of blood and tissue aspirates as erythrophagocytosis, but this is not proof of an immune-mediated process (e.g. also seen with malignant histiocytosis). Antibody-coated erythrocytes may also be lysed by complement fixation and the membrane attack complex, which can clinically be noted as intravascular hemolysis. It should be noted that the normal process of erythrocyte senescence involves antibodies, such as anti-band 3.

Clinical Evidence of Hemolysis

A diagnosis of IMHA must demonstrate accelerated peripheral destruction of erythrocytes compared to the normal senescence process with extravascular destruction of canine erythrocytes after 100-120 days. Evidence of a hemolytic anemia is suggested clinically by anemia, icterus, and pigmenturia. Typical laboratory diagnostics for hemolysis include hyperbilirubinuria/-emia and occasionally hemoglobinuria/-emia which refers to an intravascular process. Artefactual lysis of erythrocytes in blood and urine need to be carefully excluded by appropriate and repeat testing. Documenting low serum haptoglobin concentrations may suggest occult intravascular hemolysis. Serum iron parameters are high in animals with hemolytic anemias (no need for iron supplementation) and have plenty of iron stores and if the hemolysis is chronic patients may develop hemosiderosis. There may be specific morphological changes of erythrocytes on a blood smear such as spherocytes seen typically with IHMA. Other erythrocytic abnormalities, such as Heinz bodies, eccentrocytes, schistocytes, and possibly ghost cells, and erythrophagocytosis are suggesting hemolysis, but not IMHA. Macrophages with engulfed erythrocytes may be noted on cytological examination of blood and tissue aspirates as erythrophagocytosis, but this is not proof of an immune-mediated process (e.g. also seen with malignant histiocytosis).

Dogs with IMHA are typically anemia, albeit the hemolysis can be well compensated. Furthermore, depending on the breed (e.g. a greyhound with a PCV of 45% is anemic) and the specific historical (days to years before) hematocrit of a dog may permit early detection of anemia before reaching a seriously anemic range. Hemolytic anemias are typically very regenerative, however, the erythroid response may be blunted by the immune, inflammatory, and necrotic processes in the bone marrow associated with IMHA in dogs or the underlying disease process, thereby leading to poorly to non-regenerative anemias. Furthermore, during the first couple of days of acute hemolysis, the anemia remains non-regenerative until the bone marrow can respond. Anemias with erythroid hypoplasia, when thought to be due to immune targeting of erythroid precursors, are not hemolytic anemias and thus should not be called IMHA. While in those cases evidence is lacking for an immune- process (Coombs' test

negative), they may be called presumptive immune-mediated non-regenerative anemias. Patients need to be monitored to document active hemolysis and erythroid regeneration.

Clinical Evidence of Immune Destruction

Besides documenting hemolysis, one or more of the following three hallmarks must be present to support a diagnosis of immune-mediated hemolysis: persistent autoagglutination, marked spherocytosis, and a positive direct Coombs' test result. As in human medicine, the Coombs' test should be considered the best test to definitively diagnose IMHA, although marked spherocytosis and persistent/true autoagglutination (after 3x washing of EDTA blood with saline) are other important indirect parameters indicating likely immune-destruction of erythrocytes. However, a response to immunosuppressive agents is entirely insufficient, because dogs with other hemolytic anemias will also readily recover despite immunosuppression (e.g. PFK deficiency, onion poisoning). If the hallmark findings are negative, and there is still IMHA suspected, it should be considered presumptive or Coombs'-negative IMHA, and differential diagnoses for (hemolytic) anemias should be (re-) considered. Indeed, the diagnosis of IMHA should be reevaluated, even when treated as long as the animal remains anemic as other causes of anemia may ensue during treatment (e.g. drug induced bone marrow suppression, infection).

(1) Autoagglutination

Anti-erythrocytic IgM and in large quantities IgG antibodies may cause directly erythrocyte autoagglutination. The autoagglutination may be seen by naked eye in an EDTA tube or on a glass slide or may become apparent as small clumps of erythrocytes on blood smears. The severe agglutination observed is obviously an in vitro phenomenon, as such agglutination would be incompatible with life - this degree of agglutination intravascularly would quickly clog small blood vessels and be lethal. For yet unexplained reasons, canine erythrocytes have a tendency to unspecifically agglutinate in the presence of plasma and colder temperatures as well as possibly with (excessive) EDTA anticoagulant. Checking for agglutination when the blood is warm, fresh non-anticoagulated or anticoagulated with heparin or citrate may prevent agglutination formation. It should be noted that severe microscopic and of course any macroscopic agglutination will make many erythroid parameters of a CBC invalid (e.g. RBC count, mean cell volume, red cell distribution width) and potentially cause hematology analyzer dysfunction by flow obstruction.

In the 'in saline slide agglutination test', which has been practiced in veterinary medicine, mixing one drop of blood with one drop of saline may break up rouleaux formation, but not other forms of unspecific erythrocyte agglutination. More recently adding more saline to a small amount of blood (e.g. 4:1) has been suggested to remove unspecific agglutination, but there is no data. In human medicine, the 'in saline agglutination test' is not used for IMHA, but repeat washing with excess saline has been routinely practiced in human

immunohematology. It is important to determine whether the agglutination persists after 'saline washing' and potentially at warmer temperatures, which has been coined 'persistent or true autoagglutination'. This is simply accomplished by adding plenty of warm physiological saline to the tube containing a small amount of anticoagulated blood (e.g. 5:1), mixing, centrifuging, and removing the supernatant including the plasma and repeating this saline washing step 3 times. This washing is typically done in any human and veterinary laboratory prior to performing a direct Coombs' and other agglutination based tests.

While true or persistent autoagglutination is indicative of an immune process, it may preclude the performance of Coombs' test, blood typing, and crossmatching procedures and interpretation of their results which are generally based upon an agglutination reactions. Thus, in case of autoagglutination, it is recommended to wash the blood prior to pursuing these tests. Tests based upon immunochromatographic techniques do not seem to be as much affected by autoagglutination as free erythrocytes can still move along the strip and bind. If the agglutination breaks up after washing, the Coombs' test can be performed and is expected to be positive in a case of IMHA. Interestingly, the observed 'in saline slide agglutination test' has recently been shown to be rapidly removed by therapeutic plasma exchange therapy providing further evidence of a plasma and temperature effect, rather than immune-mediated process and thus no direct evidence of IMHA.

While the author has applied this more strict diagnostic criteria of 'persistent or true autoagglutination' to any agglutinating sample for decades, and, thereby, only sees a small proportion with persistent or true autoagglutination excluding properly dogs with other anemias, few other clinical studies have done so. This omission is a major drawback of published surveys on IMHA in dogs, as dogs with other anemias are likely falsely included. Moreover, there is currently no evidence that washing removes ('washes away') weakly bound antibodies on erythrocyte in dogs with IMHA.

(2) Spherocytosis

If erythrocytes are only partially phagocytized or lysed by complement in circulation, erythrocytes with reduced surface area to volume ratio, known as (micro-) spherocytes, are formed. They appear spherical and microcytic with no central pallor and are considered fragile. It should be noted that proper areas on the blood smear need to be reviewed microscopically to find spherocytes in between single regular discoid erythrocytes (i.e. with central pallor). Large numbers of spherocytes (>10/microscopic high power field) are nearly diagnostic for IMHA, whereas small numbers may be seen with other conditions (e.g. DIC, endotoxemia, and zinc intoxication). In the author's experience, nearly all dogs with marked spherocytosis and suspected to have IMHA also had a positive direct Coombs' test. However, only 60-80% of dogs with a positive direct Coombs' test or clinically diagnosed with IMHA had marked spherocytosis. Hereditary spherocytosis due to genetic membrane defects (e.g. an autosomal dominant trait due to a spectrin deficiency) has rarely been seen in dogs, but should be

considered as a differential diagnosis in dogs with persistent spherocytosis and a negative Coombs' test results.

Because of the difficulties with the direct Coombs' test (see below), it has been proposed to use the erythrocytic osmotic fragility test at a specific saline concentrations as a mean to diagnose IMHA. While this test is currently used in various clinics, there are many other reasons for increased fragility of erythrocytes beside IMHA including hereditary erythrocyte defects. This test is not used in human medicine for IMHA and has not been shown to be superior to determination of marked spherocytosis and a positive direct Coombs' test in dogs with IMHA. It should be noted the erythrocytic osmotic fragility test is also a cumbersome and not well standardized technique and is not recommended by this author.

(3) Positive Direct Coombs' or Antiglobulin Test Result

The direct Coombs' test is also known as direct antiglobulin test (DAT) and detects antibodies and complement on the surface of erythrocytes when the anti-erythrocyte antibody strength or concentration is too low to cause spontaneous macro- or microscopic agglutination (also referred to as subagglutinating titer). Separate canine-specific IgG, IgM, and C3b antibodies as well as polyvalent antiglobulin reagents are available. They are added typically at various concentrations after washing the patient's erythrocytes free of plasma (3 times as shown above). Recent immunochromatographic strip and gel tube tests may not require washing (in absence of autoagglutination) and use a fixed standard reagent concentration. Then, mixtures are generally incubated at room temperature and/or 37°C, as warm antibodies cause hemolysis. Cold agglutinins appear to be rarely of clinical importance, may be seen with other diseases, and very rarely cause hemolysis, but may cause cold agglutinin disease with peripheral skin necrosis. The strength of the observed Coombs' reaction does not necessarily predict the severity of hemolysis, but reaction changes over time can be useful in monitoring the disease process in a patient.

Typically tube or microtiter methods have been used exclusively in the reference or teaching laboratory setting, but a flow cytometric method has also been introduced in a couple of laboratories. Titrations of antiglobulins are used to overcome a possible prozon effect. A standardized, sensitive, and simple gel column method is no longer available for dogs, but can be set up by adding the appropriate reagents in the laboratory. A novel standardized antiglobulin test method with a micro gel tube succeeding the gel column and immunochromatographic strip technique has been recently introduced for in practice use apparently not requiring washing and antiglobulin titration. In a prospective study by the author's laboratory (Caviezel et al. 2014) of anemic and non-anemic dogs comparing microtiter plate assay, gel column, capillary, and immunochromatographic techniques using polyvalent antiglobulins in a laboratory setting, found excellent correlations between various direct Coombs' test methods with spherocytosis and without noticeable interference by immunosuppressive or transfusion therapy in anemic dogs were observed. It should be noted

that the Coombs' test has to be set up carefully and there is neither a gold standard test nor specific positive control samples available (also not in humans).

While in human medicine the indirect Coombs' test is also typically used, it has not been routinely applied for dogs, and there is insufficient clinical data in veterinary medicine. The presence of alloantibodies has been raised as a concern to cause false positive test results, however, there is no evidence for any clinically important naturally occurring alloantibodies in dogs. Similarly, the direct Coombs' test does not appear to become positive following transfusion in dogs, and delayed transfusion reactions caused by newly developed alloantibodies have not been documented. However, previously transfused dogs (>4 days) may be transiently Coombs' positive when again transfused.

Although many commercial laboratories offer direct Coombs' testing for dogs, clinicians have questioned the tests sensitivity and specificity and often forgo the test and/or use response to immunosuppressive therapy as a diagnostic. False negative Coombs' test results may be rarely seen because of technical reasons, insufficient quantities of bound antibodies, absence of the hapten, the presence of weakly bound antibodies (not documented), or the disease having gone into remission (normal hematocrit). However, the direct Coombs' test stays positive for days to months after initiating treatment and should be positive if the dog is still anemic and hemolyzing due to IMHA. A few days of immunosuppressive therapy will not reverse the Coombs' test result to negaitve, as unlikely a transfusion would cause a positive Coombs' test result. Thus, dogs with negative Coombs' test results should be reevaluated for other causes of hemolytic anemia. Retesting by another laboratory or method may also be considered.

While laboratory test evidence of immune-mediated hemolysis is required for a diagnosis of IMHA, these tools beyond hematocrit are also most helpful in monitoring response to treatment and disease course. Thus, evidence of autoagglutination, spherocytosis and/or a positive direct Coombs' test should be regularly followed until negative. Unless it is a secondary IMHA, these immunohematological parameters, particularly the direct Coombs' test remain positive for several weeks despite immunosuppressive therapy. It should be noted that some dogs (like humans) remain Coombs' positive for months to years without being or only mildly anemic and without requiring continued treatment. There is no evidence that a flow cytometric Coombs' test is any better, and it should be noted that low titers of antibodies by any methods may not be meaningful.

A diagnosis of IMHA requires the documentation of red blood cell destruction and an immune process. While regenerative anemia, icterus, and hyperbilirubinuria are indicating the presence of a hemolytic anemia, evidence of (1) true autoagglutination after washing, (2) marked spherocytosis, and/or (3) a positive direct Coombs' test are required to document immune destruction. The prognostic factors for IMHA are poorly defined unless IMHA is secondary to an underlying disease. Severe anemia, icterus, leukocytosis, hypoalbuminemia and thrombotic evidence are unfavorable findings. Because the severity of IMHA ranges from

indolent to life-threatening disease and serious complications seen with IMHA, therapy has to be tailored for each patient and depends in part on whether the IMHA is primary or secondary in nature. Removal of the triggering agent or treatment of the underlying condition can bring the IMHA rapidly under control.

Fluids, Blood Transfusions, Oxygen and Oxyglobin in IMHA

Restoration and maintenance of tissue perfusion with crystalloid fluids is important, even when it results in further lowering of the hematocrit. When severe anemia and a dropping hematocrit lead to signs of tissue hypoxia, packed red blood cell transfusions appear beneficial. The increased oxygen-carrying capacity provided by the transfused red blood cells may be sufficient to maintain the animal's hematocrit for a few days, while other treatment modalities have time to become effective. The notion that transfusions pose an increased hazard to animals with IMHA has been overemphasized and is not supported by retrospective clinical studies. Fresher blood products are possibly an advantage. However, the common occurrence of autoagglutination may make blood typing and crossmatching of the patient impossible. In these cases DEA 1- blood should be transfused. Additional blood types are being recognized which may be also important.

If compatible blood is not available, the bovine hemoglobin solution Oxyglobin, a highly purified bovine hemoglobin solution, if available, may be administered and provides increased oxygen-carrying capacity and plasma expansion. The original FDA study documented the beneficial effects of Oxyglobin in dogs, whereas recent retrospective studies do not allow any conclusions. In contrast to blood and Oxyglobin, oxygen inhalation therapy is of little benefit, unless the animal with IMHA is suffering form pulmonary disease such as pulmonary thromboembolism. Thanks to adequate transfusion support, animals with IMHA rarely die because of anemia, but because of secondary complications such as thromboemboli and infections.

Immunosuppressive Therapy for IMHA

The insufficient understanding of the pathogenesis, the generally guarded prognosis, the lack of good therapeutic trials, the serious drug side effects, and the high costs of intensive care greatly hamper the successful management of dogs with IMHA. The main goal of immunosuppressive therapy is to reduce (1) phagocytosis, (2) complement activation, and (3) anti-erythrocytic antibody production. Glucocorticoids are the initial treatment of choice for canine, feline and human IMHA. They interfere with both the expression and function of macrophage Fc receptors and thereby immediately impair the clearance of antibody-coated erythrocytes by the macrophage system. In addition, glucocorticoids reduce the degree of antibody binding and complement activation on erythrocytes, and only after weeks, diminish the production of autoantibodies. Thus, oral prednisolone at a dose of 1-2 mg/kg twice daily is

the mainstay treatment. Alternatively, oral or parenteral dexamethasone at an equipotent dose of 0.6 mg/kg daily can be used, but is likely not more beneficial.

There is no evidence that other immunosuppressive agents are effective. They should not be used initially as they are associated with severe side effects. Additional immunosuppressive therapy is warranted when prednisone fails, only controls the disease at persistently high doses, or when it causes unacceptable side effects. They are generally used together with prednisolone, but may eventually be used independently. Historically, cytotoxic drugs such as cyclophosphamide were added, however a small randomized study and several retrospective surveys failed to show any beneficial effects, but may be associated with greater morbidity and mortality in the acute management of IMHA. Retrospective studies and anecdotal reports with azathioprine, cyclosporine, danazol, mycophenylate, and human intravenous immunoglobulin suggest some efficacy, but controlled prospective clinical trials that document their efficacy are lacking. For instance, there is no evidence that azathioprine is effective and from a mechanistic view point it only inhibits antibody production and as it is an antimetabolite, it is only effective after a few weeks. Furthermore, the side effects of acute pancreatitis and agranulocytosis to aplasia makes this in most cases unsuitable. Cyclosporine at 5-10 mg/kg is likely the best and safest second agent but blood drug levels and in vitro immunosuppression should be determined in order to avoid toxicity and underdosing. Highly immunosuppressive agents from transplantation medicine such as mycophenylate and leflunamide are other agents which have been tried, but no definitive beneficial effects have been reported. Finally, human intravenous immunoglobulin at 2 x 1 g/kg may rescue a non-responding IMHA patient but relapses are common.

One other agent is melatonin which has been added as immunotherapy but it is unclear how it works and if this has any beneficial effects. Splenectomy may be considered particularly in refractory cases with large spleen, but even a normal spleen may excessively clear antibody-coated red blood cells. Furthermore, splenic histopathology, toxicology and infectious disease screens may offer a diagnosis of an underlying disease. Finally, because of the apparently severe agglutination and the inflammatory and necrotic process, plasma exchange therapy has been used in some cases and appeared to be helpful in expediting response and avoiding serious complications.

It should be noted that an apparent therapeutic response to immunosuppressive therapy is insufficient evidence for the diagnosis of IMHA. Response to therapy may be indicated by a hematocrit that rises or stabilizes, an appropriate reticulocytosis, diminished autoagglutination, and fewer spherocytes; this response can be expected to be seen within days to weeks. The subsiding of autoagglutination would allow the performance of a direct Coombs' test and thereby permit the direct documentation of anti-erythrocytic antibodies. As glucocorticosteroid therapy is associated with well-known side effects, the initial dose will be tapered by reducing the amount by one-third every 7-14 days and moving toward every other day therapy. In secondary IMHA with appropriate control of the underlying disease, the tapering can be accomplished more rapidly.

Thromboembolic and Other Complications with IMHA

Because of the potential of gastrointestinal ulceration by glucocorticosteroids and other immunosuppressives, gastrointestinal protectants such as sucralfate may be considered. Because dogs with IMHA suffer from an immune deregulation which may have been triggered by an infection and are treated with immunosuppressive agents, these patients are prone to experience infections; it is, therefore, prudent to administer preventative as well as therapeutic antibiotics to these dogs with IMHA on immunosuppressive therapy.

Thromboemboli and DIC are unique serious complications that greatly contribute to the morbidity and mortality of dogs with IMHA which are not typically seen in humans and cats with IMHA. Although the pathogenesis remains unknown, venipuncture, catheters, confinement, and glucocorticosteroids as well as other immunosuppressive agents may be contributing factors. Thus far, no study has definitively documented any successful prevention and/or management protocol for these life-threatening hemostatic problems in canine IMHA. Predisposing factors should, whenever possible, be limited, and adequate perfusion and tissue oxygenation should be provided with fluids and transfusions or Oxyglobin. Generally, anticoagulation therapy is instituted after there is some evidence or suspicion of thromboemboli. Unfractionated Heparin (dose of 50-300 IU/kg subcutaneously every 6 hours or by continuous intravenous infusion) or Low Molecular Weight Heparin (LMWH; Dalteperin 150 IU/kg sc every 12 hours) are the most commonly used drugs and is used. The replacement of coagulation factors and antithrombin III has not been proven to be beneficial. Antiplatelet agents may also be used and for instance an ultralow dose of aspirin (0.2-1 mg/kg once daily) has been advocated by a couple of groups, but other studies question its efficacy. Other antithrombotic agents such as modern antithrombotic agents have been used occasionally, but their efficacy and safety remain also unproven.

In conclusion, in my view a diagnosis of IMHA requires the documentation of clinical erythrocyte destruction (hemolysis) and an immune process targeted against erythrocytes. While regenerative anemia, icterus, hyperbilirubinuria and +/-hemoglobinuria are suggesting a hemolytic anemia, evidence of true persistent autoagglutination, marked spherocytosis, and/or a positive direct Coombs' test result are required to document immune-mediated erythrocyte destruction. Monitoring of IMHA patients for the disappearance of these immunological changes over days and months following initiation of therapy is also recommended to adjust and taper therapy.

The successful management of IMHA remains a challenge; immunosuppressive therapies beyond glucocorticosteroids have not been proven to be effective but can be associated with serious side effects. Furthermore, the tendency to inflammation, necrosis and thromboembolism of dogs with IMHA contributes greatly to the morbidity and mortality of dogs with IMHA and effective preventative and therapeutic interventions have not yet been established.

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Reference

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# ACUTE AND CHRONIC BLOOD LOSS ANEMIAS

*Blood loss is one of the most common clinical presentations of anemia in animals and may have different causes. The blood loss can be internal or external, localized or multifocal, induced or spontaneous, and peracute, acute, and chonic. Therefore blood loss anemias can be associated with different clinical signs and laboratory test abnormalities presenting as emergency to chronic disease. Likewise treatment, beside local hemostasis, is very different. The diagnostic approach and management of blood loss anemias is being presented here.* Bleeding may be caused by:

Trauma
Surgery
Tumors
Drugs
Infections

Vasculopathy
Thromocytopenia
Thrombopathia
Coagulopathy
Combined hemostatic defects

Spontaneous hemorrhage and excessive bleeding due to mirror trauma, and prolonged and recurring bleeding may suggest a systemic hemostatic disorder. Surface bleeding indicates a primary hemostatic defects such as a thrombocytopenia or vasculopathy. Hematomas and cavity bleedings suggest a coagulopathy – a plasma coagulation factor deficiency. The hemostatic system may be affected by many acquired causes such as drugs, toxins, and hepatic and kidney disorders. In addition, hereditary bleeding disorders should be considered such as hemophilia, Factor VII and XI deficiency as well as thombopathias and von Willebrand disease. Thus, bleeding animals may well require a hemostatic diagnostic work up, which is described in more details in another lecture.

A single bleeding site may suggest a localized disease process caused by trauma, surgery, although acquired and hereditary hemostatic disorders should not be excluded. The site of hemorrhage may be obvious when external and severe, while internal bleeds may remain unnoticed for extended times. Hence imaging studies may be needed to document hemorrhage in body cavities and organs. While local hemostasis is critical, diagnostic aspirate and surgical interventions should be done carefully and aseptically as they may cause more bleeding and secondary infections.

Classifying the blood loss into internal versus external is crucial, as chronic external blood loss also causes loss of iron and plasma. It should be noted that external blood loss includes losses through the gastrointestinal tract. Melena may be caused by gastric to small intestinal bleeding, but also be from nasal and oral regions. While epistaxis is readily recognized, a considerable amount of blood can be swallowed resulting in melena. Hematochezia would suggest bleeding

from colon and rectum. Melena and hematochezia are generally macroscopically appreciated, but intermittent or mild bleeding may require repeat fecal examination and a fecal occult blood test. If a dog is on a regular canine diet, the occult blood test is typically negative unless there is gastrointestinal bleeding.

**Temporary classification of blood loss anemias**

| Bleeding | Peracute | Acute | Chronic |
|---|---|---|---|
| Duration | Minutes – Hours | Several Hours – Days | Weeks – Months |
| PCV | N | ↓↓ | ↓↓↓ |
| CRT | ↑↑ | ↑↑ | N |
| Skin turgor | N | ↓↓ | N |
| Reticulocytes | N | ↑↑ | ↑ |
| MCV | N | ↑↑ | ↓↓ |
| MCHC | N | N↓ | ↓↓ |
| Iron | N | N | ↓↓ |

A critical differentiation is based upon time of bleeding and being seen in clinics. Within minutes to hours major bleeding will result predominantly in hypovolemia and may cause hypovolemic shock with tachycardia and thready pulses. Besides the obvious bleeding site, these patients show pale mucous membranes because of hypovolemia and vasoconstrictions and not because of anemia. In fact very early on the hematocrit and total protein concentration will be normal to increased. Changes will only be seen when fluids shift from the periphery and fluids are administered. During the first couple of days there are also no abnormalities seen regarding red cell indices and reticulocyte count – thus showing a normocytic-normochromic and non-regenerative pattern.

With acute blood loss over several hours to days, fluids shift and anemia develops. Not only the capillary refill time can be prolonged, but also the skin turgor test. Oral or parenteral fluid intact and persistent blood loss can affect the clinical and laboratory abnormalities. After 2-3 days anemia becomes macrocytic normo- to hypochromic and regenerative. There should be adequate iron stores for a strong erythropoiesis, and if there is no further loss, the anemia will resolve in a couple of weeks.

In case of prolonged internal blood loss the blood components including iron will be recycled and therefore the anemia is robust as with acute blood loss anemia. However, when there is external blood loss that continues for weeks to months, and thereby there is also iron loss, and the patient will develop a microcytic hypochromic (poorly) regenerative anemia. These patients are normovolemic and their heart is hypertrophied and working at max capacity; thus additional fluid administration would not be well tolerated. As this develops slowly the patient can frequently adapt well and may only show minimal signs until the anemia is very severe or the animal is experiencing a stressful situation.

Serum iron parameters can be assessed if unsure of the diagnosis of chronic iron deficiency anemia. Determination of serum iron concentration is simple, but values can be affected by stress and medications. Serum iron binding capacity does not change much in dogs and cats and thus is not useful. Serum ferritin concentration could be helpful but only available at a few labs as it requires species specific reagents. Iron stores could also be assessed by special Prussian blue stain of bone marrow aspirate and core biopsy except in cats, because iron stores are normally minimal.

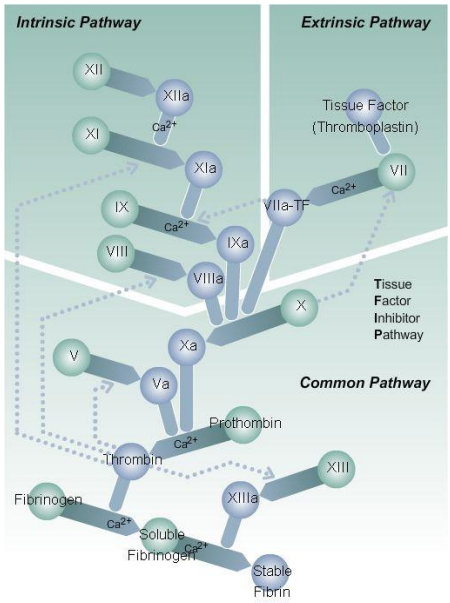
Management of blood loss anemia depends on the severity, acuteness, and cause of blood loss. Main objectives are stopping further blood loss, restoring normovolemia and correcting severe anemia. However, because there are many specific causes, treatment varies. Peracute blood loss of >20% requires immediate treatment of hypovolemic shock with crystalloid or colloid fluids and only blood later on. Note, colloid fluids may enhance the bleeding tendency. Only once the blood volume is restored and the extend of the blood loss can be assessed by measuring hematocrit and total protein concentration, severe anemia is corrected by blood transfusions.

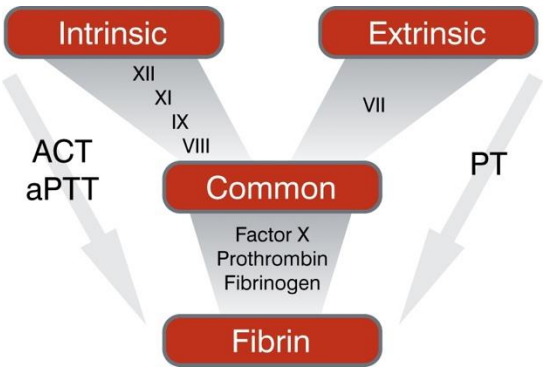
Transfusion in the form of fresh whole blood or stored packed red cells and fresh frozen plasma are considered depending on the severity of clinical signs – typically when the hematocrit is less than 15-25%. Thus rather than having a specific transfusion trigger, it is a clinical judgement. There is no need to reach a normal hematocrit. Typically animals can tolerate a hematocrit of ~20% well, but underlying disorders, disease progression or intended surgical procedures may call for a higher hematocrit. With external blood loss the hypoproteinemia could also be improved by fresh frozen plasma. Coagulopathies and von Willebrand disease are specifically treated with fresh frozen plasma. Hemophilia A and von Willebrand disease will be best controlled with cryoprecipitate. Vitamin K is a good example of a specific treatment in case of anticoagulant rodenticide poisoning, but may also help with hepatopathies. In case of chronic blood loss anemia iron supplementation over weeks to months in the form of oral iron sulfate or intramuscular iron dextran may be required.
In conclusion, there are clinical tools to diagnose blood loss anemias and many practical therapeutic interventions including transfusions for a successful outcome.

# DIAGNOSTIC APPROACH TO BLEEDING DISORDERS

*Bleeding disorders are a common presentation in dogs and less commonly in cats and may be inherited or acquired. Furthermore, thrombotic conditions are being increasingly recognized. This lecture will focus on the clinical diagnostic approach to a bleeding animal. There are several point-of-care and reference laboratory tests permitting the separation between primary and secondary hemostatic defects as well as a specific diagnosis. Particularly challenging is the diagnosis of Disseminated Intravascular Coagulation (DIC), a syndrome observed with a variety of disorders.*

Bleeding diatheses are generally separated into primary and secondary hemostatic disorders and in some cases both systems are affected, such as in disseminated intravascular coagulation (DIC). Primary hemostatic disorders include not only the common thrombocytopenias but also thrombopathias, vasculopathies, and von Willebrand disease. Secondary hemostatic disorders include all coagulation factor deficiencies involved in fibrin formation and are strictly speaking the coagulopathies. Platelet and vascular problems often present with surface hemorrhage, while coagulopathies generally cause hematomas and cavity bleeds. Excessive hemorrhage at an injury or surgery site and bleeding from multiple places are suggestive of bleeding disorder, and there are a several breed predilections for specific hereditary defects.




Hemostatic tests are indicated whenever an animal is bleeding excessively, prior to surgery when an increased bleeding tendency is suspected, to monitor therapeutic interventions, and for genetic screening in certain breeds or families with a known bleeding disorder. Hemostatic abnormalities should be assessed prior to instituting therapy whenever possible or at least appropriate blood samples should be collected pretreatment. Excellent venipuncture with discarding of the first few drops of blood (to avoid platelet activation and tissue factor) and extended compression over jugular, saphenous or femoral vein is required. The **cuticle bleeding time** crudely assesses overall hemostasis, but is not standardized and painful and is, therefore, not recommended. A minimal database includes a packed cell volume and total protein evaluation, and **evaluation of a blood smear** can provide a platelet estimate and identify platelet size and clumping as well as schistocytes. The results can also provide some measure of the extent of blood loss and red blood cell transfusion requirement.

**Tools for Primary Hemostastic Defects**

Platelet counts can be estimated on a blood smear or specifically counted by a hematology instrument. Since 8-15 platelets (1 platelet equals 20,000/µl) are normally found per high power oil emersion microscopic field, an absence to low number of platelets suggests a severe thrombocytopenia. Various modern impedance and laser hematology instruments have the ability to count platelets

and measure their mean size including platelet size distribution and platelet crit; they may have been validated, but some have difficulties in differentiating large platelets from erythrocytes (particularly in cats). Furthermore, platelets can readily be activated which results in platelet aggregation, hence, platelet counts need to be confirmed by a careful review of a blood smear including the feather edge for platelet clumps (preferably on fresh non-anticoagulated blood). Hemorrhage is generally not observed unless the platelet count is <40,000/µl (normal 150-500,000/µl) or there is also a coagulopathy like DIC.

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

A diagnosis of thrombocytopenia is made by a platelet estimate on a blood smear or complete blood cell count, but any thrombocytopenia must be verified by a review of a blood smear. Spurious thrombocytopenia may due to instrument limitations; e.g. megaplatelets in Cavalier King Charles and few other breeds, and platelet aggregates with many illnesses and collection techniques; also Greyhounds have generally a mild thrombocytopenia. Classic signs of thrombocytopenia include petechiation, ecchymosis, epistaxis, and gastrointestinal blood loss. The most severe thrombocytopenias, seen with IMT/ITP, often cause only mild hemorrhage. Following a careful history, a search for an underlying cause is warranted to identify an infection (blood smear, serology, PCR) or cancer (also involving lymphnodes and spleen). Bone marrow examination is safe, but may rarely reveal a specific cause on initial presentation. A diagnosis of ITP is mostly based upon excluding other causes of thrombocytopenia, but platelet-associated antibodies can also be determined to support an immune mechanism for thrombocytopenia. Detection of platelet-associated antibodies further supports an immune-mediated thrombocytopenia, but this test is rarely available. Serum titer, antigen and PCR tests for tick-born (ehrlichiosis, babesiosis, leishmaniasis, Rocky mountain spotted fever) and other infectious diseases are indicated in certain countries or areas. The presence of schistocytes and thrombocytopenia suggests intravascular disseminated

coagulation, where intravascular fibrin strands fragment erythrocytes. Because von Willebrand disease is such a common mild primary hemostatic defect in dogs, plasma vWF measurements by ELISA through a commercial laboratory are indicated. For breeding purposes, DNA testing is also available for some canine breeds.

Finally, in light of normal platelet count and plasma vWF values, a prolonged buccal mucosal bleeding time (BMBT) indicates a thrombopathia. Disposable devices are available that facilitate making 1-2 standard 1 mm deep mucosal incisions. The platelet function analyzer (PFA100) is a simple tool to functionally assess primary hemostasis. Electron microscopic and platelet aggregation and nucleotide studies allow further characterization of platelet dysfunctions in specialized laboratories. For a couple of hereditary thrombopathias even a DNA test is now available such as for Glanzmann thrombasthenia in Great Pyrenees and Otterhound, and thrombopathia in the Spitz, Basset, Landseer and Swiss Mountain dog, and macrothrombocytopenia in Cavalier King Charles and others.

**Coagulation Tests**

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

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

Until recently the ACT tube test was the only point-of-care test available for clinical practice, whereas PTT and PT tests were performed in commercial laboratories. There are now new point-of-care coagulation instruments (e.g. IDEXX Coag DX and the Abaxis VetScan VSpro) introduced that are capable of determining without delay on small amounts (50 µl) of fresh citrated whole blood the aPTT and PT, thereby making separation of citrated plasma and shipment of frozen plasma to the laboratory for initial coagulation screening unnecessary. In practice, a reasonable and simple approach for a bleeding animal to be screened for a coagulopathy would be to measure the ACT or PTT first as either test detects all coagulopathies (except for hereditary factor VII deficiency in Beagles, Scottish

Deerhounds and Alaskan Klee Kais), but the aPTT is more standardized and the ACT can only be run on fresh whole blood. If the aPTT (or ACT) is prolonged, a PT test would be indicated to differentiate between an intrinsic and common pathway defect or a combined coagulopathy involving several coagulation factors.

**Hemostatic screening tests and groups of bleeding disorders**

| | Platelets | BMBT | PTT | PT | TT |
|---|---|---|---|---|---|
| **Thrombocytopenia** | **D** | **I** | **N** | **N** | **N** |
| **Thrombocytopathia & vWD** | **N** | **I** | **N** | **N** | **N** |
| **Intrinsic coagulopathy** | **N** | **N** | **I** | **N** | **N** |
| **Extrinsic coagulopathy (FVII)** | **N** | **N** | **N** | **I** | **N** |
| **Combined coagulopathies (DIC, liver, rodenticide)** | **D** | **I/N** | **I/N** | **I/N** | **I/N** |

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

Although hereditary coagulopathies can be suspected based upon the pattern of coagulation test abnormalities, specific factor analyses are needed to confirm a diagnosis. A young male animal who is bleeding and has a mildly prolonged aPTT but normal PT likely has hemophilia A or B (factor VIII or IX deficiency), an X-chromosomal recessive disorder. However, factor XI deficiency is associated with the same test abnormalities and is inherited by an autosomal recessive trait (e.g. Kerry blue terriers). For several hereditary coagulopathies DNA tests are already available (http://research.vet.upenn.edu/penngen), while for others the specific plasma factor deficiency can be determined through the Comparative Hemostasis Laboratory at Cornell University. Finally, factor XII deficiency, particularly common in domestic shorthair cats, and prekallikrein deficiency causes marked aPTT prolongations but no excessive bleeding tendency. Rodenticide poisoned animals that are bleeding or are at risk for bleeding will have severe prolongations in all of the above coagulation tests, but would have a normal thrombin time (TT). The thrombin time is independent of vitamin K-dependent coagulation factors and is a functional assay for fibrinogen to form fibrin. The protein induced by vitamin K antagonism or absence (PIVKA) test is a modified PT test and not diagnostic for rodenticide poisoning, but a toxicological investigation (product identification, blood toxicology analysis) may confirm the rodenticide poisoning. Moderate thrombocytopenia may be associated with rodenticide poisoning. All liver diseases may result in varied coagulopathies due to impaired coagulation factor synthesis and vitamin K malabsorption.

Similarly, disseminated intravascular coagulopathies due to many different disorders is associated with variably prolonged coagulation times. More helpful to the diagnosis of DIC are the recognition of schistocytes, thrombocytopenia, low fibrinogen and antithrombin III levels, and increased D-dimers and fibrin split

(degradation) products. Finally, thromboelastography (TEG or ROTEM) techniques can now be used in the emergency room, intensive care units, and referral centers to assess overall hemostasis and particularly thrombotic/fibrinolytic tendencies of citrated whole blood.

Supported in part by a grant from the NIH (OD 010939). The author's laboratory PennGen is offering some advanced hemostatic testing.

# TREATMENT OF BLEEDING DISORDERS

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

**Therapeutic considerations for the bleeding dog include:**

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

The general principles of resuscitation and emergency care apply to dogs with hemorrhage such as restore hydration, open airway, oxygenation, and body temperature. For rehydration, crystalloid fluids are typically used as colloids have anticoagulant effects and may worsen the bleeding. In case of dangerously low oncotic pressures, fresh frozen plasma (FFP) may be used. With peracute blood loss PCV changes are not observed for hours until fluid shifts occur or after the animal is rehydrated with fluids. Dogs with acute hemorrhagic gastroenteritis may lose more fluid than RBCs and become hemoconcentrated until they are rehydrated. Thereafter, they are anemic and often severely hypoproteinemic.

While ligatures, hemostats and compression can stop visual bleeding from trauma or surgery, surgical intervention should be cautiously considered to not cause more harm to the patient. Thus, adequate hemostatic function should be first assured or restored with appropriate blood products or medical treatment, whenever possible. There are also a variety of commercially available local hemostatic agents that might be applied at a wound, such gelatin, thrombin, bone wax, and fibrin glue.

Animals with massive blood loss may benefit from pRBCs or whole blood transfusions. Ideally, dogs are initially DEA 1 typed to provide type specific blood products and possibly crossmatched, if they had received blood previously (>4 days). There is no specific PCV at which to transfuse, but rather the overall

clinical assessment of tissue oxygenation is determining the transfusion trigger in each patient. The simple formula of volume to transfuse = desired PCV rise x kg Body Weight x 2 is adequate to estimate the target PCV. In case the expected PCV rise is not achieved continued blood loss, fluid shifts, and an acute hemolytic crisis may account for the deficit. Animals with chronic blood loss generally have well adapted to their low hematocrits and may cope well with a PCV as low as 10%. Their heart, however, functions at maximal capacity (large cardiac output) to compensate for the anemia. They are generally not dehydrated and additional fluids may result in severe volume overload and cardiac decompensation. Thus, the fluid and blood volume should be appropriately chosen, and the dog's cardiovascular system should be carefully monitored. Interestingly, it has been shown that a rise in PCV will also ameliorate bleeding, likely due to the fact that red cells are a major part of any clot.

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

There are a variety of specific treatments for thrombocytopenia but there is no clinically available drug truly stimulating platelet production. As many thrombocytopenias are caused by infections dogs need to be serologically and by Real-Time PCR examined for infections. And accordingly they are potentially presumptively treated for instance with doxycycline until the specific microorganism is found a specifically treated. It should be noted that Babesia is more frequently causing thrombocytopenia than hemolytic anemia. And indeed there are many emerging infections and double infections cause more serious signs.
With respect to immunosuppression glucocorticosteroids remain the best option despite their negative side effects. Aside dexamethasone and prednisolone/prednisone at their respective immnosuppressive doses (dex is 6-8 times more potent than pred), a dexamethasone pulse regiment could be tried but likely has considerable side-effects. On the other hand vincristine is a useful additional agent. It is inexpensive, safe, and rapidly effective massively increasing the platelet count. It is a tubulin inhibitor permitting more rapid release of platelets from marrow and inhibiting macrophage activity particularly in spleen and without bone marrow suppression. The main concern is perivascular necrosis which can be readily avoided if a catheter is placed and flushing is used.

A single dose is useally sufficient but could be repeated after one week. Other alternatives are limited except for human intravenous immunoglobulin which seems to work similar well as vincristine but is extremely expensive and not approved for dogs. Additional medications may include melatonin but there is no data. Platelet transfusions raise the platelet count less than in other diseases likely due to the rapid antibody-coating of platelets and their removal, but may still ameliorate the bleeding if serious. Splenectomy may be a last resort and offer also another means of diagnosing an underlying cause.

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

While for any coagulopathy fresh or fresh frozen plasma could be administered (10ml/kg or to effect) for some coagulopathies other therapeutic options should be considered. Coagulopathies due to rodenticide poisoning and several hereditary coagulation factor deficiencies can be treated with cryo-poor plasma, while Hemophilia A and fibrinogen deficiency require cryoprecipitate. Depending on the cause of vitamin K deficiency higher or lower doses of vitamin K are administered (1-5mg/kg BID). Vitamin K1 rather than K3 should be used. Oral absorption is very fast and effective and subcutaneous injections may be considered if nothing per os can be administered or gastrointestinal absorption is impaired (cholestasis, inflammatory bowel disease, antibiotics). Porcine and human coagulation factors have been experimentally studied in bleeding dogs and have also been used anecdotally in clinics. Human recombinant FVIIa may be used if FFP is not available in some coagulopathies although its efficacy and safety have not been extensively studied in dogs. The cuticle bleeding time was normalized in Beagle dogs with FVII deficiency. Finally, the dog has served as an excellent large animal model to develop and assess the efficacy and safety of hemophilia A and B and the initial experiments are promising with plasma factor levels of >5% already being beneficial. Once a vector and protocol has been established and the administration of a coagulation factor gene product could be simple and affordable, and it is foreseeable that this could be applied to the canine patients.

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

Supported in part by a grant from the NIH (OD 010939). The author's laboratory PennGen is offering some advanced hemostatic testing.

# CANINE TRANSFUSION THERAPY

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

## Canine Blood Types

Blood types are genetic markers on erythrocyte surfaces that are antigenic and species specific. A set of blood types of two or more alleles makes up a blood group system. Dogs have likely more than a dozen blood group systems mostly known as dog erythrocyte antigens (DEA). However, there is no DEA 2 blood group and some may be rather labeled high frequency or common red blood cell (RBC) antigens (e.g. DEA 4) and some have not yet received a DEA designation (e.g. Dal). Canine erythrocytes are either positive or negative for a blood type (e.g., DEA 4+ or DEA 4-), and these blood types are likely codominantly inherited. The DEA 1 system was thought to be an exception with DEA 1.1 (A1), DEA 1.2 (A2) and potentially DEA 1.3 (A3) being allelic. Thus, a dog could apparently be DEA 1.1+ or DEA 1.1- and DEA 1.1- dogs can be DEA 1.2+ or DEA 1.2-. However, these studies were based upon weak polyclonal antibodies (DEA 1.1 and 1.X) requiring Coombs' reagents. Recent studies with a monoclonal antibody showed that the DEA 1 blood group is a continuum from DEA 1- to weakly to strongly DEA 1+; hence DEA 1.2 typing is no longer offered. The degree of DEA 1 expression is constant and DEA 1+ appears to be dominantly inherited. A recent survey in North America indicates that most dogs are either DEA 1- or strongly DEA 1+ with fewer dogs being weakly to moderately DEA 1+. The biochemical structure of the DEA 1 remains still unknown, but a genome wide association study has identified a likely single locus.

Recent surveys revealed that the Dal- type is not restricted to Dalmatians but is also seen in Doberman Pinschers, Lhasa Apsos and Shih Tzus and thus typing for this blood type is becoming more important particularly for those requiring multiple transfusions. In a related study dogs from North America were screened for two new blood types, preliminarily called Kai 1 and Kai 2. Most dogs were Kai 1+ and only few dogs were Kai 2+ or Kai 1-/Kai2-. The clinical importance is yet to be determined albeit anecdotally dogs can develop anti-Kai 1 alloantibodies. The PennGen Laboratory currently offers Dal and Kai 1 and Kai 2 typing.

The clinically most important canine blood type is DEA 1, which elicits a strong alloantibody response after sensitization of a DEA 1- dog by a transfusion and thus can be responsible for a transfusion reaction in a DEA 1- dog previously transfused with DEA 1+ blood. It is currently unknown if DEA 1- dogs are equally

sensitized by weakly to strongly DEA 1+ blood, or if weakly DEA 1+ dogs are sensitized by strongly DEA 1+ blood. Furthermore, transfusion reactions against other blood types or common antigens have rarely been observed and reported. They include reactions against the DEA 4, Dal, Kai 1 and other common RBC antigens; other clinically important blood types may be found in the future. No reagents currently are available against several antigens or are only available on a limited basis, and additional blood types continue to be recognized. Only limited surveys on the frequency of these blood types have been reported, which suggest possible geographic and breed-associated differences.

Strongly antigenic blood types are of great clinical importance because they can elicit a potent alloantibody response. These alloantibodies may be of the immunoglobulin G (IgG) or IgM class and may be hemagglutinins or hemolysins. Based upon experimental and clinical data, dogs can become sensitized after receiving a mismatched transfusion (i.e., a blood unit positive for one or more blood types not found on the recipient's RBCs). There are no clinically important, naturally occurring alloantibodies (also known as isoantibodies) present before sensitization of a dog with a transfusion. Sensitizing dogs in experimental studies in the 1950s led to the documentation of some transfusion reactions caused by blood group incompatibilities and to the characterization of new blood types.

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

**Canine Blood Typing Procedures**

Because of the strong antigenicity of DEA 1, typing of donors for DEA 1 is recommended. Whenever possible, the recipient also should be typed to allow the use of DEA 1+ blood for DEA 1+ recipients. Canine blood typing tests are generally based on serologic identification by agglutination reactions but chromatographic strip methods are also offered. Originally serum from sensitized dogs has been used for typing, but such polyvalent alloantibodies vary from batch to batch, may require Coombs' reagent to enhance agglutination, and may not be always available and are therefore not optimal. Two monoclonal antibodies against DEA 1 have been developed. The gel column technology, widely used in human blood banking, was found to be an excellent standardized laboratory

method (DiaMed), but is unfortunately no longer commercially available. A blood typing card has been available with modifications since the mid-1990s as a simple in-practice kit to classify dogs as DEA 1- or DEA 1+ (degree of reaction can vary). a standardized simple immunochromatographic technique became available in the mid-2000s from Alvedia. Another cartridge with a similar strip technique was introduced by DMS/AgroLabo, but has not been evaluated. Moreover, a third cartridge method in which blood flows through the cartridge is also available (DMS/Abaxis) but seems to produce inconsistent results.

Polyclonal reagents against other DEA types are currently only available on a limited bases for DEA 3, 4 and 7 from Animal Blood Resource International (prior Michigan state University and Midwest Blood Services). And only limited anti-Dal reagents from sensitized dogs are currently available in a couple of laboratories like Montreal University and PennGen, monoclonal anti-Kai 1 and anti-Kai 2 alloantibodies have been developed in South Korea. DEA 1 typed and matched patients in need of a transfusion may be typed for DEA 4, Dal and Kai 1/2, which may then permit the localization of a type-matched donor dog.

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

**Blood Crossmatching Test**

Whereas blood typing tests reveal the blood group antigens on the red blood cell surface, blood crossmatching tests assess the serologic compatibility or incompatibility between donor and recipient. Thus the crossmatch test checks for the presence or absence of naturally occurring and induced alloantibodies in serum (or plasma) without determining the blood type and thus does not replace blood typing. These antibodies may be hemagglutinins and/or hemolysins and can be directed against known blood groups or other RBC surface antigens. Many laboratories commonly use a standardized tube crossmatching procedure, but the interpretation of the agglutination reaction is highly variable. The crossmatching test requires some technical expertise, may be accomplished through a veterinary laboratory along with blood typing, and is done with washed

EDTA-anticoagulated blood from recipient and potential donor(s). The DiaMed gel column technique and more recently the in-clinic DMS gel tube assay have been evaluated and were found to be simple, sensitive, and standardized methods to crossmatch dogs and cats. In addition, Alvedia introduced a simple strip crossmatch test with a Coombs' phase.

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

The initial blood crossmatch between two dogs that have never before received a transfusion should be compatible, because dogs do not have naturally occurring alloantibodies. Therefore, a crossmatch may be omitted before the first transfusion in clinical practice for dogs. Because the crossmatch does not determine the blood type of the patient and donor, a compatible crossmatch does not prevent sensitization of the patient against donor cells within 1 to 2 weeks. Thus, previously transfused dogs should always be crossmatched, even when receiving again blood from the same donor. The time span between the initial transfusion and incompatibility reactions may be as short as 4 days and the induced alloantibody can last for many months to years (i.e., years after the last transfusion alloantibodies may be present). Again, a blood donor never should have received a blood transfusion to avoid sensitization. The practice of transfusing patients with the least compatible unit does not have any scientific basis. Nevertheless, some minor agglutination results in crossmatching a patient may be unrelated to alloantibodies and unspecific (e.g., patient's RBC damage by uremia and other illnesses, donor cells after extended storage of unit in the refrigerator). Of course, any patient with true/persistent autoagglutination may not be matched to any donor.

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

**Transfusion Reactions**

While transfusion of blood and its components is usually a safe and temporarily effective form of therapy, there is always a risk for potential hazards. Adverse reactions usually occur during or shortly after the transfusion and can be due to any component of whole blood. Most transfusion reactions can be avoided by carefully selecting only healthy donors, using appropriate collection, storage, and administration techniques, performing blood typing and crossmatching, and administering only needed blood components. The most common clinical sign of transfusion reaction is fever, followed by vomiting and hemolysis. Hemolytic transfusion reactions can be fatal and are, therefore, most important, while fever and vomiting are usually self-limiting. Adverse effects of transfusions can be divided into non-immunologic (pyrogen-mediated fever, transmission of infectious agents, vomiting, mechanical hemolysis, congestive heart failure, hypothermia, citrate toxicity, pulmonary complications) and immunologic reactions (acute and delayed hemolytic transfusion reactions, urticaria to anaphylaxis, acute respiratory distress, graft versus host disease). Note that some clinical signs may be caused by both mechanisms. Despite the variety of blood types and the limited degree of compatibility testing in clinical practice, transfusion reactions are rarely reported.

**Blood Donors and Sources**

Many larger veterinary hospitals have permanent canine and/or feline blood donors to cover their transfusion requirements or in case fresh whole blood or platelet-rich plasma (concentrate) is needed. Several larger voluntary blood donor programs have emerged with client or staff owned dogs. More than a dozen commercial canine blood banks have been established in the United States and deliver overnight blood products. Autologous (self) transfusion refers to the donation of blood by a patient four weeks to a few days prior to surgery when major surgical blood loss is anticipated. Blood can also be collected immediately prior to surgery. The patient will be hemodiluted with crystalloid and colloid solution and receives the blood when excessive bleeding occurs or after surgery. Autotransfusion is another autologous transfusion technique in which freshly shed blood salvaged intra-operatively or following trauma can be reinfused after careful filtering.

Blood donors should be young adult, lean, and good tempered animals, and weigh at least 23 kg for dogs (to donate 450ml); have no history of prior transfusion; have been regularly vaccinated and are healthy as determined by history, physical examination, and laboratory tests (complete blood cell count, chemistry screen, and fecal parasite examination every 6-12 months) as well as free of infectious diseases (testing depends on geographic area but may include regular microfilaria, Brucella, Hemomycoplasma, Babesia, Ehrlichia, Anaplasma, Borrelia, Leishmania spp. testing in dogs. Donors should receive a well-balanced, high performance diet, and may be supplemented twice weekly with ferrous sulfate (Feosal, 10 mg/kg), if bled frequently. Packed cell volume (PCV) or hemoglobin (Hb) should be >40% and >13 g/dl in canine donors.

**Blood Collection and Component Preparation**

Canine donors are generally not sedated. Blood is collected aseptically by gravity or blood bank vacuum pump from the jugular vein over 5 to 10 minute period. Plastic bags containing citrate-phosphate-dextrose-adenine (CPD-A1) with or without satellite bags for blood component separation are optimal. These commercial blood bags represent a closed collection system in which the blood does not come into contact with the environment at any time during collection or separation into blood components, thus minimizing the risk of bacterial contamination and allowing storage of the blood products. The maximal blood volume to be donated is 20 ml blood/kg or one regular blood bag unit of 450 ± 45 ml per ≥ 25 kg dog.

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

**Administration of Blood Products**

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

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

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

Rate of transfusion depends on the hydration status, degree of anemia, and general health condition of an animal. Initial rate is slow, starting with 1-3 ml over the first 5 minutes to observe for any transfusion reactions, even with blood

typed and/or crossmatched transfusions. In animals with cardiac failure, do not exceed 4 ml/kg/hr. Transfusion of a single bag should be completed within 4 hours to prevent functional loss or bacterial growth. Volume of blood component to be administered depends on the type of deficiency and size of the animal. In anemia: Volume (ml) of whole blood = 2 x PCV rise desired (%) x body weight (kg) or in other words, administration of 2 ml whole blood/kg body weight raises the PCV by 1%. If packed red cells are used without prior resuspension in a red cell preservative, closer to half the volume is administered, since packed red cells have a PCV of 70-80%. In the absence of bleeding and hemolysis, at least 80% of transfused erythrocytes survive 24 hours (required blood bank standard) and transfused erythrocytes may be thereafter expected to have a normal life-span (~110 days in dogs). Response to transfusion is carefully monitored by obtaining PCV/TP readings prior to, immediately, 2, 4, 6 and 24 hours post-transfusion, and observing the clinical parameters of a patient.

In thrombocytopenia or thrombopathia, platelet transfusions are only used with life-threatening bleeding. One unit of Platelet Concentrate, Platelet Rich Plasma or Fresh Whole Blood will increase the platelet count by 10,000/µL in a recipient weighing 30 kg. Platelet counts are monitored prior, 1 hour and 24 hours after the platelet transfusion.

In coagulopathies and von Willebrand's disease, Fresh Frozen Plasma at 6-10 ml/kg is an initial dose to stop bleeding or avoid excessive bleeding during surgery. In some cases, larger volumes may be needed to control bleeding. Depending on the coagulopathy, repeated administration of FFP may be required. Because of the short half-life of factor VII and VIII and von Willebrand factor, deficient animals need to be treated twice to four times daily. Other coagulopathies may be treated daily. Cryoprecipitate at a dose of 1 Cryoprecipitate unit/10 kg or 2-4 ml/kg body weight twice daily is ideal to treat hemophilia A and von Willebrand's disease. Plasma support should be provided for an additional 1-3 days after the bleeding has been controlled to allow for healing and prevent rebleeding.

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# ANATOMÍA DE LA CÓRNEA DEL OJO

La córnea es uno de los órganos más sensibles de nuestro cuerpo. Representa una parte de la capa superior del globo ocular (membrana fibrosa), tiene transparencia y sirve tanto para refractar los rayos de luz como para proteger las estructuras internas del ojo debido a su densidad. En su estructura, se asemeja a un pastel de capas, que está cubierto con una costra densa en ambos lados, y el interior son capas más delgadas de pastel.
La superficie interna de la torta es el epitelio interno, que está unido a la membrana de descemet, es una capa de células poligonales que están estrechamente adyacentes entre sí. La parte mediana es la estroma corneal, que consiste en tejido conectivo fibroso denso. Contiene una gran cantidad de fibrillas de colágeno, con células incluidas entre ellas, los queratinocitos. La estroma es hidrófilo, por lo tanto, si el epitelio externo o interno está dañado, las fibras de colágeno absorben la humedad y la córnea puede perder su transparencia. La capa más externa está representada por un epitelio no queratinizado de múltiples capas. Consta de 5-6 capas de células y se encuentra en la membrana basal, unida a ella por semisdesmosomas. A su vez, la membrana basal proporciona una estrecha conexión del epitelio con el estroma subyacente, que muestra una organización clara y reflexiva de los tejidos de los organismos vivos que la naturaleza ha creado de manera inusual y correcta.
Pero las criaturas biológicas ideales, como el tejido corneal del ojo, están sujetos a diversos cambios patológicos en la arquitectura, que son característicos de todos los organismos vivos en nuestro complejo hábitat. Las condiciones en las que se viola la integridad de la córnea, los principios de diagnóstico de las patologías de la córnea y el tratamiento de los pacientes con sus patologías se analizarán en detalle en nuestras conferencias.

**Condiciones de urgencia en oftalmología veterinaria.**
La capacidad de navegar rápidamente en el lugar y prescribir el tratamiento correcto es una de las habilidades exitosas de un profesional practicante. Esto es especialmente importante en condiciones agudas, cuando el tiempo es muy importante. El oftalmólogo veterinario muy a menudo tiene que lidiar con afecciones agudas graves en los pacientes, que van desde conjuntivitis, reacciones alérgicas e inflamatorias agudas, que terminan con lesiones y ceguera aguda.
Todas estas condiciones pueden llevar a la pérdida de la vista del animal y, por lo tanto, a una violación de su calidad de vida y estado en la sociedad. Nuestro objetivo es hacer todo lo posible para que el paciente encuentre consuelo y no pierda de vista.
En la conferencia, consideraremos condiciones tales como conjuntivitis aguda, edema alérgica del párpado, erosión y úlceras corneales, ataques agudos de glaucoma y ceguera aguda.
Aprendemos cómo comportarnos en tales situaciones y cual tratamiento prescribir para la rápida recuperación del paciente.

**Glaucoma en perros y gatos.**
El glaucoma es una enfermedad crónica caracterizada por una presión intraocular elevada y neuropatía óptica glaucomatosa.
El glaucoma en perros y gatos tiene muchas causas: desde el desarrollo deficiente del globo ocular y la predisposición genética hasta el proceso inflamatorio secundario y la

oncología. Los bloques hidrodinámicos, que tienen diferentes etiologías, también desempeñan un papel importante en el ajuste de la presión intraocular. La identificación de signos tempranos de glaucoma permite el diagnóstico en etapas tempranas del desarrollo, pero también para prescribir un tratamiento patogénicamente sano de manera oportuna.

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# EXAMINING THE HORSE WITH COLIC

Evaluation and decision making for a horse with colic can be influenced by numerous factors – some medical, some financial and some emotional. Veterinarians have to be prepared to contend with all of these influences and attempt to make decisions that are good for the horse and the horse's owner. As no hard and fast rules exist for many of these colic scenarios, it is important to have a general plan of how to provide for the horse in medically correct and humane ways, as well has help the client navigate through some of the emotional and ethical decision making.

It is important to note that trends have continued to hold true that 95% or greater of horses with colic do not need to leave home and will recover to return to original roles. The greatest majority of these cases require only one veterinary visit. This is perhaps why so many horses are treated with flunixin meglamine by an owner/trainer with little or no veterinary assistance. Yet in this common use of certain medications lies complicating factors that can make a veterinarian's job difficult – interpreting a horse with colic in the face of owner administered medications. Noting that most horses do not require referral to a hospital, this potential should be discussed at some point early in the history taking or examination.

A reality that can be very frustrating for everyone involved with working up colic cases, is that nailing down an absolute, accurate diagnosis of the cause for most colic cases is not possible at home. So decisions about what to do with an affected horse can become uncomfortable as a veterinarian makes the best informed and examination-driven decisions that may become a "best guess". It's not fun, but it is a reality of the current state-of-the-art of colic diagnosis. Very often, a surgical exploration, or a post mortem examination are required for an anatomically correct diagnosis.

All good decision making should begin with as complete an understanding of medical history as possible. The question "When was your horse last normal" has served well to get an accurate replay of what the horse with colic has experienced. So many thought processes can be influenced by the answers to historical questions that this should not be overlooked. For example:

1. Does the horse have a history of colic?
2. When did the current symptoms begin?
3. Description of colic signs?
4. Any feed changes occur?
5. Medications administered?
    a. What?

b. When?
c. How much?
d. What kind of response has been observed?

A thorough physical examination is indicated for every horse with colic. If a horse is well known to a veterinarian, some short cuts can be made in the examination that may be inappropriate for a first time or relatively unknown horse. Determining vital signs is essential to a working data base. Getting the body temperature before any medications are administered, and before a rectal examination is performed is important. Fever is a cardinal sign of a certain subset of disease processes that will influence management decisions. Being uncertain of real temperature can be frustrating. The importance of heart rate in colic cases cannot be overstated. Sustained heart rates at 60 or more beats per minute indicate that the potential to survive the current colic episode are declining. Once again, it is important to determine heart rate before the administration of medications that could alter a baseline reading (IE: sedatives for analgesia).

Every horse with colic signs, especially horses that an owner has declared cannot leave home for referral to a hospital , should have a nasogastric tube passed and a rectal exam performed. Passing a stomach tube for horses with severe colic pain, that originates from small intestinal obstruction, can be life-sustaining or lifesaving due to stomach decompression prior to rupture. This can also be viewed as a good diagnostic test for potential involvement of the stomach and small intestine. A thorough examination per rectum can provide limited, but predictable information in regard to potential causes of colic symptoms.

Abdominal ultrasound examination can also be a very valuable asset to narrowing a diagnosis. Many keys have been determined that help improve colic diagnosis. Included, but not limited potential findings are:

1. Small intestinal distention
2. Stomach distention
3. Nephrosplenic entrapment
4. Intestinal wall thickness status
5. Free peritoneal fluid
6. Right dorsal colon displacement witnessed by visualization of colonic vessels on the right side

Abdominocentesis can be an asset to the examination of the horse at home. Negative attempts to harvest fluid can be an encouraging and normal finding. Ultrasound guided placement of a needle or chosen instrument can help find fluid. Peritoneal fluid samples that becomes cloudy, opaque, color changes toward orange and red, and frank particulate matter demonstrate increasing concern and likely decreasing prognostic thoughts.

With the advent of "horse-side" diagnostic testing, many points of data can be determined today that not long ago required an elaborate laboratory and many hours of time. When possible, PCV, TP, WBC, lactate, and other cellular and chemistry information can aid diagnostic, therapeutic and prognostic determinations.

Veterinarians develop techniques and procedures that become comfortable and familiar with more and more colic cases experienced. One of these assessment tools that has become predictable and useful for many is the administration of alpha 2 sedative agents in lower than label doses. The drug of choice for this use is most often Xylazine. The following protocol has been very useful once a sound physical exam has been completed and analgesia of colic pain is desired:

For the typical adult1000-1200 lb horse:

1. 200 mg (2 ml) Xylazine IV
    a. Expected sedation duration is 20-30 minutes)
2. If horse becomes painful again before expected end of drug sedative effects:
    a. Second 200 mg dose of xylazine
3. If horse becomes painful again before expected end of drug sedative effects:
    a. Third 200 mg dose of Xylazine
4. If the horse fails to remain comfortable and painful symptoms recur, this horse is unlikely to respond to conservative treatment or do well staying at home. This is a reasonable time to revisit referral away from home or have more directed discussion of a possible decision for euthanasia.

With as much information and data from examination as possible, a veterinarian's role is to advise the client and perform appropriate treatment for an affected horse. Commonly, veterinarians also become the source for advisory information as well. Clients want numbers that address cost and also prognosis. While these are often difficult to narrowly define, a general rule is that the more intense the medical needs, the higher the costs and the lower the prognosis for long term recovery. Therefore, the veterinary team becomes the initiator of discussion on:

1) How "far" does an owner want to go with diagnosis and treatment, including likely costs
2) How "much" is the owner comfortable with the horse experiencing colic pain
3) How to define "humane" treatment and expectations
4) When considerations of euthanasia are appropriate and acceptable

# COLIC EXAM

Historical information is important to final diagnosis of the causes of colic in horses. A complete physical examination, including vital signs is also essential. Other examination techniques that can assist diagnostic understandings include: passage of a nasogastric tube, rectal examination, abdominocentesis, ultrasound examination of the abdomen and systemic blood cell and chemistry assessments. In some instances abdominal radiography and use of an endoscope can also help determine causes of colic.

**Angular and Flexural Limb Deformities**

Angular limb deformities (ALD) and Flexural limb deformities (FLD) can occur at predictable times in a horse's life. Congenital presence of these abnormal limb conformations can be self-correcting with close monitoring of grow and control of exercise. When ALDs and FLDs develop with grow, or are acquired, veterinary intervention is often required to achieve normal limb conformation as adult horses. Appropriately timed and specific medical and surgical treatments are often successful in returning young horses to normal skeletal structure.

**Synovial Wounds**

Wounds that penetrate to the depths of synovial compartments can be devastating to future soundness of affected horses. Therefore, early detection and complete diagnostic understanding of such wounds is essential for successful treatment and outcome. A septic synovial environment can destroy articular cartilage and encourage fibrous adhesion formation so timely sterilization of wounded synovial compartments is the goal such that these complications can be avoided and normal function can be returned.

**Respiratory Biosurveillance**

A corporate-sponsored Biosurveillance program of equine respiratory disease in North America is now in its 10$^{th}$ year. Over 8500 horses have had blood and nasal swabs submitted for diagnostic assistance during the presence of upper respiratory disease. Horses need to be febrile with at least one other symptom of respiratory disease to participate. To date Equine Herpes Virus 4 and Equine Influenza are the

most common pathogens isolated from horses in North America. This has led to the development of vaccines with more relevant Equine Influenza strains included.

**Zoonotic Diseases**

Veterinarians working with horses that have symptoms of infectious and contagious disease must be aware that some of the responsible pathogens can also cause disease in humans. Some of these can be lethal (IE: Rabies). Therefore, appropriate biosecurity practices must be defined and closely followed such that animal owners, caretakers and veterinarians do not become affected. Good hygiene and limiting contact to potential zoonotic diseased animals is the best way to start management of suspect cases.

**Vaccination**

The American Association of Equine Practitioners has developed guidelines for vaccination practices in North America. Two general recommendations are suggested: Core Vaccines and Risk-Based Vaccines. The Core Vaccination program is suggested for all horses and includes Rabies, West Nile Virus, Eastern and Western Equine Encephalitis and Tetanus. Risk-based vaccine suggestions are made for regional and seasonal concerns and often may be sport regulated by oversight boards. These can include: Equine Herpes, Equine Influenza, Botulism, Potomac Horse Fever, Strangles, Equine Viral Arteritis, Rotavirus and others. Vaccination is an important tool in preventative health care practices. Sound immunologic understandings can help guide veterinarians and horse owners to best decisions for individual horses, and herd management practice as well.

# ANGULAR AND FLEXURAL LIMB DEFORMITIES

Foals and young horses with angular limb defects have long been treated with hemicircumferential periosteal transection and elevation ("periosteal stripping") or with more aggressive treatment based on orthopedic implant management. New studies have questioned the efficacy of periosteal stripping and required veterinarians to take another look at this procedure in the management of angular limb defects in growing horses.

Periosteal stripping has been considered to stimulate growth on the growth-retarded or concave aspect of the limb. Several descriptions of how this occurs have been theorized through time. The first was that transecting and elevating the periosteum would create a release phenomenon. This would release an inhibitory role of the periosteum at the physis and allow the physis "catch up" to the convex aspect of the limb resulting in correction and straightening of the angular defect. However, it has been interesting to note that periosteum over these sites does not spring or "release" when incised and will actually heal in place over a relatively short period of time. This has called into question any physical role the periosteum may have. A second theory associated with periosteal stripping is that local disruption or stimulation of this tissue may result in local growth factor release and that this may have a stimulatory effect on the physis under the incised periosteum. This is interesting in light of the fact that even "key hole" periosteal incisions and repeated puncture of the periosteum with hypodermic needles have appeared to deliver similar results as the classic surgical stripping procedure.

It is also interesting to note that many foals that did not have any periosteal manipulations performed have straightened angular limb defects over time. Classically this has been observed in foals with less severe angulation, however, many foals with difficult deformities have been witnessed to correct partially or completely. This has lead investigators (Wilson, et al) to question if periosteal stripping procedures or other factors are actually responsible for limb straightening. To pursue their question these investigators used age-matched siblings and created angular limb defects with the implantation of transphyseal bridges of screws and wires. These were removed when equitable angular limb defects occurred. The groups were then split to treatment groups receiving either periosteal stripping or no treatment. The finding that has called into question the efficacy of periosteal stripping is that the two groups appeared to correct to similar degrees. The conclusion of this study was that hemicircumferential periosteal transection and elevation may not be a growth stimulation procedure and may not be indicated for foals with angular limb defects.

At this time, however, there remain several questions related to this study and our understanding of the best treatment for foals with angular limb defects. One large question is: Does an experimentally arranged model of angular limb defects really reflect the spontaneous condition in growing foals? This is a very debatable question at this time and may require larger numbers of naturally occurring cases to finalize a sound opinion. Included in this questioning is: "Do physes associated with naturally occurring angular defects behave similarly to normal physes forced into angular conformation?" It is conceivable that physeal behavior and response to weight bearing forces is different in these two scenarios. Severe angular limb deficits can result in physeal inflammation and periosteal new bone production resulting in even more severe angular defects. Defects of far less severity have been observed to spontaneously correct. Perhaps a better understanding of the molecular biologic environment at the physes of these

challenged limbs will help with this understanding. Until then, it is difficult to completely condemn periosteal stripping as an efficacious procedure. Many foals over the years have appeared to be positively assisted with this procedure. Yet the question does remain about how some foals do spontaneously improve.

It has been widely accepted that angular limbs in foals of advancing age and those with severe deformities at earlier ages can be improved with the implantation of devices that cross the physes on the growth rich or convex aspect of the limbs. Transphseal bridging is still the standard. The down side of this procedure is the requirement of appropriately timed removal of implants. This places a lot of responsibility on owners and veterinarians to time the second surgical procedure such that over-correction of the original defect does not happen. Foals and young horse from several weeks of age to over 18 months of age have had angular limb defects corrected with transphyseal bridging. The two classical means to accomplish this is either with transphyseal staples or screws and wires across the targeted physes. Recently, Drs. Hunt. Spirito and Rodgerson of Lexington, KY, have discussed the placement of a single screw across the convex aspect of the physes of foals with angular limbs. Results equitable to those achieved with staples or screws and wires have been reported. The encouraging aspect of this new procedure is the fact that the same good result can apparently be accomplished quickly with less soft tissue disruption and thereby less potential for complications.

Young growing horses with flexural limb deformities, what have often been referred to as “contracted tendons”, can present many frustrations. Firstly, tendons do not possess contractile properties so the old terminology does not apply well. Yet, why do these limb deformities occur. The best explanation is likely the presence of pain originating somewhere in the affected limb. The most common cause is physeal pain. Again an old term is “epiphyisitis” but this is probably best described by the term “physitis”. The pain from these sites may not be sufficient to produce overt lameness, yet young growing horse can become flexurally deformed if not treated appropriately and in a timely manner. These deformities are referred to as Type 1 when the limb approaches a vertical alignment and Type 2 when the limb flexes beyond 90 degrees. Most defects are observed at the distal interphalangeal joint and at the fetlock.

The first avenue of treatment is a reduction in exercise and judicious administration of NSAIDs for analgesia. This will correct many young horse defects and normal practices can soon be resumed. If no response is obtained then the transaction of distal and proximal check ligaments (desmotomies) can be considered. These procedures can be successful with milder deformities of short duration. Type 2 defects and flexural deformities that have been present for extended periods of time carry a less encouraging prognosis. If flexor tendons and joint capsules become involved the prognosis for soundness is poor.

# WOUNDS NEAR SYNOVIAL STRUCTURES

Wounds involving the synovial compartments of joints, tendon sheaths, and bursae can be debilitating and career if not life threatening injuries. Unlike juvenile forms of joint sepsis the most common route for inoculation of adult synovial structures is via direct penetration during wounding. Inoculation of these structures can be obvious from an open wound or more subtle from puncture wounds or extension from distant injury. It is vital to treatment success that wounds associated with synovial structures are considered contaminated until proven otherwise.

Horses with wounds of synovial structures can have obvious trauma with tissue disruption and/or loss or they may require examination due to very subtle wounds as with puncture trauma. Lameness is usually present but can vary in severity. Acute wounds that open a joint may not have lameness that would be typical of synovial sepsis but more consistent with the pain of only the wound itself. Many horses with open and draining septic joints do not demonstrate severe lameness until the outflow is occluded with granulation tissue. When this occurs or the wound is such that a closed synovial environment remains, the horse can demonstrate lameness of grades 4-5/5.

Physical examination of horses with this type of wound should include determination of the type of wound and then concentrate on determination of synovial compartment involvement. Lacerations, de-gloving injury, and puncture wounds are the most common means of involving equine joints and synovial sheaths and bursae. Extension from wounds distant from these structures can occur and the possibility should be investigated. Other supporting tissue and normal interior tissue (ie; tendon) should be evaluated to determine the total extent of the traumatic wound. Lameness can again be variable dependant on the timing of evaluation in relation to wounding, the tissues involved, and the ultimate presence of contaminants. The horse should be examined for systemic repercussions from the wound and any resultant complications.

The diagnosis that a wound does indeed involve a synovial structure can be obvious on physical examination or may require some extensive investigation. When performing an examination on the suspected tissue it is recommended to handle the tissue in an aseptic manner to avoid iatrogenic inoculation of these special tissues. A rule of thumb would be to handle the tissue as if it remains sterile when examining it and assume it is infected when treating that structure. It may be essential to clean the wounded region before further diagnostic procedures can be safely performed. Lavage with sterile aqueous solutions is recommended unless heavy contamination is obvious, when tap water is acceptable. When the wounded tissue is appropriately cleaned, a sterile probe can assist diagnosis by investigating the depths of a particular wound. It is preferable to probe gently so as not to puncture into an otherwise normal structure. A sterile hypodermic needle can be placed into the structure under question to aspirate

synovial fluid for evaluation and to administer a sterile balanced polyionic solution. It is best to place the needle as distant from the wound as possible to avoid inadvertent contamination. Sterile solution is injected with volume and pressure sufficient to distend the synovial compartment. The wound should be observed during this procedure. If the fluid is seen to flow from the depths of the wounded tissue then the synovial structure should be considered contaminated and potentially infected even if synovial fluid samples demonstrate normal cellular and protein contents. Definitive diagnosis continues to rest on culture and sensitivity identification of microorganisms from the synovial environment. Cytology and gram stain results can provide a preliminary working diagnosis.

After physical examination and manipulations, imaging studies may be necessary either for diagnosis or for establishment of a baseline imaging study. Plain film radiography is the most common imaging modality used. Gas patterns with in the synovial compartment in question can be consistent with involvement with a wound. Obvious disturbance of related osseous structures can confirm joint involvement. If the examination is performed after sufficient time, loss of cartilage and lysis of subchondral bone may be evident as repercussions of synovial compartment sepsis. If a needle can be placed in the joint, a positive contrast intra-synovial study can demonstrate communication with a wound. After proper cleansing preparation, a catheter (large IV or small animal urinary) can be placed into the depths of the wound and positive contrast medium injected. The resulting fistulogram may also demonstrate communication between the wound and the synovial structure in question.

When a wound is confirmed or under strong suspicion to involve a synovial structure, treatment should be initiated at the earliest possible opportunity. When faced with an open wound into a synovial compartment, two options are immediately possible. Primary closure of the capsule of these structures requires that the internal environment be as clean as possible and ideally sterile. This decision is usually made based on the amount of obvious contamination of the tissue and the duration since wounding when treatment can be initiated. If the synovial compartment has been sharply opened with minimal trauma and contamination and the horse is available for immediate post-injury treatment, primary suture closure can be successful. The ability to appropriately close wounds of this type is infrequent and may be most dependant on husbandry practices. Wounds with obvious contamination and longer duration may be best treated as open wounds or have drainage systems placed within the synovial compartment. The goals of treatment are to remove the contaminant, prevent it from establishing infection, preserve the synovial environment, and return the tissue to the functional status of pre-wounding. These goals are best achieved by thorough lavage to physically remove debris and microorganisms, systemic antibiotic administration, and anti-inflammatory therapy. The reduction in the inflammatory insult to the synovial structure can be accomplished by administration of systemic non-steroidal anti-inflammatory drugs (NSAID) and local administration of dimethylsulfoxide (DMSO) and sodium hyaluronate (HA). The use of HA has been clinically beneficial in the face of sepsis, however, there may be some early

evidence that it may bind compliment in a similar manner as polysulfated glycosaminoglycans. Therefore caution is suggested.

Treatment of puncture wounds and wounds that contaminate a synovial structure from indirect extension require similar treatment as open wounds. Lavage can be best accomplished with arthroscopic guidance and administration. Greater volumes of lavage solution can be delivered and debris can be visualized and removed from the intra-synovial space. This may also be the best way to lavage structures involved with large open wounds. A schedule of lavage is difficult to prescribe as each wound can be very different in nature and response to treatment. Every other day lavage has been suggested. This can be amended to more or less frequent administration dependant on the horse's clinical improvement and results of serial synovial fluid analyses. Steadily decreasing lameness and return to a normal synovial fluid profile is solid evidence of improvement. Indwelling positive suction drains have been reported as successful in horses with septic arthritis and tenosynovitis. Long term antibiotic therapy is often necessary (up to 8 weeks) to totally rid the synovial environment of microorganisms.

Regional perfusion of antibiotics is an accepted modality for increasing local antimicrobial treatment in a specific site. With a tourniquet placed above the septic site, antibiotics can be administered intravenously, into joint spaces and in to the medullary cavity of long bones. Dosing schedules have been somewhat arbitrary but most practitioners repeat doses every 24 to 48 hours. Dosage quantities have also been somewhat variable (full systemic body does to 1/3 this dose at each administration). The benefit of regional perfusion is gaining higher local presence of antibiotics at the septic synovial site and therefore, more likely effect of the chosen drug.

Horses that survive the treatment of synovial structure wounds can benefit from additional ancillary therapy. Passive motion and staged active use of the wounded limb(s) can encourage return to a normal synovial compartment. Adhesions can be modified with exercise and reduced in severity or lengthened so as to not influence range of motion in tendon sheaths and joint capsules. Recent evidence supports the use of HA in tendon sheaths to reduce or prevent adhesions after insult to these tissues. The same may be true for joints. The administration of PSGAG may assist the synovial compartment return to normal but care must be taken that this agent is not placed into the synovial space when microorganisms are still present. The compliment binding of the PSGAG can allow complications or reestablishment of infection.

The prognosis for horses with wounds into synovial structures id always guarded to poor for return to athletic soundness. This prognostic picture can change dramatically with appropriate treatment. This is especially true when aggressive treatment can be initiated in as early and timely a manner as possible.

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# HOW TO DEAL WITH CASTRATION COMPLICATIONS

**Objectives of the Presentation:**

- To review the different techniques of castration
- To review the different complications that may be encountered and how to deal with them
- To discuss peri-operative management strategies that may help prevent the development of complications

**Overview of the Issue and Introduction:**

Castration is one of the most common surgical procedures performed in equine practice. Open, closed, and semiclosed techniques are used for castration of horses and the procedure may be performed in a standing, sedated animal or in a recumbent animal under general anesthesia.[1-4] Although the procedure is considered to be routine, complications can occur and remain the most common cause of malpractice claims against equine practitioners in North America.[2] The majority of complications encountered after castration tend to be mild and resolve easily with treatment, but more serious or life-threatening complications, such as eventration, peritonitis, and hemorrhage, can also occur. A thorough knowledge of male reproductive anatomy and physiology combined with a good surgical technique help to reduce the rate of complications associated with the procedure.[2,3]

**Pre-operative Considerations:**

All equids to be castrated should undergo a full physical examination prior to surgery including palpation of the testicles. Equids to be castrated under injectable general anesthesia should have an intravenous (IV) catheter placed in a jugular vein via aseptic technique prior to surgery. To facilitate catheter placement and palpation of the testicles prior to castration, animals in our practice are generally administered a combination of xylazine hydrochloride (0.5 mg/kg) and butorphanol tartrate (0.01 mg/kg IV) for sedation.
All equids undergoing any surgical procedure should be current on tetanus prophylaxis. Some veterinarians chose to administer one dose of procaine penicillin (22,000U/kg) prior to surgery. The use of antibiotics to prevent post-operative infections is debatable and generally based on clinician preference. Pre-operatively use of non-steroidal anti-inflammatories (phenylbutazone 2.2mg/kg; flunixin meglumine 1.1mg/kg) are recommended by some clinicians.

**Anaesthetic and Surgical Techniques:**

Horses to be castrated under general anesthesia are pre-medicated with xylazine hydrochloride (1.1 mg/kg, IV), and when sedation is deemed adequate, anesthesia is induced with ketamine hydrochloride (2.2 mg/kg IV) and diazepam (0.05 mg/kg, IV). The horses are placed in lateral recumbency with the hind limbs restrained to facilitate surgery. Anesthetic depth is monitored on the basis of heart rate, respiratory rate, movement, palpebral reflex, and presence of nystagmus. When an additional dose of anesthetic agent is deemed necessary to maintain an adequate plane of anesthesia (i.e. if anesthetic depth was determined to be too light), ketamine (1.1 mg/kg, IV) is typically administered in combination with xylazine hydrochloride (0.5mg/kg IV). The scrotal area is routinely prepared for surgery with dilute povidone-iodine followed by intra-testicular injection of 2% lidocaine hydrochloride, the dose of which may vary according to size of horse (typically 10-15 mLs per testicle).
For horses castrated under standing sedation chemical restraint is achieved using a combination of detomidine (0.01 mg/kg, IV) and butorphanol (0.01 mg/kg, IV). A twitch may also be applied to facilitate restraint. Lidocaine is always injected intratesticularly and locally along the planned incision sites[7] on each side of the median raphe.
In one study[8] thirty-one horses were castrated while standing, of which 5 (16%) developed complications, compared with 28 of 293 (9.6%) castrated under general anesthesia; however, the odds of developing a complication did not differ between these 2 categories. These findings are similar to those in a previous study [9] in which horses castrated while standing had a complication rate of 22%, compared with a complication rate of 6% for those in which castration was performed under general anesthesia with primary closure of the scrotal incisions. Castration in standing horses minimizes the risk of death associated with general anesthesia and traumatic injury during recovery; it is also less expensive than surgery with general anesthesia and can be performed in the field. In general the horses chosen to be castrated while standing are young adults with a good temperament or of a larger breed type.

The three surgical techniques include open, closed and semi-closed. The open technique requires less dissection than does the closed technique and is therefore preferred by some veterinarians.[3] In one study[8], a higher proportion of horses that underwent semiclosed castration (18/77; 23.4%) went on to develop complications, compared with those that underwent closed castration (15/247; 6.1%). To date, no controlled study has been performed to investigate the superiority of either technique. Investigators in another retrospective study[10] found that use of a semiclosed technique resulted in a higher occurrence of infection, edema, and excessive hemorrhage, compared with open or closed techniques. Potential reasons for an increased complication rate associated with the semiclosed technique may include increased tissue handling, increased contamination, or longer duration of surgery, compared with the closed or open techniques. Scrotal incisions are generally allowed to heal by second intention and left unsutured. Primary closure may also be performed, however, this is not typically performed in the field.

The most commonly used emasculators include Reimer, Serra and improved White's emasculators. The Reimer emasculator crushes the spermatic cord and a blade operated on a separate handle cuts the cord distally. The improved

White's and Serra emasculators simultaneously crush and cut the spermatic tissue.[3] One study[10] demonstrated a significantly higher rate of hemorrhage associated with the use of the Reimer emasculator compared with the Serra emasculator; however, to the author's knowledge no prospective study directly comparing the use of instruments has been performed. The importance of properly maintained surgical instrumentation, regardless of which emasculator is used, should be emphasized. Thorough cleaning following use and regular maintenance can help improve longevity and functionality. The Henderson Equine Castrating Instrument is another available instrument to facilitate castration. When using this instrument, one hand grasps the testis and the instrument is clamped across the entire cord proximal to the testis such that a closed castration is performed. Slight tension is placed on the drill and the instrument is held parallel to the cord. The testis, which is grasped within the instrument, is rotated slowly for about 5 turns and then the speed of the rotation is increased gradually while keeping tension on the cord. After approximately 20–25 rotations, the cord separates about 8–10 cm proximal to the instrument. The twisting action of the spermatic cord effectively seals the severed vessels.[3]

Some veterinarians will use ligatures around the vasculature of the spermatic cord in order to reduce the incidence of post-operative hemorrhage. It has previously been recommended that all donkeys have ligatures with absorbable suture placed as part of the procedure as a preventative measure against any possible hemorrhage, because blood vessels of the spermatic cord are typically larger in donkeys than in horses.[11] In a recent study[8] only 17 (5.2%) cases of a total of 324 had ligatures placed as part of the castration procedure. The overall rate of hemorrhage as a complication in this study was (6/324; 1.8%) indicating that the use of ligatures may not be necessary to prevent post-operative hemorrhage.

## Complications

*Post-operative swelling and seroma formation*

Post-operative swelling affecting the preputial and scrotal regions is common following castration and is usually greatest 4-5 days after surgery has been performed.[13] In previous studies[10,12,14] the incidence of swelling and seroma formation was 27.6%, 3.8% and 24.3%. Excessive swelling may be attributed to inadequate drainage, inadequate exercise following surgery, excessive tissue trauma at the time of surgery, or infection.[13] Older horses have also been reported to be more prone to development of excessive edema following castration, compared with younger horses.[15] Following castration, exercise, cold-water treatment of the area, and administration of NSAIDs can help to minimize swelling.[4] Excessive postoperative swelling can be painful and may result in an unwillingness to exercise, causing premature closure of the surgical wound, further compounding the problem.[3,13] Adequate postoperative exercise consisting of handwalking or trotting daily for 10 to 14 days can help prevent premature closure of the surgical wound and seroma formation. Treatment involves administration of NSAIDs to reduce swelling and increase the tolerance of the animal to exercise and move around. Where seroma formation has occurred it is beneficial to digitally re-open the scrotal wounds to facilitate drainage in a sterile manner. Therapy with systemic antibiotics is indicated

where signs of infection are present such as purulent discharge although they are usually administered prophylactically in cases of seroma formation to prevent the development of an infection.

*Infection*

Infection is a commonly reported complication of castration.[3,9,10] Infection may not be evident until days after the surgery was performed. Clinical signs may include fever, swelling, lameness or discomfort when exercising and drainage from the incisions. Infection may also follow formation of a seroma allowing the development of a 'septic seroma'. The use of ligatures has been implicated as a cause for post operative infection potentially acting as a nidus.[10,15] Treatment involves opening of the scrotal incisions to facilitate drainage, similar to that performed for a seroma. Exercise to help prevent premature closure of the incisions and promote drainage should also be started. Administration of broad-spectrum systemic antibiotics should be instituted. A sample taken from deep within the scrotal incisions may be taken and submitted for culture and sensitivity to help direct antimicrobial therapy. Infections that do not resolve with initial medical therapy should be referred to a surgical facility as surgical resection of infected tissue may be warranted to resolve the issue completely.[2,16] Scirrhous cord, which may also be referred to as funiculitis, refers to the chronic infection of the spermatic cord stump where the scrotal incisions heal but the stump continues to be infected or abscess eventually forming a draining tract. It may develop as an extension of a scrotal infection or from a contaminated emasculator or ligature. This is generally caused by a *staphylococcus* spp. It is usually palpable as a firm mass in the inguinal region and may not evident for months to years. In the early stages treatment with appropriate antimicrobials may be sufficient but occasionally treatment involves surgical resection of the infected stump.[2,3] Removal of an infected cord within a few weeks after castration is generally much easier than removal of a chronically infected cord due to the presence of fibrous adhesions to the parietal tunic and their associated blood supply. *Champignon* is a term used to describe a type of infection of the spermatic cord caused by *Streptococcus*. It is characterized by a mushroom shaped nodule of granulation tissue that protrudes from the scrotal incisions with an associated purulent discharge. This was a more common complication before the advent of emasculators to help control hemorrhage but is now rarely seen.[3]

*Eventration*

Eventration is an uncommon complication of castration that occurs when a portion of intestine prolapses through the inguinal canal and out of the scrotal incision. It typically occurs within 4 to 6 hours after castration[13] but has been reported to occur up to 12 days following surgery.[17] Investigators in other studies[10,18,19] found the incidence of eventration to be 2.96%, 0.4%, and 0.2%. In another study[8], eventration occurred in only 1 of 324 (0.3%) horses. In that study, the incidence of eventration was low, despite the lack of use of ligatures as part of the routine procedure in most horses. This suggests further investigation may be needed to determine whether ligatures provide an advantage when castrating horses of breeds other than those reported to be at an increased risk of eventration. Eventration has been hypothesized to result from increased abdominal pressure, presence of a large inguinal ring, leg

position during recovery from general anesthesia, and possibly excessive exercise[1]. One study[12] found that common vaginal (parietal) tunic ligation significantly reduced the incidence of omental herniation and eventration, with only 1 of 131 (0.8%) evaluated horses developing eventration. That study focused on the castration of young draft horses, a breed type reported to be at increased risk of eventration after castration.
Protrusion of omental tissue through the inguinal rings can also occur following castration. A thorough examination in a well sedated horse should be performed to assess the type of tissue protruding as occasionally subcutaneous tissue may be found protruding through the scrotal incision. In most cases of minor omental prolapse emasculation of the tissue can be performed. The animal should be confined to a stall to prevent more tissue prolapsing and systemic antimicrobial therapy should be instituted to prevent an ascending infection or peritonitis. Where severe herniation of omentum has occurred surgery under general anesthesia may be necessary to facilitate ligation and transection of the tissue. It is also advisable to perform a rectal examination to allow examination of the inguinal rings and ensure there is no intestinal prolapse through the rings.[15,16]

*Hemorrhage*
Some hemorrhage is normal following castration in the immediate post-operative period when the horse stands up from anesthesia or immediately after the emasculators have been removed. When bleeding occurs in the form of a steady drip or stream for an excessive period of time (>15 minutes) it should be addressed.[2] The most common source of bleeding post-operatively is the testicular artery but can also occur from the testicular vein or subcutaneous vessels. Initial therapy should be aimed at identifying and eliminating the source of hemorrhage. The stump of the spermatic cord can be identified and the individual bleeding vessel isolated and ligated or if enough of the cord can be exteriorized the entire cord can be emasculated again. This, however, can be difficult in the standing animal and may necessitate general anesthesia. If the source of the bleeding cannot be identified the scrotal incision can be packed with sterile gauze which can be left in place for 24-48 hours by suturing the incisions closed. In general these horses should be placed on oral systemic antibiotics as a precautionary measure to reduce the incidence of infection.
Other therapies reported as adjunctive treatments include use of aminocaproic acid, that acts to decrease fibrinolysis, given at a dose of 20-100mg/kg IV.[8,16]
Other treatments reported include the use of diluted formalin (0.5-1.0%) IV to decrease hemorrhage post-operatively.[3] Referral should be considered where substantial blood loss has occurred or signs of hypovolemic shock are evident.

*Peritonitis*
The vaginal tunic derived from the peritoneum continues through the inguinal canal to line the interior of the scrotum. It is composed of 2 layers, the visceral tunic which attaches firmly to the *tunica albuginea* around the testis and the parietal tunic, which is continuous with the parietal peritoneum of the abdomen. As a result of this communication many horses exhibit a non-septic peritonitis, characterized by elevated cell counts >100 x $10^9$/l, for up to 5 or more days following castration.[3] Although peritoneal inflammation is common post

castration, bacterial peritonitis is a rare complication where an elevated nucleated cell count with presence of degenerative neutrophils (>90%) and intracellular bacteria on abdominocentesis confirms the diagnosis. Clinical signs may include fever, depression, inappetance or mild signs of colic. Culture of peritoneal fluid is recommended if possible.[2] Clinical signs may include fever, depression, inappetance or mild signs of colic. Treatment should involve administration of systemic antimicrobials and anti-inflammatories, intra-venous fluid therapy and peritoneal lavage through the use of an indwelling abdominal drain if indicated.[3,16]

*Hydrocele formation*

A hydrocele, which may also be referred to as a vaginocele, is a painless accumulation of fluid within the vaginal cavity in stallions; however, it may also be seen in geldings up to months or years following castration.[3] They occur uncommonly after castration and are reportedly more likely to occur in mules. They are more likely to form after castration is performed using the open method as the parietal tunic is not removed using this technique. The swelling that develops may resemble a scrotal testis or hernia and on aspiration a clear, amber colored fluid will be obtained. On palpation, the swelling may be reduced by squeezing the fluid into the abdominal cavity.[2] Drainage of the fluid will only temporarily relieve the condition. Treatment involves the removal of the parietal tunic under general anaesthesia with the horse placed in dorsal recumbency. However, this is only usually necessary when the swelling interferes with functionality of the animal or for cosmetic purposes.[2]

*Penile Damage*

Penile damage during castration is almost exclusively iatrogenic and usually occurs when the penile shaft is mistaken for a testicle. If the penis is transected the horse should be referred immediately to a surgical facility for surgical repair or phallectomy.[2,16]

*Continued stallion-like behavior*

Serum concentrations of testosterone and oestrogen decline within 6 h after castration; however, castration may not always be successful in eliminating masculine or stallion-like behavior. These geldings are often referred to as ‘false rigs’.[3] While causes such as retention of epididymal tissue, adrenal cortex production of testosterone and heterotopic testicular tissue have been implicated, it is more likely that this persistent behavior is innate and represents normal social interaction among horses.[2] In cases where the continued masculine behavior is excessive or there is little information pertaining to the actual castration itself, hormonal testing can be performed to establish if there is residual testicular tissue present. Hormonal assays that may be useful include basal plasma or serum testosterone concentrations, basal oestrone sulfate concentrations or testosterone concentrations following human chorionic gonadotropin stimulation.[2] In general, males should be isolated from mares for 2 days following castration under routine circumstances. After 2 days, ejaculates are highly unlikely to contain sufficient numbers of spermatozoa to cause pregnancy.[20]

**Summary/Key Points:**

- The incidence of complications associated with castration is considered low and the mortality rate associated with the procedure very low with few fatalities occurring.
- However prompt recognition and management of any complications encountered should be instituted to prevent further morbidity, death or malpractice claims.
- The importance of client communications cannot be over-emphasized when dealing with complications to help prevent misunderstandings and lawsuits.
- While most complications encountered are mild and can be resolved relatively quickly with appropriate therapy, eventration, haemorrhage or signs of peritoneal infection should be considered emergencies and strong candidates for referral.

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# EMERGENCY CONDITIONS OF THE EQUINE HOOF

**Objectives of the Presentation:**

- Briefly review the anatomy of the hoof.
- To outline diagnostics and management of common emergency conditions of the equine hoof.
- Describe how to place a hoof cast in the field.

**Overview of the Issue and Introduction:**

Distal limb injuries are frequently encountered emergencies in equine medicine. The most commonly encountered injuries include heel blub/pastern lacerations, penetrating injuries of the sole and fractures of the distal phalanx. Rapid diagnosis and appropriate management of these conditions can result in quicker healing and a more rapid return to function.

**Penetrating Injuries of the Sole:**

Puncture wounds of the equine hoof are potentially serious injuries and are diagnosed frequently in equine practice. While the majority of penetrating solar injuries are superficial and respond well to conservative treatment, deeper penetration of the foot, especially in the frog region, can lead to serious and potentially life threatening complications. In cases where the penetration is relatively superficial, an abscess can develop between the solar horn and corium, but generally does not cause damage to the underlying structures. However, deeper penetration can result in damage to vital underlying structures such as the distal phalanx, deep digital flexor tendon sheath, navicular bursa, and/or the distal interphalangeal joint. Several studies have emphasized the importance of prompt recognition and aggressive treatment of deep puncture wounds to the foot involving synovial structures[1,2,3]. To avoid these potentially life - threatening complications, careful physical examination and radiological evaluation of the injured foot to decide the best course of treatment and management is essential.

The most common penetrating foreign body is a nail[1]. Often horses will present with a non-weight bearing lameness but lameness may be variable depending on the duration and the site of puncture. There may be palpable swelling of the soft tissue proximal to the coronary band with an increase in digital pulses also apparent. The solar surface of the foot can be divided into two regions, the central region (frog and collateral sulci) and the sole. Steckel *et al.* found that 95% of horses with a puncture through the sole returned to soundness,

whereas only 50% of the horses receiving a puncture wound through the frog or collateral sulci regained soundness reflecting a poorer prognosis[3]. In another study by Kilcoyne *et al*. horses with a puncture wound in the caudal third and middle third of the central foot were twice as likely to have penetration of one or multiple synovial structures versus the cranial region[1]. The location of the puncture wound is an important variable in determining a prognosis early in the evaluation and deciding the best course of treatment. Identification of a tract in the frog and sulci can be difficult if the penetrating object is no longer in place as the elastic tissue of the horn tends to seal over once the object is no longer in situ[2]. Any time lapse between the introduction of bacteria and treatment can lead to establishment of a serious infection with marked tissue destruction and extension of infection into synovial cavities such as the navicular bursa, digital flexor tendon sheath or distal interphalangeal joint. The longer the duration of infection, the higher the incidence of permanent damage especially where synovial structures are concerned. It has also been shown that horses which have a hindlimb affected carried a better prognosis than those which were affected in the forelimb[1].

A complete radiographic examination of the affected foot is warranted. If the penetrating object is still in place orthogonal views can help accurately detirmine the location (the direction and depth) of the penetrating object and determine involvement of any underlying structures. If the object has been removed already use of a sterile probe inserted through the tract can be useful in determining depth and direction. If synovial structure involvement is suspected a contrast study can be performed by injecting a radiopaque contrast agent into the synovial structure using aseptic technique and detirmining if there is communication with the tract. Computed tomography (CT) and magnetic resonance imaging (MRI) can also be useful to determine if damage or injury to underlying soft tissue structures such as the deep digital flexor tendon or impar ligament has occurred or if there has been osseous damage not detectable on radiographs. The gold standard for determining involvement of a synovial structure is to obtain a sample via synoviocentesis and perform a cytological analysis. Culture and sensitivity of this fluid should also be performed to ascertain the best direction for antimicrobial therapy[2].

All horses should receive broad spectrum antibiotic therapy until the results of any culture and sensitivity are available. The most common organisms isolated include *E-coli* sp., *Streptococcus* sp., *Proteus* sp., *Pseudomonas* sp. and *Enterococcus* sp. Anaerobes are often implicated also[1,2]. Use of procaine penicllin G and gentamicin is usually an effective starting point. Intravenous regional limb perfusions (IVRLP) provide high doses of appropriate antimicrobials to the infected area and greatly contribute to elimination of infection. In simple cases without underlying synovial structure involvement the penetration in the sole should be debrided to remove any devitalized tissue after a thorough cleaning the foot. Systemic antibiotics should be maintained until granulation tissue completely fills in the defect and the hoof should be kept in a

clean bandage until the defect cornifies. Alternatively the use of a treatment plate can be used. Deeper penetrations to the distal phalanx may result in septic osteitis or sequestrum formation. If sufficient time has passed radiographic examination may be useful in detirmining the presence of such an infection. Treatment involves use of systemic antibiotics, IVRLP and in certain cases necessitates currettage and debridement of the affected bone. Where there has been penetration of deeper structures such as to the navicular bursa surgical intervention is required. Bursoscopy of the navicular has now been advocated as the treatment of choice for these injuries and allows copious lavage of the bursa. In all these cases antibiotics should be instilled into the synovial cavities at the end of surgery[2].

Multiple studies have shown that synovial structure involvement in penetrating hoof injuries carry a worse prognosis. Our study reported an overall success rate of 76% in treated horses with penetrating injuries to the foot with only 28% of horses with synovial structure involvement returning to their previous level of soundness[1].

**Heel Blub Lacerations:**

Heel bulb lacerations occur commonly in equine practice. A thorough diagnostic work-up is required to ascertain the involvement of underlying structures such as synovial structures, bone, collateral cartilages or the presence of a foreign body. A considerable number of synovial structures (distal interphalangeal joint, proximal interphalangeal joint, navicular bursa, digital flexor tendon sheath) are present in the equine distal limb; therefore, all synovial structures close to a distal limb injury should be thoroughly examined to determine whether there is communication with the wound[4,5,6]. Arthrocentesis and synovial structure distention with sterile saline may be necessary to determine synovial structure involvement, radiographs, contrast radiographs, and ultrasonography are adjunctive diagnostic modalities that may help assess the severity of the injury and whether synovial structures are involved. If a synovial structure is involved, then appropriate therapy to treat the infected synovial structure should be performed. It is important that the clinician is confident that the infected synovial structure has been eliminated before a distal limb cast is applied. These wounds are usually very contaminated and copious lavage and cleaning is required. If the wound is very contaminated it is the author's choice to place a hypertonic dressing for 24 hours and perform delayed primary closure at 24-48 hours after presentation. Immobilization of the wound (i.e. the distal portion of the limb) by application of a cast may enhance healing by limiting movement of the injured tissue, decreasing tension on sutures, and limiting development of excessive granulation tissue[6].

As with penetrating injuries of the sole systemic antibiotics and use if intravenous regional limb perfusions in the initial stages of treatment can help reduce the level of infections and improve healing. Debridement of the wound using a #15 blade or curette to remove all devitalized tissue is important prior to

closure. Closure is usually performed using 0 or 2 non-absorbable monofilament suture in a simple interrupted pattern. If there is considerable tension present the use of the larger no. 2 suture is preferred by the authors and the use of tension relieving sutures such as the near-far-far-near pattern may be employed. Debridement and closure may be performed under general anesthesia or may be facilitated standing using sedation and an abaxial sesamoid nerve block. Following closure a light dressing is placed and the foot is place in a cast. In general, only a single cast is required, and most distal limb casts are worn for 3 weeks[6]. It is important that horses be confined to a clean, dry stall while wearing a cast to minimize cast complications. Elastic bandage material around the proximal cast should be changed every 3 to 4 days but should be changed immediately if it becomes wet. Casts need to be monitored daily for signs of fluid discharge from the proximal cast or through the cast, cast breakage, cast sore development around the proximal cast, excessive cast "wearing" around the toe or solar surface, or the development of lameness[5].

Overall, treating uncomplicated heel bulb lacerations that do not involve synovial structures is associated with a good prognosis for return to soundness (90%) and an acceptable cosmetic appearance (90%)[6].

**Distal Phalanx Fractures:**

Fractures of the equine distal phalanx are quite common, can occur in all breeds and usually have a favorable prognosis. Treatment is indicated in all cases except those with intra- articular fractures with significant incongruency of the articular surface and severely comminuted fractures. Generally, a conservative approach is adopted, consisting of immobilizing the hoof wall and a prolonged period of complete box rest. They can be caused by acute trauma, such as a kick toward a hard, non-movable object. Most often fast or excessive work induces fractures of the distal phalanx. Laceration of the hoof capsule may result in fractures as well. The forelimb is more commonly involved than the hindlimb. Fractures of the distal phalanx are classified into the following types[7]:

1. Abaxial/paramedian fractures without joint involvement
2. Abaxial/paramedian fractures with joint involvement
3. Axial/sagittal and parasagittal fractures with joint involvement
4. Fractures of the extensor process
5. Multi-fragment (comminuted) fractures with joint involvement
6. Solar margin fractures

The patient usually shows an acute, moderate to severe lameness accentuated during turns. The hoof and distal phalangeal region are warm to the touch, and an increased pulse can be palpated over the palmar or plantar arteries. There may be sensitivity to hoof testers. Diagnosis is usually confirmed by radiographs. Fractures of the distal phalanx can be managed with fragment removal, cast application and special shoeing, compression screw fixation, and neurectomy. Foals are best treated with stall rest.

Type 1 and 2 fractures are usually treated with by application of a fiberglass cast around the hoof capsule. Alternatively, a bar shoe with large side clips is applied to the hoof, providing support to the heels to limit hoof expansion during loading. NSAIDs are administered to reduce the pain level and allow the horse to bear weight on the foot. Stall rest for 2 to 4 months is required. Follow-up radiographs are taken to evaluate fracture healing. Usually after 4 months, the horse can be ridden at a walk on even terrain. A reasonable prognosis can be given for future use. It usually takes 4 to 6 months for the fracture to heal. However, radiographically the fracture line is visible much longer. Initially a fibrous union develops, which ossifies at 6 to 12 months[8]. If there is displacement of a Type 2 fracture then surgical intervention using lag screw technique is required to restore the congruity of the joint surface.

For Type 3 fractures it is important to prolong the rest period: 4 months of stall rest followed by 4 months of hand-walking exercise. The horse should be shod for 6 to 8 months with a bar shoe. A guarded prognosis is given for horses older than 3 years that are to be used as future riding animals, whereas horses younger than 2 years have a good prognosis[9]. Surgical reduction of the fracture may also be employed.

Type 4 small extensor fragments should always be removed arthroscopically because they are mobile and have contact with the articular surfaces. There is no ideal treatment for large fragments, therefore, conservative therapy is usually tried. Insertion of one or two screws in lag fashion has been described, but only rarely is a rigid fixation achieved. Therefore, if lameness persists after conservative management, surgical removal of the fragment is recommended[10]. Generally, a good prognosis can be given.

Type 5 fractures are usually always associated with severe lameness. Application of a hoof cast can be tried; however, these fractures usually carry a poor prognosis.

Type 6 solar margin fractures occur commonly and are usually the result of blunt trauma or may occur as the result of chronic laminitis. These usually heal with time and rarely require removal[11].

According to a recent study[11] horses with a non-articular type 1 fracture had a better prognosis (91.7%) for return to original or expected level of use than horses with an articular type 2 or 3 fracture (69.6% and 74.1%, respectively). The prognosis for types 4 and 5 fractures was fair (57.7% and 57.1%, respectively) and for type 6 good (80%). Horses with a hindlimb fracture had a significantly greater chance of a successful outcome. The best treatment option for types 1–3 fractures was a conservative approach (stall rest). Type 4 fractures were best treated by arthroscopic removal of the fragment.

**Summary/Key Points:**

- All puncture wounds to the foot should be considered an emergency with aggressive treatment instituted early on for a favourable prognosis for a full return to athletic performance.
- Puncture wounds of the hind-limb carry a better prognosis than the forelimb.
- Use of a foot cast protect wounds by limiting movement of wound edges, providing tension relief of suture lines, decreasing development of exuberant granulation tissue, and providing a moist environment for re-epithelialization. They can be applied standing in the field.
- Fractures of the distal phalanx can occur commonly and usually have a good prognosis if there is no concurrent joint involvement.

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# CLINICAL APPLICATIONS OF INTRAVENOUS REGIONAL LIMB PERFUSIONS IN THE FIELD

**Objectives of the Presentation:**

- To outline the main indications for using intravenous regional limb perfusion in the field
- To describe how to perform the procedure and the rationale behind the methods used
- To discuss different choices for antimicrobials

**Overview of the Issue and Indications:**

Regional limb perfusion of medications originated in human medicine to facilitate surgical procedures of the extremities and was first described as regional anesthesia in 1908 by August Bier. The technique was later studied and used to administer antimicrobials and anti-cancer drugs, however it wasn't until 1990 that Dietz and Kehnscherper[1] first described regional perfusion of antimicrobials in horses.

Traumatic wounds involving the limbs of horses are very common in equine practice and deep punctures or lacerations can threaten the life and athletic career of the animal.
Wounds and lacerations of the distal limb frequently affect underlying synovial structures, as well as soft tissues such as tendons or ligaments and bone. Thorough examination of the wound, including diagnostics such as radiographs, ultrasound and synoviocentesis in cases where synovial involvement is suspected, can aid in prompt and aggressive treatment for a better outcome.
Puncture wounds of the equine hoof are potentially serious injuries and are frequently diagnosed in equine practice. While the majority of penetrating solar injuries are superficial and respond well to conservative treatment, deeper penetration of the foot, particularly in the frog region, can lead to serious and potentially life threatening complications. Deep penetration of the solar surface of the hoof can result in damage to vital underlying structures such as the distal phalanx, deep digital flexor tendon sheath, navicular bursa, and/or the distal interphalangeal joint.
To try to eliminate the pathogenic bacteria, antimicrobial agents must reach adequate concentrations at the site of injury. As there is a relatively poor blood supply to the distal limb of the horse, systemic administration of antimicrobials may not reach adequate synovial concentrations at the site of injury. During intravenous regional limb perfusion (IVRLP), high concentrations and pressure gradients between the intravascular and extravascular compartments are obtained which facilitates diffusion of the antimicrobial into the surrounding tissues, including poorly vascularized tissues where bacteria may be protected

from systemically circulating antimicrobials. Additionally, regional application of antimicrobials allows delivery of a high concentration of antimicrobial to the site of injury while maintaining low systemic drug levels thereby minimizing potential side effects.

**Antimicrobial Choice:**

The goal of antimicrobial therapy is to achieve antimicrobial concentrations above the minimum inhibitory concentration (MIC) in infected tissue without causing any unwanted systemic or local effects. Aminoglycosides, such as amikacin and gentamicin, are concentration-dependent drugs, therefore a higher peak maximum concentration ($C_{max}$):MIC ratio is associated with a greater bactericidal effect.[2] Human studies evaluating systemic aminoglycosides for the treatment of Gram-negative sepsis have shown that the peak systemic aminoglycoside $C_{max}$:MIC ratio should be at least between 8:1 and 10:1 in order to maximize the effect of these drugs.[3-5] High concentrations are essential when treating infections caused by less susceptible pathogens with higher MIC of the antibiotic, therefore the goal of treatment should be optimization of peak concentrations by use of the highest possible nontoxic dose.[6] Ideally, synovial $C_{max}$ should be eight to 10 times higher than the MIC to be efficacious. These high concentrations of antimicrobials are typically impossible to achieve safely by systemic administration but are readily attainable by IVRLP.
Multi-drug resistant bacteria are an ever-growing problem in people and in recent years have become a serious threat in equine medicine.[7] High antimicrobial concentrations (>10 times MIC) do not only serve to increase therapeutic effect but also to prevent the emergence of a population of resistant bacteria.[8] Ideally the choice of antimicrobial should be based on culture and sensitivity results, however a positive culture of synovial fluid is not always achievable and usually culture results take up to 48 hours to get back.
Amikacin is the most commonly used antimicrobial for IVRLP[8], not only because it is an aminoglycoside and concentration dependent drug, but also because of the spectrum of action which includes gram negative aerobes and some *staphylococcus* species. The most common isolate from a retrospective study of 206 adult horses (older than 6 months) with synovial infection was *Staphylococcus aureus* (34.3%).[9] Earlier studies recognized that *S. aureus* is more common in cases of sepsis that develop after intra-articular injection or after surgery, and *Enterobacteriaceae* species are more common after traumatic wounds.[10] Various doses of amikacin have been reported in the literature (250mg-3g).[8] Typically, at the author's clinic 2g is the routine dose of amikacin used in an adult horse.
Other antimicrobials have been studied for use in IVRLP and are outlined in Table 1.[11-15] These antimicrobials are usually chosen based on culture and sensitivity results which may indicate a susceptible bacteria or resistance to amikacin.

**Type of Tourniquet:**

The efficacy of RLP depends upon the function of the tourniquet, so it is essential to use a wide rubber tourniquet (>10cm) or a pneumatic

tourniquet.[8,16,17] It is equally important to prevent motion of the treated limb by use of the sedation and if possible, local anesthesia. Movement during IVRLP is considered to be detrimental because it causes leakage of the perfusate and lowers the antimicrobial concentrations in the targeted region. Means to prevent this movement include general anesthesia (GA), peripheral nerve blocks and adding local anaesthetic to the perfusate. However, a recent study by Mahne et al.[18] revealed that adding local anaesthetic to the perfusate did not prevent movement and a peripheral nerve block was just as effective as GA in preventing movement. Furthermore, a recent study by Aristizabal et al.[19] actually showed higher synovial concentrations of antimicrobials after standing sedation than after GA. Thus, performing IVRLP under standing sedation is both practical clinically and supported by up-to-date research. It is the author's preference to add local anesthetic (lidocaine 2%) to the perfusate rather than performing a regional nerve block as it has been our clinical experience that this works sufficiently with reduced time required for the peripheral nerve block to be performed.

Regarding the duration required for tourniquet application, most studies have used application times of 25-30 minutes[8,16-18]. Two studies evaluating different tourniquet times found no significant difference in mean synovial concentrations between groups where the tourniquet was maintained for 20 minutes versus 30 minutes[19] or 10 minutes versus 30 minutes[20] respectively. A more recent study[21] looking at the time to peak synovial amikacin concentration in the distal interphalangeal joint (DIPJ or coffin joint) has shown that despite maintenance of the tourniquet, the median peak concentration did not increase past 15 minutes, indicating that application of the tourniquet for 15 minutes should be sufficient to achieve peak concentrations of antibiotics within the distal interphalangeal joint of the distal limb while performing intravenous regional limb perfusion.

**Vessel Choices:**

Multiple perfusions, typically 24 hours apart, are usually required to resolve infection in the distal limb. There are no concrete guidelines as to how many are necessary and the decision is usually based on clinician preference and how the horse is responding clinically i.e. degree of lameness, improvement in cytological parameters of synovial fluid, appearance of the wound etc. The majority of studies looking at intravenous regional limb perfusions have sued the cephalic or saphenous vein which has been shown to be as efficient and effective as using the digital palmar/plantar vessels. Both the cephalic and saphenous veins are more accessible and as a result of their larger diameter they are easier to catheterize than smaller vessels, resulting in fewer complications such as thrombosis. Either a 23g butterfly catheter or 22g 2.5cm catheter can be used to facilitate injection. One study[22] showed that use of an indwelling catheter in the cephalic or saphenous vein provided prolonged venous access and facilitated successive perfusions with minimal complications associated with its use.

**Volume of Perfusate:**

The main theory is that the volume of perfusate should be high enough to increase the intravascular pressure, which results in sufficient drug diffusion to the surrounding tissues. Different volumes have been used in different studies and vary from 20 ml to 250 ml[8]. A study by Hyde et al.[23] found no difference in synovial antimicrobial concentration after using three different volumes of perfusate during IVRLP. A more recent study[24] found the use of the higher perfusate volume (60-100 mL) resulted in a significantly higher antimicrobial concentration in the synovial fluid compared to lower perfusate volumes (30 mL). These findings highlight the possible importance of venous distention during IVRLP on the antimicrobial concentration in the distal limb, and emphasize the advantage of using a high volume of perfusate (60-100 mL). Typically, at the author's clinic the total volume of perfusate used for regional limb perfusion performed at the level of the cephalic/saphenous veins is 60 mLs consisting of 20 mL 2% lidocaine, 2g amikacin and ~35 mL sterile saline. A lower total volume of 35 mLs perfusate is used for the digital palmar/plantar vessels.

**Summary/Key Points:**

- Intravenous regional limb perfusion is a safe and efficacious modality to deliver high concentrations of antimicrobials to the distal limb of horses.
- It is an easy procedure to perform in the field
- It can significantly improve clinical outcomes in horses with traumatic injuries to the distal limb.
- The typical dose of an average 500 kg horse using the cephalic/saphenous vein would be 2g amikacin diluted to 60mls using 20mLs 2% lidocaine and 30mLs sterile saline.
- Tourniquet applications for 15-20 minutes is sufficient.

**Table 1: Less commonly used antimicrobials for IV-RLP.**

| *Drug* | *Dose* | *Spectrum* | *Cidal/Static* | *Reference* | *Comments* |
|---|---|---|---|---|---|
| **Gentamicin** | 1g | Gram – aerobes | Cidal | Werner et al. 2003[11] | Usually next choice if Amikacin not available<br>No action against *staphlococcal* spp. |
| **Vancomycin** | 300mg | Gram + bacteria *Clostridial* spp. Resistant *staphlococcal* and *enterococcal* spp. | Cidal | Rubio-Martinez et al. 2006[12] | Limited Gram – activity |
| **Ceftiofur** | 2g | Gram + and – aerobes | Cidal | Pille et al 2005[13] | After RLP synovial fluid ceftiofur concentrations remain above MIC for common pathogens (1 µg/mL) for > 24 hours |
| **Enrofloxacin** | 1.5 mg/kg | Gram – aerobes and *staphylococcal* spp. | Cidal | Parra-Sanchez *et al.* 2006[14] | May cause irritation/vasculitis at injection site |
| **Chloramphenicol** | 2g | Gram + and – aerobes and anaerobes | Static | Kelmer et al. 2015[15] | Half life much shorter – only 3 hours |

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# DIAGNOSIS AND MANAGEMENT OF EQUINE UROLITHIASIS

**Objectives of the Presentation:**

- To describe the common presenting clinical signs associated with urolithiasis in horses
- To outline different methods of diagnosis and subsequent management
- To outline indications for perineal urethrotomy and how to perform one in the field

**Overview of the Issue and Indications:**

Conditions of the urinary tract are common presentations in equine practice with cystic calculi reported to represent 8% of diagnoses relating to the urinary system[1]. Previous studies report the prevalence of urolithiasis to be low ranging from 0.04% to 0.5% with cystic calculi being the most common type of calculi encountered followed by urethral calculi[1]. Renal or ureteral calculi are found less frequently with clinical urolithiasis, but it is not uncommon to detect uroliths in more than one location[2,3].

**Types of Calculi:**

In horses, there are two basic forms of cystoliths, and both are primarily composed of calcium carbonate crystals. More than 90% are yellow-green spiculated stones (type 1) that can easily be fragmented. Less commonly, uroliths are gray-white smooth stones (type II) that are more resistant to fragmentation. These type II stones often contain phosphate in addition to calcium carbonate. The crystalline composition of normal equine urine sediment and uroliths is similar. Calcium carbonate ($CaCO_3$) in the form of calcite (a hexagonal crystal form of $CaCO_3$) is most common, followed by vaterite (a metastable, hexagonal crystal form in which $CaCO_3$ is partially replaced by magnesium or to a lesser extent by manganese, strontium, and sulfur)[1].
It is well known that horses excrete large amounts of $CaCO_3$ crystals in their urine[4] and that their urine pH is alkaline[1], allowing for calcite crystal formation. Relatively little is known about formation of urinary calculi in horses; however, as in other species, mineralization around a nidus under conditions favoring crystal growth (ie, supersaturation of urine) is thought to be the inciting cause[5]. Desquamated epithelial cells may provide a nidus in animals with urinary tract disease. It is also likely that damage to renal medulla as a result of use of nonsteroidal anti-inflammatory drugs and irritation of the mucosa of the lower tract with urinary tract infection can provide a scaffold for urolith formation[1]. Subsequent enlargement of urinary calculi proceeds by aggregation of microscopic $CaCO_3$ crystals to the surface of the stone. A second means of

urolith growth is precipitation of crystals as cement onto the surface of the calculus[1].

**Clinical Signs and Diagnosis:**

The classic presenting complaint for cystolithiasis is hematuria or dysuria after exercise. An affected male horse may also demonstrate stranguria by repeatedly dropping his penis and posturing to urinate but voiding little or no urine. Although cystoliths are less common in mares, stranguria and incontinence are common presenting complaints and urine scalding of the hindlimbs may be apparent. Less common signs which may be seen with nephroliths or ureteroliths include an irritable attitude, recurrent colic, and loss of condition[1]. Male horses with colic signs attributable to bladder distention from an obstructive urethrolith frequently have their penis partially dropped and may repeatedly posture to urinate.
Diagnosis of a bladder stone is usually made by rectal palpation. If a smaller stone has made its way into the urethra and is causing a blockage of urine the calculus may be palpated in the perineal area with distention/pulsing of the urethra proximal to the blockage. On rectal palpation these horses will have large distended bladders[5].
When performing a rectal examination in a horse with a suspected bladder stone, it is important to recognize that cystoliths are commonly found within the pelvic canal in the neck of a small bladder. They can usually be palpated with a hand inserted no further than wrist deep into the rectum and can be missed if the examination is focused on structures beyond the pelvic brim. The bladder in these horses is usually small due to frequent voiding as a result of irritation.
Renal and ureteral calculi are often more difficult to diagnose, but abnormal rectal palpation of the kidney or dilation of the ureter can sometimes be detected by means of rectal palpation[1].
Transabdominal and transrectal ultrasonographic imaging have substantially improved antemortem diagnosis of urolithiasis of the kidneys or ureters.

**Treatment:**

Surgical removal is the treatment of choice for equine bladder stones. Most surgeons consider laparocystotomy the method of choice to remove cystic calculi, but poor exposure and abdominal incisional dehiscence are reported complications. Approaches include caudal ventral midline, caudal paramedian and parainguinal incisions. The parainguinal approach[6], which is the approach favoured by the author for the removal of cystic calculi, eliminates the need for tedious dissection and ligation of branches of the external pudendal and caudal superficial epigastric vessels and the need to reflect the prepuce in male horses, creating less dead space.
Surgery may need to be performed on the urethra to divert urine flow in horses with urethroliths that are causing urethral obstruction or to access the bladder for cystolith removal via a perineal urethrotomy (PU)[3,5]. Obstructive urethrolithiasis is essentially a male horse problem because mares are generally able to void small stones through the urethra. Careful palpation of the urethra at the level of the ischial arch may reveal a firm obstructing urolith, although some stones travel more distally into the penis. In horses that have

been obstructed for more than 1 to 2 days, bladder leakage or rupture may occur, leading to abdominal distention from uroabdomen. Affected horses typically have a decreased appetite, a large volume of echolucent free peritoneal fluid on transabdominal ultrasonography, and serum electrolyte concentrations typical for uroabdomen (hyponatremia, hypochlo- remia, and mild to moderate hyperkalemia). Peritoneal fluid creatinine concentration twofold or greater than serum creatinine concentration confirms uroperitoneum. Obstructive urethrolithiasis is an emergency condition (to prevent bladder rupture) that is generally treated by performing a PU into the distended urethra. If the offending urolith is at or just beyond the ischial arch, it can often be removed at the time of surgery; however, if it has traveled more distally, removal may be more challenging.

**Perineal Uretrotomy Procedure[3]:**

1. In cases where the procedure was performed standing the horses is ideally restrained in standing stocks and sedated with a combination of detomidine hydrochloride (0.01 mg/kg IV) and butorphanol (0.01 mg/kg IV).
2. Caudal epidural anesthesia should be provided by administration of 2% lidocaine (0.22 mg/kg) either alone or in combination with 10% xylazine hydrochloride (0.15-0.2 mg/kg) diluted to a volume of 7-10 mL with sterile preservative free saline (0.9% NaCl). Alternatively or additionally, local instillation of 2% lidocaine may be placed along the proposed line of incision.
3. Feces should be removed from the rectum and the tail bandaged and secured overhead to the stocks.
4. The perineum is prepared aseptically for surgery. If possible, a stallion urinary catheter was passed from the urethral orifice into the bladder or to the level of the obstruction.
5. A vertical incision starting 4-6 cm distal to the anus, extending 8-10 cm ventrally is made on midline and extended subcutaneously.
6. The retractor penis muscles are separated on midline and reflected laterally.
7. The bulbospongiosus muscle is then exposed and incised.
8. The incision is continued through corpus spongiosum penis and then the caudal urethral wall.
9. Hemorrhage is controlled with ligation and digital pressure as necessary.
10. The placement of a urinary catheter may help to prevent deviation off midline and penetration of the cranial urethral wall.
11. In general, care should be taken to not extend the initial incision ventral to ischium in order to prevent urine scalding post-operatively.

**Prevention:**

Despite the success of dietary management (low protein, phosphorous, and magnesium) for medical dissolution of uroliths in small animals, dietary management is unlikely to replace surgical treatment of cystic urolithiasis in horses. This can be attributed to the fact that dietary management for small animals has been directed at struvite urolithiasis, and these stones are not

common in horses. Nevertheless, dietary management should not be overlooked following cystolith removal to decrease the risk of recurrence. At a minimum, legume hays and dietary supplements containing calcium should be avoided. Additional recommendations may include addition of salt to the diet to increase water intake and urine output as well as allowing access to grass at pasture. Unfortunately, acidification of equine urine is not easily accomplished and is not a routine postoperative recommendation[1]. It is also a good idea to have the local water on the farm tested for levels of calcium in hard water areas as an alternative source of water may be required.

**Summary/Key Points:**

- Calcium carbonate is the most common composition of urolith in horses.
- Uroliths are most frequently seen in the bladder or urethra, less commonly in the kidneys and ureters, HOWEVER, the presence of uroliths in multiple locations is common.
- Obstructive urethrolithiasis in males may result in bladder rupture if not treated as an emergency.
- Perineal urethrotomy can be a life-saving procedure in the event of obstructive urethrolithiasis to facilitate diversion of urine from the bladder.

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# COLIC: MEDICAL VS SURGICAL

**COLIC INITIAL ASSESSMENT AND DIAGNOSTICS:** We will perform a thorough review of your initial clinical assessment and diagnostic evaluation of a colic case. This will include:

- Taking a thorough history
- Physical examination
- Rectal examination
- Nasogastric intubation
- Abdominal ultrasound
- Abdominocentesis
- Abdominal radiography
- Gastroscopy +/-

The most important factor to consider as you piece together the "colic puzzle" is the horse's response to analgesics. Those horses that are not responding to analgesics at appropriate repeated doses should have an abdominal exploratory if there is a surgical option.

A consistent and methodical approach is best when assessing response to analgesics. Choose the analgesics that you are most comfortable with and consistently have with you. My choices most commonly are:

- Xylazine: .25mg/kg (100mg) and Butorphanol: .02mg/kg (10mg) for the average 1000 pound horse with mild to moderate colic symptoms.
- Xylazine: .35mg/kg (150mg) and Butorphanol :.035mg/kg (15mg) for the average 1000 pound horse with moderate to marked colic symptoms.
- Detomidine: .035mg/kg (15mg) for the average 1000 pound horse with violent colic symptoms.

As a general rule, those horses that require 3 doses of analgesics to remain comfortable in less than 90-120 minutes will require surgical intervention. Many other physical exam findings must be interpreted in conjunction with the response to analgesics to arrive at a final decision to take a horse for an abdominal exploratory.

It is worth noting that if referral is an option, it should be strongly considered for any horse that does not respond to the initial dose of Flunixin Meglumine +/- the administration of mineral oil via nasogastric tube.

Multiple case discussions to follow.

# FRACTURE FIRST AID

**EMERGENCY FIRST AID:** Because horses are not stable on three legs, when a limb fracture occurs, the inherent instability can cause the horse to additionally injure the already fractured limb. The objectives of emergency first aid are to minimize secondary damage and are as follows:

1) prevent damage to the vessels and nerves of the limb
2) keep the fracture from becoming open (skin penetration)
3) stabilize the limb to relieve the horse's anxiety over an unstable limb
4) minimize further damage to the fractured bone ends and surrounding soft tissue.

These objectives will best be accomplished with appropriate sedation and limb stabilization with splints. Horses will make repeated attempts to put the limb in a normal position. This lifting and replacing of the limb can further damage the bone ends or penetrate the skin. Once the limb is stabilized, most horses will become more manageable and easier to work with even if they are still not weight bearing on the affected limb. The most important tissue to protect initially is the skin. If the fracture is not contaminated, our success rate with repair is significantly increased. If the fracture is already open, then apply an antibiotic ointment and sterile dressing to minimize further contamination.

**SPLINTING TECHNIQUES:** The ideal splint will neutralize damaging forces as much as possible, will not be so large and awkward that the horse can't move, can be applied under all circumstances, doesn't require general anesthesia to apply, and is economical and accessible.

**Phalanges and distal metacarpus fractures:** Align the dorsal cortices of the bones and splint in a straight line. Kimzey "Leg Saver" is ideal but in the absence of this commercial unit you can use a piece of PVC pipe that is bi-valved, or a wooden board. First apply a light bandage (1 cm thick) and then tape the splint to the dorsal surface of the limb from the carpus to the toe. A combination of elastic tape and duct tape work well. I also like to tape a block to the heel prior to applying the dorsal splint and incorporate the block into the splint. This will keep the horse on his toe and prevent fetlock flexion and instability. If transporting the horse add cast material to the splint for additional stability.

**Mid-forelimb fractures:** Apply a thick Robert Jones bandage with each layer no more than 1 " thick. I prefer to use roll cotton covered with brown gauze and vetwrap for each layer. The bandage should go from the coronary band to as high on the forearm as possible. A rule of thumb is to have the Robert Jones bandage be 3 times the thickness of the limb at the fracture site. Then apply a rigid splint from the elbow to the ground on the lateral side of the limb and another on the caudal surface of the limb from the ground to as high as possible. You can again use wood or bi-valved PVC pipe. The material is

not important as long as it is rigid and thick enough that it won't break. Use non-elastic tape such as duct tape to attach the splint to the Robert Jones bandage.

**Fractures of the mid and proximal radius:** Apply a similar Robert Jones bandage but the lateral splint will have to extend up the lateral aspect of the chest and secured to the limb as proximally as possible in the axilla. This lateral splint extension will lie against the ribs and will prevent limb abduction. This is important because there is minimal musculature on the medial side of the limb and if an unstable limb abducts the bone ends will easily penetrate the skin.

**Fractures proximal to the elbow:** Humerus, ulna and scapular fractures are well protected by muscle covering. However these fractures usually will disrupt the triceps apparatus and the horse cannot fix it's elbow for weight bearing. The horse will frequently stand with a "dropped elbow" appearance because of this. They are much less anxious about this than with the instability of the distal limb. They are more comfortable however if the carpus is fixed in an extended position. Apply a padded bandage (not a complete RJ) and a caudal splint to maintain the carpus in an extended and locked position. The limb can then be used for balance and the horse is less anxious.

**Distal hind limb fractures:** These will be treated identical to the forelimb distal limb fractures if a Kimzey splint is available. If it's not, it may be easier to apply the PVC pipe or board to the plantar surface. You will tape the board or bi-valved pipe to the sole of the foot and then to the plantar surface of the limb to the hock.

**Fractures of the mid and proximal metatarsus:** The calcaneus (point of the hock) can be used as a functional extension of the metatarsus. Apply a Robert Jones bandage from the coronary band to the hock and then apply a lateral and caudal splint from the calcaneus to the ground using non elastic tape.

**Fractures of the hock and tibia:** The reciprocal apparatus makes these fractures especially difficult to splint. In addition the angulation of the hock and stifle joints prevent the use of a cranial or caudal splint. The tibia is similar to the radius in that there is minimal musculature medially so the goal is to keep the limb from abducting and resulting in skin disruption. Apply a thick Robert Jones bandage and then apply a rigid splint to the lateral aspect of the limb that extends proximally to the ilium. A broad board is best used in this instance (15-20cm wide) or an aluminum bar that can be bent to follow the angulation of the limb across the hock and stifle joints.

**Femur fractures:** The muscle mass protects these fractures and temporary splinting does little to improve the inability to bear weight.

Once the fracture is stabilized, broad spectrum antibiotics should be started if the skin has been broken or if there is significant soft tissue damage. NSAID's should also be administered prior to transport. Remember that the duration of

the trailer ride is relatively insignificant if the horse is properly supported. However even a short trailer ride can be catastrophic without proper limb support.

# GASTROINTESTINAL INFECTIOUS DISEASES: RECOGNITION, TREATMENT, MANAGEMENT

Infectious gastrointestinal (GI) disease almost always results in colitis. Colitis can be a diagnostic and therapeutic challenge for both veterinarians and owners alike. The presenting clinical symptoms of colitis are usually similar regardless of the etiology, yet the diagnostic tests can vary based on the disease process the clinician suspects. We will review diagnostics for some of the most common causes of equine colitis and will then discuss treatment which will include endotoxin targeted therapy, supportive care, antimicrobials and probiotics.

**COLITIS:** The clinical presentation of colitis can range from sudden death to depression, fever, endotoxemia, inappetence, colic, and profuse diarrhea. Early in the course of the disease or in horses with focal colitis, diarrhea may be absent.

**General diagnostics:** After a thorough physical examination, a complete blood count, serum chemistry profile, and abdominocentesis should be performed. The CBC will frequently reveal a leukopenia with a neutropenia. Changes in the chemistry profile will usually include hypoproteinemia with hypoalbuminemia and electrolyte derangements. If available, a venous blood gas and lactate should be performed to assess the acid-base status of the horse. A rectal is also helpful to assess for a large colon impaction, gas accumulation, or palpable colon thickening. Additional diagnositcs would include ultrasonography, radiography, and fecal samples.

**Etiologies:** The list of possible etiologies is very long and often times, much to the disappointment of the treating clinician, the final diagnosis on the case summary is listed as “idiopathic”. With that said, in order to support the well being of the remaining horse population on the affected farm, etiologic diagnosis should always be attempted when possible. Other causes that we will review are Salmonella, Clostidium, Cyathostomes, and although they are not infectious, we will briefly touch on Sand Enteropathy, Right Dorsal Colitis, and Antibiotic induced colitis.

**Salmonella:** Salmonella are gram negative bacteria that are common gastrointestinal pathogens in horses. Many serotypes have been reported to infect horses, but Group B seem to be more commonly associated with disease. Horses shedding Salmonellae are a potential source of infection to susceptible horses, and are environmental reservoirs, making Salmonellosis one of the most common nosocomial disease in horses. The emergence of multidrug resistant Salmonella isolates are a significant cause for concern due to its importance as a nosocomial pathogen and its zoonotic potential. Clinical syndromes associated with salmonellosis include inapparent infection, atypical

salmonellosis (depression, fever, and neutropenia without diarrhea), traditional enterocolitis with diarrhea, and septicemia +/- diarrhea (primarily in foals).

The diagnosis of salmonella can be done with fecal culture of 5 consecutive fecal samples or PCR of 3 or more consecutive fecal samples. The reason for repeat samples is that salmonella are shed intermittently and can't be isolated with culture or PCR consistently. PCR seems to have the greatest agreement with bacterial culture when 2 or more positive PCR results are used to define active shedding. It must be noted that detection of salmonella in feces does not prove a diagnosis, but the positive predictive value is high in horses with compatible clinical signs.

**Clostridial Colitis:** Clostridial species are an important cause of enterocolitis in both foals and adults. C. difficile and C perfringens (types A and C) are most commonly associated with enterocolitis, but other clostridium species have been isolated from horses with colitis as well. Clostridiosis is commonly associated with antibiotic associated as well as nosocomial causes of equine colitis.

**C. difficile**: Disease from C. difficile results from exotoxin production. Toxin A (enterotoxin) and toxin B (cytotoxin) act synergistically to cause intestinal disruption and secondary inflammation with associated clinical signs.

The diagnosis of C. difficile is based on bacterial culture AND toxin assays (ELISA). Culture is a sensitive test but is not specific due to non-toxin producing isolates. Fecal samples should be several grams and should be refrigerated in an airtight container to be sent out.

**C. perfringens:** Disease is seen more commonly in foals than adults. Types of C. perfringens are differentiated based on the production of four different toxins: alpha, beta, epsilon and iota .

The diagnosis of C. perfringens is based on fecal culture in combination with identification of the toxin.

**Cyathostomes:** Small stongyles are the most commonly implicated parasitic etiology of colitis. Cyathostomiasis is a well recognized cause of chronic diarrhea, but acute colitis may also be seen. The diagnosis is difficult because the disease is caused by the larval stages making fecal egg counts minimally helpful. Specific treatment is moxidectin or fenbendazole (10mg/kg PO daily for 5 days).

**Sand Enteropathy:** Sand can result in diarrhea secondary to irritation of the colonic mucosa. Horses pastured in coastal regions and fed on the ground should be considered at risk. Horses will commonly present for acute or chronic diarrhea, colic or weight loss. There are rarely abnormalities on CBC or serum Chemistry. Sand can be definitively diagnosed with abdominal radiographs. Sand auscultation, fecal sedimentation, and abdominal ultrasonography can also be useful. Specific treatment is psyllium mucilloid (1g/kg via NGT daily) in mineral oil for 5-7 days.

**Right Dorsal Colitis (RDC):** This disease is most commonly associated with NSAID administration. It is an ulcerative inflammatory disease of the right dorsal colon that may result in fibrosis and stricture formation. NSAID's inhibit

COX/PG synthesis which disrupt mucosal blood flow and other mucosal protective mechanisms in the GI tract. There are two primary forms of RDC: 1) acute colic, diarrhea, depression and endotoxemia. 2) Chronic weight loss, lethargy, edema, intermittent diarrhea often of “cow-patty”consistency. The most common serum chemistry abnormality is hypoproteinemia with hypoalbuminemia. Diagnosis is commonly via abdominal ultrasonography showing a thickened colon wall (>.5cm) on the right side of the abdomen in the $11^{th}$-$13^{th}$ ICS. Specific therapy is daily psyllium to increase the production of short chain fatty acids, a complete pelleted feed, and corn oil. In addition, Sucralfate may be helpful (20mg/kg PO QID), Metronidazole (15mg/kg PO TID-QID), Plasma (2-10 liters), and Misoprostal (2-2,5 mg/kg PO BID-TID).

**Treatment of colitis:** Regardless of etiology, supportive care and maintenance of hydration and normal electrolyte status are critical in the successful management of equine colitis. Intravenous polyionic fluid therapy may be required at 100 mls/kg/day or higher for horses with significant fluid losses through diarrhea or with evidence of azotemia on serum chemistry. Of course, fluid support must take into consideration protein losses, and occasionally colloid therapy, such as plasma, is required. Electrolyte supplementation should be based on serum chemistry results or blood gas analysis. Supportive care must also include laminitis prophylaxis and pain management as needed.

**Endotoxemia:** Endotoxemia and its sequelae can result in rapid deterioration of the colitis patient. Patients with endotoxemia will require additional therapy. Their fluid support may include hypertonic saline (7.5% NaCl @ 4ml/kg), and in addition they may benefit from Polymixin B(1000-6000 u/kg IV q 8-12 h), Flunixin Meglumine (.25mg/kg IV 1 8 hr), Hyperimmune plasma, and Pentoxyfylline (8 mg/kg).

Antibotic therapy is controversial in colitis cases. They can disrupt normal microflora so each case should be assessed individually. Metronidazole (15mg/kg PO q 6-12 h) should be administered if Clostridial colitis is suspected. My personal preference is to give antibiotics to those horses with profound neutropenia, those that are septic, and to all foals.

# PREVENTION OF INFECTIOUS DISEASES WITH BIOSECURITY MEASURES

**BIOSECURITY:** With the rise in outbreaks of equine infectious respiratory and neurologic disease in the media, the term "biosecurity" has become more common place. Biosecurity could be considered a catch all term for "How not to get sick or spread disease". In other words, we are trying to prevent infectious disease from happening in an individual animal and also take steps to avoid spreading the disease to other animals.

The key to biosecurity is proper preparation. This is focused at the veterinary practice as well as the farm. Biosecurity is much more than just proper vaccination. We must train and educate our staff on the concept of biosecurity. We must also train and educate our clients about not only vaccination, but also closely monitoring individual animals, segregating animals according to their travel and use, quarantine of new animals, frequent hand washing, and not sharing water and feed buckets. It is also important to remind horse owners not to transport sick horses in addition to isolating any horses that are sick whenever possible.

Although it seems intuitive to us, we must remember to stress that horse handlers wash their hands between horses, and use individual water buckets instead of a common tank or trough. Once there are sick animals on a farm then barrier precautions come into play such as separate barns if possible, changing clothes in between horses or wearing a disposable gown, using disposable foot wear or foot baths, and again, meticulous hand washing.

**Travel:** Take only healthy horses to events, shows or races. Always consider exposure potential BEFORE you travel. Make sure all horses are vaccinated with appropriate antigens at least 14 days prior to travel. All horses should have their temperatures taken prior to travel and no horse should travel with a fever (health certificates should be taken very seriously). And, once again, plan for your water and feed sources so that there is no sharing. When arriving at a show facility (or before is even better) look at the facility layout and try to put your horse in a location with minimal nose to nose contact. The "big show tents" for stabling are perfect for aerosolized transmission of infectious agents and avoid these tents whenever possible.

When returning from a show it is ideal to wait before introducing the show animals to the rest of the home herd if at all possible. It is ideal to isolate those horses coming from the show for 3-5 days in a separate barn. Monitor them closely with twice daily temperature checks in addition to monitoring for other potential symptoms of disease. If the show horses do bring an infectious disease home with them, the odds of transmission to the remainder of the herd will be greatly decreased if these protocols are enforced.

# TENDON-LIGAMENT

**SUMMARY:** This discussion will include an overview of superficial digital flexor (SDF) and deep digital flexor (DDF) tendinitis, suspensory desmitis, and desmitis of the accessory ligament of the deep digital flexor tendon (inferior check ligament). We will look at etiology, therapy, and potential shoeing recommendations.

**Tendinitis:** Tendinitis occurs when there is a strain to the structure. This is frequently associated with a tendon overload. Tendon fibers tear (or rupture) which results in hemorrhage. These lesions will fill in with granulation tissue and ultimately fibrose. We know that tendon/ligaments respond to repeated loading and will strengthen and resist injury with repeated strain application. Therefore it makes sense that we frequently see these injuries in young horses in their early training or in older horses that are coming off of a period of lay up.

Tendinitis is typically acute in nature and can range from a mild tear to complete disruption of all fibers. Classic clinical symptoms include lameness of varying degrees and swelling that can result in the classic "bowed tendon" appearance. The superficial digital flexor tendon (SDF) is most commonly affected, but the deep digital flexor tendon (DDF) can also be involved either on it's own or in combination with the superficial flexor. Although often times a diagnosis can be made on appearance alone in more severe lesions, the more subtle lesions usually require ultrasonography to confirm the suspicion. Ultrasonography should always be performed to assess the amount of tendon involved and help to develop a treatment and controlled exercise plan.

Treatment for tendinitis in the acute phase includes support (bandage or splint), ice, and NSAID's. Once the acute inflammation has resolved, additional therapies can be considered such as surgical options of tendon splitting or check desmotomies, and intra-tendinous treatment with a variety of products such as sodium hyaluronate, corticosteroids, autologous stem cells, platelet rich plasma, etc. Shockwave thereapy is included in many treatment protocols as well as a variety of therapeutic shoes based on the structure that is injured. No matter what ancillary therapies are tried, the key factor in a successful rehabilitation program is controlled exercise.

**Tendon Lacerations:** Trauma to tendons can be sharp in nature and result in a lacerated tendon, or may be blunt and result in tendon tearing. Complete tendon lacerations or tears results in limb malpositioning. Complete extensor tendon lacerations will result in knuckling over at the fetlock. Complete flexor tendon lacerations will result in a dropped fetlock with an SDF tear, an elevated toe with a DDF tear, and the fetlock completely on the ground with a complete suspensory ligament tear in addition to SDF, and DDF. Lacerations around the palmar fetlock and pastern region almost always involve the digital tendon sheath. This breach of the synovial structure should be treated aggressively just as you would for a septic joint.

Treatment for extensor tendon lacerations is typically supportive in nature. Sutured tenorrhaphy is not usually necessary. Flexor tendon lacerations however are surgical emergencies. Immobilization will be required and is usually best done with a Kimzey splint or a distal limb cast. Surgical intervention may be delayed as long as the limb is supported. Sutured tenorrhaphy is ideal to attempt to bring the tendon ends back into apposition. Limb immobilization is required in the postoperative period and will continue for weeks to months pending the degree of injury and structure(s) involved. The prognosis is guarded initially for return to athletic function. This is largely because of the "one wound-one scar" concept. However, rehabilitation efforts can be rewarding and many horses can return to some degree of athletic function.

**Suspensory Desmitis:** Proximal suspensory desmitis (PSD) is different in the forelimb than the hind limb. It is a common injury in the forelimb and may be unilateral or bilateral. Lameness varies from mild to moderate and is rarely severe. Lameness is usually worse on soft surface and when the affected limb is on the outside of a circle. Diagnostic analgesia followed by ultrasound is required to confirm forelimb PSD. Most horses with PSD of the forelimb respond well to rest and controlled exercise and a return to full athletic function is seen in about 90% of horses. Additional therapies such as intralesional injections with various products as well as shockwave therapy may be of benefit.

In the hind limb, proximal suspensory desmitis may be either insidious or a sudden onset lameness that ranges from mild to severe. It is frequently bilateral. Unlike the forelimb, horses with hindlimb PSD may have severe lameness that does not respond to stall rest. This is thought to be secondary to a compartment-like syndrome with pressure on the plantar metatarsal nerves. Diagnostic analgesia followed by ultrasound is required to confirm proximal suspensory disease. The return to athletic soundness is much lower in horses with hind PSD that are treated only with rest and controlled exercise as compared to the forelimb especially when the condition becomes chronic. Intralesional injections with PRP or stem cells in conjunction with shockwave therapy may be beneficial, but most horses respond best to surgical intervention with a neurectomy of the deep branch of the lateral plantar nerve.

Suspensory branch lesions, both medial, lateral, fore and hind are relatively common injuries in all types of sport horses. Foot imbalance may be a predisposing factor. These injuries are easier to diagnose than proximal suspensory lesions because of the obvious swelling and sensitivity to palpation. There may or may not be associated effusion of the fetlock joint and/or the digital tendon sheath. Treatment is similar to what has already been discussed although corrective shoeing can also be a key part of therapy along with rest, controlled exercise +/- intralesional injections and/or possible surgical splitting of the branch.

**Desmitis of the Accessory Ligament of the Deep Digital Flexor Tendon:** This ligament may also be referred to as the inferior check ligament. Injuries to this ligament usually occur in middle aged horses. Desmitis is usually in the

forelimb and is usually unilateral. Clinical symptoms are usually acute onset, moderate to severe lameness with obvious swelling in the region and sensitivity to palpation.

As with the other soft tissue injuries, diagnosis is confirmed with ultrasound. Treatment is similar to what has been discussed: rest, controlled exercise, intralesional injections with PRP or stem cells, shockwave therapy, and if chronic and non-responsive, some horses will respond to desmotomy of the accessory ligament of the DDF as long as there are no concurrent soft tissue injuries.

# WOUNDS: CLOSURE OR NOT

Wounds will always be a prominent part of equine veterinary practice because horses are naturally inquisitive animals whose protection mechanism is “flight from fright”. These wounds range from a simple scratch to life threatening injuries. The veterinarian’s approach to wound evaluation and management should be methodical and consistent.

**HISTORY:** Try to find out where the wound is located, where the horse is located, how old the wound is and what the owner has done for therapy to date. This is much more important than “what happened”. The horse has a wound and how it got there is irrelevant. If that information is available it may be helpful, but while most clients will obsess on how the wound occurred, the real important information is what structures are involved and can the wound be managed effectively. If at all possible, try to have the owner send you a video of the wound and more importantly how the horse moves (if she can move). This can help you triage before arrival if the owner should try to move the horse and if any cleansing or bandaging should take place before your arrival.

**INITIAL ASSESSMENT:** The most important part of the initial assessment is to remember that there is a horse attached to the wound. Don’t have tunnel vision focusing solely on the wound/s. Assess the entire horse first to be certain that the horse is stable before turning your primary attention to the wound.

-Is the horse’s behavior amenable to wound exam and management?
-Is the horse systemically stable?
-Is the horse weight bearing in all 4 limbs and are all limbs stable?
-Can you work where the horse is currently located?
-What kind of help do you have?

**WOUND EXAMINATION:** Begin with a visual exam of the wound to determine if the wound is a simple laceration or a multi-tissue laceration. Is there tissue loss? Is the wound location conducive to vital tissue involvement (synovial structures, vascular or nerve involvement, bone exposure or damage, tendon or ligament involvement)? After assessing as much as possible visually, properly sedate and restrain the horse and then begin your physical exam of the wound. Clip and clean prior to exploring deeper wounds. Wear gloves! Use sterile probes as needed and radiograph all wounds of limbs if the wounds are deep or significant tissue trauma is evident.

**IMPORTANT CONSIDERATIONS:** Because the limbs of horses have minimal soft tissue covering, joint and tendon sheath involvement is common with limb wounds. Remember that when you are assessing a synovial structure for wound communication to always inject into the synovial structure from non-wounded tissue. If you can’t, it’s not worth checking and you need to assume the structure is involved. When you perform synoviocentesis, collect fluid aseptically for analysis and culture/sensitivity. Then distend the synovial structure with sterile saline or LRS and determine if the fluid egresses from the wound.

Vital tissues must be prioritized in your wound management. These will determine long term soundness and success. Your beautiful skin repair is meaningless if the horse has a septic joint beneath it.

**PRIMARY CLOSURE OR SECOND INTENTION MANAGEMENT:** This is truly determined on a case by case basis with a multitude of factors considered. My personal preference is to close all wounds primarily (at least partially) as long as I have addressed any underlying pathology. Client communication is key to manage their expectations. When the situation dictates, let them know that sometimes we are simply applying a "biologic bandage" to damaged tissue, and that the wound will ultimately be managed by second intention healing. For wounds involving deeper tissues, always leave room for drainage at the most ventral or distal aspect of the wound.

**SUPPORTIVE CARE:** Systemic antimicrobials and anti-inflammatories are almost always a part of wound care. Local antibiotics can be important as well especially when synovial structures are involved. This can be in the form of regional limb perfusion, PMMA beads, antimicrobial infusion pumps as well as many other forms of local antibiotic delivery. Bandaging is mandatory for many distal limb wounds.

**HUSBANDRY MANAGEMENT:** Exercise restriction is often part of the post injury protocol. This can involve prolonged periods of time with more complex wounds. It is important to adjust the horse's diet to correlate with the decreased exercise to try and avoid colic or other GI disturbances.

# SHARON SPIER

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# GENETIC DISEASES OF HORSES

## INTRODUCTION AND DEFINITIONS

### Congenital Defects

Congenital defects include all undesirable traits and pathologic conditions present at birth whether they are genetic or due to intra-uterine events that results from extra-uterine influences. Congenital defects do not necessarily indicate inheritance; they simply indicate that the defect was present at birth.

### Inherited Tendencies

There are characteristics in horses that are influenced by a wide variety of genes, whose pattern of inheritance is complex and whose expression has strong environmental influences. Horses have been selectively bred for centuries to promote or discourage these characteristics. The selection for or against these inherited tendencies is the basis for our current breed registries. Size, power, color, speed, conformation and many other characteristics that are genetically influenced are selected for or against by certain breed registries. Variations from ideal may be undesirable but they are not deemed to be genetic defects.

### Genetic Defects

Genetic defects are pathologic conditions of proven genetic origin. These may be the result of a mutation in a gene of major effect or mutations in multiple genes (polygenic) whose effects combine to produce a deleterious or undesirable result. The degree to which some traits are expressed in horses carrying particular mutations can be influenced by environmental factors. This is called incomplete penetrance.

### Undesirable traits

An undesirable trait, as designated by certain breed registries, is a condition or behavior that may or may not be present at birth, may develop over time, may or may not be a genetic defect, but precludes registration of that animal. A variation in color is an example of a characteristic that may be considered by a breed to be undesirable. Concealment of such undesirable traits by any means, including surgery, is prohibited by breed registry. It is therefore unethical for a veterinarian to perform such treatments, except when the treatment is intended to improve the health of the horse, and when the veterinarian reports the treatment to the breed registry.

## GENETIC TESTS AVAILABLE FOR HORSES

Tests for mutations in single genes are currently (February 2019) available for 21 diseases.

*Autosomal Dominant*

1. Hyperkalemic Periodic Paralysis (HYPP) in the Quarter Horse
2. Type 1 Polysaccharide Storage Myopathy (PSSM) in numerous breeds,
3. Malignant Hyperthermia in Quarter Horse related breeds,

*Autosomal Recessive*

4. Overo Lethal White Syndrome in the Paint Horse
5. Combined immunodeficiency in Arabian Horses
6. Glycogen Branching Enzyme Deficiency (GBED) in Quarter Horse related breeds
7. Junctional Epidermolysis Bullosa (JEB) in Belgians
8. JEB in Saddlebred horses

9. Hereditary Equine Regional Dermal Asthenia (HERDA) in Quarter Horse-related breeds
10. Cerebellar Abiotrophy (CA) in Arabians
11. Lavender Foal Syndrome (LFS) in Arabians
12. Occipitoatlantaoaxial Malformation (OAAM) in Arabians
13. Connemara Pony Hoof Wall Separation
14. Dwarfism in Friesians and Friesian Cross
15. Hydrocephalus in Friesians and Friesian Cross
16. Ocular Squamous Cell Carcinoma (SCC) in Haflinger and Belgian Horses
17. Skeletal Atavism in Shetland Ponies and American Miniature Horses
18. Warmblood Fragile Foal Syndrome (WFFS)
19. Leopard Complex and Congenital Stationary Night Blindness in Appaloosas
(Other breeds around the world that exhibit this pattern include the British Spotted Pony, Knabstrupper, Noriker, and Tannu Tuva Pony)
20. Naked Foal Syndrome in Akhal Teke
21. Immune mediated myositis (IMM) and MYH1 Myopathy in Quarter Horses

There are numerous other conditions strongly suspected to be due to mutations in genes of major effect, but genetic tests for these conditions are not yet available. New information in equine genetics is being generated very quickly, and any document of this type will require frequent updates, at least for the next few years.

**AAEP POSITION STATEMENT ON GENETIC DEFECTS**

**Surgical Correction of undesirable traits and genetic defects**

According to the American Veterinary Medical Association, Surgical correction of "genetic defects" for the purposes of concealing the defect is unethical. If surgical correction is undertaken for the purpose of improving the health of the individual, then it should be accompanied by sterilization to prevent the perpetuation of the genetic defect. The AAEP agrees with the intent of this position. Further, surgical correction of any characteristic specifically named by the breed organization as being prohibited, with the purpose of concealing the characteristic for obtaining registration, would be considered fraudulent and unethical. Such procedures offer no benefit to the horse and are intended only to deceive the breed organization. The AAEP does support surgical correction of conditions that are in the best interest of individual horses.

**Identification of genetic traits**

AAEP supports the use of genetic testing by veterinarians or breed associations to identify genetic mutations in animals so that owners can make informed decisions about breeding, purchase and specific treatments. Breed associations should be contacted to determine if there are any restrictions on registration of horses with genetic defects. Licensed laboratories should be used for genetic testing.

**More information on equine genetic diseases is available at these websites:**

**http://www.vgl.ucdavis.edu/services/horse.php**
**http://www.cvm.umn.edu/umec/lab/home.html**
**http://www.ca.uky.edu/gluck/ServEPVL.asp**

**SELECTED DIESEASES WITH GENETIC TESTS AVAILABLE FOR HORSES**

## SEVERE COMBINED IMMUNODEFICIENCY

**Breeds affected:** Arabian
**Bloodlines:** unknown
**Prevalence**: 8% carriers
**Age affected**: 3-4 months of age when colostral immunity wanes
**Clinical signs**: lymphopenia (low numbers of lymphocytes in the blood), absence of the circulating immunoglobulin IgM and hypoplastic lymphoid tissue (few lymphocytes in the lymph nodes)
**Mode of inheritance:** Autosomal recessive.
**Mutation:** defect in the catalytic subunit of the DNA dependent protein kinase. A truncated unstable protein results that impairs the molecular mechanism necessary to create an almost limitless number of unique immune receptors. As a consequence SCID foals lack the ability to generated B lymphocyte and T lymphocytes.
**Testing:** The Arabian Horse Registry recommends that all breeding stock be tested and interbreeding of carriers avoided. Vetgen Ann Arbor Michigan tests for this mutation (www.vetgen.com)

## JUNCTIONAL EPIDERMOLYSIS BULLOSA (JEB)

**Breeds affected:** Belgian Draft horses, Breton, Comtois, Vlaams Paard, and Belgische Koudbloed Flander draft horse breeds. A separate mutation occurs in American Saddlebreds.
**Bloodlines:** unknown
**Prevalence**: 17% of Belgian horses in North America are carriers and in European breeds 8-27% of horses are carriers. About 3% of Saddlebred are heterozygous.
**Age affected**: Homozygotes show signs shortly after birth
**Clinical signs:** Foals are typically born alive, but irregular, reddened, erosions and ulcerations develop in the skin and mouth over pressure points or after mild trauma with common secondary infections.
**Mode of inheritance:** Autosomal recessive.
**Mutation:** Drafts have a cytosine insertion (1368insC) creating a premature stop codon in the LAMC2 gene on chromosome 5, which encodes for the laminin γ2 chain. Saddlebreds have a 6589-bp deletion spanning exons 24-27 in the LAMA3 gene. These defects in LAM subunits result in an absence of laminin 5 which anchors the basement membrane zone of the dermal-epidermal junction.
**Testing:** University of California at Davis tests for this mutation (www.vgl.ucdavis.edu)

## OVERO LETHAL WHITE FOAL SYNDROME (OWLS)

**Breeds affected:** American Paint horses
**Bloodlines:** Paint Horses with Overo ancestry
**Prevalence**: >94% of frame overos are heterozygotes, and present in highly white calico overo and frame blend overos as well as broodstock with no white spots
**Age affected**: Homozygotes show signs shortly after birth

**Clinical signs:** All white colored foals develop colic within 12 hours of birth, pass no fecal material and show pain that is not responsive to analgesics. There is a complete absence of intrinsic myenteric plexus in the terminal small intestine, cecum and entire colon, with the ileum most severely affected.
**Mode of inheritance:** Autosomal recessive.
**Mutation:** Point mutation that results in an isoleucine/lysine substitution at codon 118 of the endothelin receptor B (EDNRB) gene located on chromosome 17. Endothelin B receptor is essential for normal development of the enteric ganglia and melanocytes within the neural crest.
**Testing:** University of California at Davis tests for this mutation (www.vgl.ucdavis.edu)

**HYPERKALEMIC PERIODIC PARALYSIS (HYPP)**

**Breeds affected:** Quarter horse-related bloodlines
**Bloodlines:** Horses descendant from Impressive.
**Prevalence**: 4% of the Quarter Horse breed is affected.
**Age affected**: Signs usually begin by 2 to 3 years of age.
**Clinical signs:** Range from asymptomatic to intermittent muscle tremors and weakness. Horses homozygous for HYPP may present with difficulty swallowing or respiratory distress.
**Mode of inheritance:** Autosomal dominant.
**Mutation:** A point mutation that results in a phenylalanine/leucine substitution in a key part of the voltage-dependent skeletal muscle sodium channel alpha subunit that controls channel activity (*SCN44*).
**Testing:** Veterinary Genetics Laboratory at the University of California, Davis on mane or tail hair roots.

**GLYCOGEN BRANCHING ENZYME DEFICIENCY (GBED)**

**Breeds affected:** Quarter horse-related bloodlines
**Bloodlines:** Horses descendant from Zantanon and King
**Prevalence**: 8% of the Quarter Horse breed are carriers
**Age affected**: Signs usually present in utero or at birth
**Clinical signs:** Abortion or stillbirth; may be born alive and are weak at birth. With supportive care may live to up to 18 weeks of age. Death may be sudden when exercised on pasture, associated with weak respiratory muscles or the result of euthanasia due to persistent recumbency. Treatable flexural deformities of all limbs and recurrent hypoglycemia (low blood sugar) and seizures occur in some affected foals.
**Mode of inheritance:** Autosomal recessive.
**Mutation:** A point mutation in exon 1 changes a tyrosine to a premature stop codon in the glycogen branching enzyme gene (*GBE1*) that is expressed in numerous tissues.
**Testing:** Histopathological tissue samples (muscle and heart) stained for Periodic acid Schiff's (PAS) show a variable amount of abnormal PAS positive globular and crystalline intracellular inclusions. Veterinary Genetics Laboratory at the University of California, Davis or Vetgen in Michigan does genetic testing on mane or tail hair roots.

## POLYSACCHARIDE STORAGE MYOPATHY (PSSM)

Two forms appear to exist. The mutation for the most common form type 1 PSSM has been discovered by Stephanie Valberg and investigations are underway for Type 2 PSSM.

**For the *GYS1* form of PSSM**

**Breeds affected:** Quarter horse-related bloodlines, Belgians, Percherons, Morgans, Mustangs and some Warmblood breeds

**Bloodlines:** Present in founders of QHs and therefore widespread in all QHs.

**Prevalence**: 36-50% of Belgians and Percherons, 8% of the Quarter Horse related breeds

**Age affected**: Signs usually begin by 2 to 3 years of age but may occur in Weanlings. Some horses are subclinical

**Clinical signs:** Firm painful muscles, stiffness, skin twitching, sweating, weakness and reluctance to move with light exercise. Sometimes gait abnormalities, mild colic, and muscle wasting. Serum CK and AST activity elevated except in Drafts

**Mode of inheritance:** Autosomal dominant.

**Mutation:** Point mutation that results in an arginine to histidine substitution in the *GYS1* gene that codes for the skeletal muscle form of the glycogen synthase enzyme.

**Testing:** Muscle biopsy samples evaluated for presence of amylase-resistant crystalline polysaccharide
Genetic testing on mane or tail hair roots, or unclotted blood samples at the Neuromuscular Laboratory at the University of Minnesota.

**Second form of PSSM**

**Breeds affected**: Quarter Horse-related breeds, a few Arabians and possibly other light breeds

**Age affected**: Signs usually begin by 2 to 3 years of age but may occur in Weanlings. Some horses are subclinical

**Clinical signs:** Rhabdomyolysis with or without exercise.

**Mode of inheritance:** unknown.

**Mutation:** Unknown. Work in progress.

**Testing:** Muscle biopsy samples evaluated for presence of abnormal polysaccharide at the Neuromuscular Laboratory at the University of Minnesota.

## MALIGNANT HYPERTHERMIA (MH)

**Breeds affected**: Quarter horse-related bloodlines

**Bloodlines:** Present at a very high frequency in one QH bloodline (also in others), Often co-exists with PSSM

**Prevalence:** <1% of the Quarter Horse breed is affected

**Age affected:** Adults

**Clinical signs**: High temperature, metabolic failure and death under anesthesia. Exertional rhabdomyolysis especially if present with GYS1 PSSM mutation.

**Mode of inheritance:** Autosomal dominant.

**Mutation:** Point mutation that results in an arginine to glycine substitution in the *RYR1* gene.

**Testing:** Genetic testing at UC Davis (mraleman@ucdavis.edu) or Neuromuscular Diagnostic Laboratory at the University of Minnesota.

**HEREDITARY EQUINE REGIONAL DERMAL ASTHENIA (HERDA OR HC)**

**Breeds affected:** Quarter horses
**Bloodlines:** Working cow and cutting horses
**Prevalence**: 3.5% of the Quarter Horse breed are carriers
**Age affected**: Signs usually begin by 1.5 years of age
**Clinical signs:** Wounds or sloughing skin, loose easily tented skin that does not return to its original position, scars, and white hairs at areas of hair re-growth found along the back and saddle area or areas with trauma. Healing is slow.
**Mode of inheritance:** Autosomal recessive.
**Mutation:** Point mutation that results in a glycine to arginine substitution in the equine cyclophilin B gene (*PPIB*) that plays a role in the processing of collagen for the anchoring of the skin to underlying tissue.
**Testing:** University of California at Davis tests for this mutation (www.vgl.ucdavis.edu)

**CEREBELLAR ABIOTROPHY (CA)**
**Breeds affected:** Arabians, lower frequency in other breeds that have used Arabians as foundation stock
**Blood lines:** Egyptian
**Prevalence**: Estimated 14% of the Arabians are carriers (needs further study)
**Age affected:** Signs usually begin by 1.5 months of age
**Clinical signs:** Head tremor (intention tremor) and a lack of balance equilibrium (ataxia), among other neurological deficits. Affected horses may show exaggerated action of the forelegs, a wide-based stance, and be unable to rise from a reclining position. They tend to startle easily and often fall due to ataxia.
**Mode of inheritance:** Autosomal recessive
**Mutation:** SNP found on ECA2 which down regulates MUTYH expression causing cerebellar cortical degeneration of Purkinje cells (neurons in the cerebellum)

**Testing:** University of California at Davis tests for this mutation (www.vgl.ucdavis.edu)

**For additional information on the available genetic diseases with DNA tests please visit the University of California, Davis Veterinary Genetics Laboratory website. https://www.vgl.ucdavis.edu/services/horse.php**
**Import permits can be obtained by contacting the laboratory.**

**AQHA 5 Panel Test for Genetic Diseases**
To help breeders make informed decisions and reduce genetic diseases, AQHA now offers a panel test for five genetic diseases: glycogen branching enzyme deficiency (GBED), hereditary equine regional dermal asthenia (HERDA), hyperkalemic periodic

paralysis (HYPP), malignant hyperthermia (MH) and polysaccharide storage myopathy (PSSM1).
When the test is ordered, AQHA will send a DNA kit to the owner, who then mails it with mane and/or tail hair to the Veterinary Genetics Laboratory at the University of California-Davis for testing. Once the tests are complete, AQHA will notify the owners and put the results on the horse's record.
As of 2018, The 5 panel tests cost $100 USD for AQHA members and $155 USD for nonmembers. For the panel test in conjunction with the DNA test required for most breeding stock, the cost is $125 USD for members and $175 USD for nonmembers.

## GENETIC IMPLICATIONS OF CLONING HORSES

The subject of equine clones is fraught with controversy and has polarized members of breed organizations – for or against. Questions, scientific, ethical, and moral are numerous. Will it ultimately help or harm the equine breeds? Will it increase the incidence of genetic disease by even more overuse of popular bloodlines, or potentially decrease disease if disease-free geldings that can then be used as breeding stallions? Should clones be registered? Are the cloned foals healthy? Is cloning morally wrong? Some owners have used the cloning process, which was first performed on horses in 2003, to preserve their animals' bloodlines, particularly those of high-performance equines. In response to cloning as a way to preserve bloodlines, some breed associations ruled on whether or not cloned horses can be included in their breed registries.

Cloned horses and their progeny are allowed to compete at FEI sanctioned events and other events such as Polo, Barrel Racing, and Reining.

### What is a Clone?

Simply speaking, a clone is an exact copy (like an identical twin) of an original animal. Just like identical twins, the clones do not look exactly alike and will have different face and leg markings from the original. The most famous mammalian clone was "Dolly" the sheep, born in 1996. From that date to the present day, there has been an ongoing debate regarding the legality of cloning and whether scientists should be allowed to clone humans.
The first equine clone was produced in 2003 in Italy and two years later Texas A&M University produced the first North American horse clone. A commercial equine cloning company ViaGen Inc offers gene banking and cloning services for a fee of $150,000.
All horse clones have been produced from adult donors using a method called somatic cell nuclear transfer, or SCNT. In SCNT, a veterinarian takes a sample of subcutaneous tissue from a skin sample, cultures the cells (fibroblasts), and then transfer nuclear DNA material from the donor into an oocyte (egg) that has had its nuclear DNA removed. The embryo is then cultured for a few days, cell division begins and then the embryo is transferred into a recipient mare. The viability of embryos varies but approximately one live foal is produced from every four embryos (this will vary considerably and will likely improve with time). Blake Russell, vice president of business development of ViaGen Inc, reports a remarkable 50% pregnancy rate for each transferred embryo.
The foals are healthy, however problems have been reported in the first week of life, resembling placental insufficiency according to Katrin Hinrichs, DVM, PhD of the Texas A&M group.
The egg donor can come from any mare and has only a tiny strand of mitochondrial DNA that will be passed on by female clones only. Offspring of a male clone will not carry the

donor mare's mitochondrial DNA. What this means is that the offspring of the cloned colt will have the identical DNA as the original.
Little information is available at this time about the performance of the clones as they are so valuable that many are used for breeding only. The clone's environment will, of course, also determine the performance and personality of the clone, as well as how it is raised and trained. There are clones currently competing in reining events and their success could be traced through the NCHA.

**Why Clone Horses?**
If disease – free, exceptional individuals from underutilized pedigrees were cloned (geldings or mares), then clones could offer potential benefits by continuing these genetics. Several cattle registries are currently registering clones and advertise the animals as disease free for specific genetic diseases where tests are available.
Cloning could also potentially be used to produce embryonic stem cells to be used to repair tendon, ligament, cartilage and bone damage in horses. Embryonic cells could be taken from an embryo cloned from the adult. Since stem cells are currently harvested from other means (such as fat or bone marrow), there appears to be no benefit at present to using embryonic stem cells for therapy.

**Why Not Clone Horses?**
The reason most horse owners use for not cloning horses are ethical, frequently stating "it just doesn't seem right to experiment with Mother Nature" or feel it is commercial exploitation of animals. The general public is fearful of potential adverse health effects from cloning, both short-term for the clone itself, and long-term for the health of future generations. Opponents believe that conventional breeding practices introduce new genetic material to continually improve the breed and health of the horse.
The biggest reason against cloning is due to the real risk of increasing the incidence of inherited diseases due to the "Popular sire effect". Cloning, especially making several copies of one animal, amplifies one individual's impact on the gene pool. Along with line breeding, artificial insemination, embryo transfer and other assisted reproductive techniques, cloning has the potential to increase the prevalence of disease causing mutations in the breed. Line-breeding and specialization for certain disciplines has increased the occurrence of genetic diseases, as has "genetic bottlenecking". Examples include HERDA and HYPP in Quarter Horses, Severe Combined Immunodeficiency and Cerebellar Abiotrophy (SCID) in Arabians, and Junctional Epidermolysis bullosa (JEB) in Belgians.

Various equine diseases that have available genetic tests will be reviewed in the presentation. The use of clones in breeding programs should be considered very carefully, and breed associations should encourage genetic testing, education and research.

# CORYNEBACTERIUM PSEUDOTUBERCULOSIS IN THE HORSE - INCREASING INCIDENCE THROUGHOUT THE AMERICAS

**DEFINITION**

*Corynebacterium pseudotuberculosis* infections occur worldwide and cause external and internal caseous lymphadenitis in sheep and goats; cutaneous excoriated granulomas and mastitic, visceral, or mixed infection in cattle; and ulcerative lymphangitis and external and internal abscesses in horses.[1-4] Subacute to chronic lymphadenitis and pneumonia have been reported in humans handling infected sheep.[5,6] Several zebras in the United States developed severe or multiple internal abscesses and died weeks after being exposed to horses in California.[7] There have been reports of the disease in camels, alpacas, and buffalo.[8,9]

**MICROBIOLOGY**

*C. pseudotuberculosis* infection is caused by a 2-µm gram-positive, intracellular, nonmotile, pleomorphic, rod-shaped facultative anaerobe.[10] *C. pseudotuberculosis* grows well at 37° C on blood agar in 24 to 48 hours, and it forms small, pinpoint in diameter, whitish, opaque colonies that are surrounded by a weak zone of hemolysis. Because of the high lipid content in the bacterial cell wall, particularly corynomycolic acid, the colonies spatter in a flame pushed across the agar surface.[11] High lipid content may facilitate survival of the organism in macrophages.[12] Two species-specific biotypes of *C. pseudotuberculosis* have been identified based on differences in nitrate reduction[5] and DNA fingerprinting techniques.[11, 13,14] Strains isolated from small ruminants are nitrate negative, strains from horses are nitrate positive, and both strains have been isolated from cattle.[1,5,13,15] From the results of DNA studies, the terms *biovar equi* for nitrate-positive and *biovar ovis* for nitrate-negative strains were proposed.[11] Molecular studies revealed that there is considerable heterogeneity of the isolates of *C. pseudotuberculosis* from small ruminants and from horses[13,14,16] and concluded that nitrate reduction may not absolutely distinguish between the isolates, as does ribotyping.[13] On the basis of genome sequencing, sheep and goats have specific isolates throughout the world, and horses and cattle have distinct groups of isolates depending on geographic locations.[13] Natural cross-species transmission between small ruminants and horses does not seem to occur.

1. *C. pseudotuberculosis* produces various exotoxins: phospholipase D (PLD), sphingomyelinase, inhibitory factor of staphylococcal β-hemolysin, hemolysis factor, dermanecrotoxins, and mouse lethality toxins.[17] Phospholipase D and sphingomyelinase are important in the pathogenesis of the disease, because they hydrolyze lysophosphatidylcholine and sphingomyelin, respectively, enabling degradation of the endothelial cell wall and increasing vascular permeability.[18] The synergistic activity of sphingomyelinase with the exotoxin of *Rhodococcus equi* in lysing red blood cells in agar forms the basis for the synergistic hemolysis inhibition (SHI) test. The SHI test measures IgG to PLD exotoxin. [19]

2. Molecular characterization, including genome sequencing of *C. pseudotuberculosis* isolates causing various clinical forms of disease have been reported. At present, phenotypic and genotypic strain differences have not been linked to clinical disease presentation (such as internal or external abscesses), suggesting that other environmental or host factors determine the course of disease.[20,21,]

## CLINICAL SIGNS AND DIFFERENTIAL DIAGNOSIS

### *Sheep and Goats*

*C. pseudotuberculosis* causes caseous lymphadenitis (CLA) in sheep and goats worldwide. Caseous lymphadenitis is a major cause of poor production, premature culling, and mortality. There are two forms of CLA which include external and internal abscesses.[22] The infection in small ruminants is primarily characterized by suppuration and necrosis of the large superficial lymph nodes. External abscesses are found more commonly involving the mandibular, parotid, prefemoral, or prescapular lymph nodes. The exudate present in those abscesses is thick or inspissated and may appear white in sheep and greenish in goats.[4] A breed association with the type of CLA cutaneous lesion was observed in an outbreak in a commercial ram stud in Scotland.[23] The disease is commonly known as “cheesy gland” in Australia. Differential diagnosis should include abscesses caused by other organisms, trauma, seroma, hematoma, foreign body, injection reaction, and less commonly, tumors. *C. pseudotuberculosis* infection represents a major herd health problem, so abscess culture to determine the precise causative agent is important. Mastitis occasionally develops.[2]

3. Internal abscesses can be found in the lungs, kidneys, and mediastinal, bronchial, mesenteric, and lumbar lymph nodes.[22] Chronic weight loss is the most common presenting complaint. Other clinical signs are related to the organ or tissues affected. Other diagnostic procedures may be necessary for the differentiation of internal abscesses as the cause of weight loss. Signs of spinal cord compression by vertebral abscesses have been seen in lambs born in unsanitary conditions.[4] Knowledge of the local prevalence can aid diagnosis of the infection when uncommon anatomic locations are affected. The prevalence in large breeding operations in endemic areas is estimated to be between 5% and 10%.

### *Cattle*

*C. pseudotuberculosis* infection in cattle occurs as a herd problem with sporadic incidence. The most common clinical form affecting cattle is cutaneous excoriated granulomas; other forms are mastitis, visceral, and mixed infections.[2] In the most common form, the lesions do not occur as abscesses but as ulcerative, exuding granulomatous lesions as large as 20 cm in diameter, with necrotic areas that are easily surgically removed, leaving granulation tissue underneath.[3,4] Lesions are usually located in the lateral exposed areas of the body: face, neck, thorax, and flanks. The exudate varies from bloody to thick greenish in color. Lesions heal spontaneously in 2 to 4 weeks and do not appear to cause significant illness or decrease milk production in cattle in California.[4] However, monthly milk production was decreased by 6% in Israeli cattle.[3] The prevalence of the infection has been reported to be up to 10% in California dairies.[4] Morbidity was reported to be up to 35% in Israeli herds.[3] Management problems like broken posts or exposed wires traumatize the skin of cattle, allowing penetration of the organism. Young cattle appeared to be less susceptible to the disease than older cattle in Israel.[3] Differential diagnoses include trauma, foreign body, and other masses like tumors. Cutaneous lesions and mastitis were seen in 6%, and cutaneous lesions with concurrent visceral involvement in 1.6% of the Israeli cases.[3] The rest of the cows (92%) only had the cutaneous form.[3] The most affected organ in the visceral form was the lung.[3] The infection has been reported in bison from Egypt, resulting in severe emaciation and edema in the ventral areas and flanks.[24]

### *Camels and Camelids*

Caseous lymphadenitis has been reported in old and new world camelids worldwide.[25] One study documented five young alpacas (aged 22 days to 14 months old) in North America with caseous lymphadenitis or subcutaneous abscesses that developed during late summer and early fall.[9] The alpacas did not appear clinically ill but developed swellings that progressed to abscesses. The abscesses (1 to 3 per alpaca) were located in the submandibular and cervical areas, and in one case adjacent to the eye. Abscess excision appeared to be the most effective treatment in those cases. Differential

diagnoses include abscesses caused by *Streptococcus* spp., *Corynebacterium* spp., and *A. pyogenes*.[26] Severe lymphadenitis with internal and external abscesses was reported in camels in Asia and Jordan.[8] A study of experimental infection of adult alpacas resulted in abscesses at the inoculation site and renal lymph nodes.[27]

***Horses***

Three forms have been described in horses: ulcerative lymphangitis and external and internal abscesses. In a previous study of *C. pseudotuberculosis* infection in horses from California, ulcerative lymphangitis was diagnosed in 1%, external abscesses in 91%, and internal abscesses in 8% of the cases.[28] There appears to be no breed or sex predilection for development of infection. Ulcerative lymphangitis appears as a severe cellulitis, where the lymphatics are affected in one or more limbs, with multiple draining ulcerative lesions. Horses often develop a non–weight bearing lameness, fever, lethargy, and anorexia. This form of the disease occurs worldwide and often becomes chronic, resulting in limb edema, lameness, weakness, and weight loss.[4] The differential diagnosis should include blunt trauma, fracture, foreign body, puncture wounds, nonseptic cellulitis, staphylococcal cellulitis, and other septic cellulitis. Musculoskeletal infection can result in marked lameness (grade 4 to 5 out of 5) and most commonly involves the axillary and triceps areas, followed by the stifle area.[29] Besides diffuse lymphangitis of the limbs, it can also cause osteomyelitis and septic arthritis.[28,29]

4. The median age for horses with external abscesses is 5 years (range, 3 months to 28 years).[28] Young horses appear to be predisposed to infection; 52% of the cases in a large retrospective study in California were 5 years old or younger.[28] Few cases involved foals younger than 6 months of age, suggesting that foals born to mares in endemic areas may be protected for several months by colostral antibodies.[28] External abscesses located primarily in the pectoral and ventral abdominal regions are most commonly diagnosed in areas of the western United States (Texas, Oklahoma, New Mexico, Colorado, Nevada, Utah, California, Wyoming, Arizona, Oregon and Washington), however disease incidence is increasing and spreading to all regions of the United States, including Hawaii, with reports in Mexico and Western Canada.[1,4,20,28,30,31] This clinical form of external infection is commonly known as “pigeon fever” because of the large size of pectoral abscesses, giving the appearance of a pigeon's breast. “Dryland distemper” is another name that reflects its geographical distribution in arid areas. Other common anatomic locations are the prepuce, mammary gland, axilla, inguinal region, limbs, and head.[28] Abscesses involving the head include the ears, eyelids, forehead, maxillary, and mandibular regions.[28] Severe facial suppurative cellulitis and panniculitis with skin sloughing have also been reported.[32] Other less common areas are the thorax, neck, parotid gland, guttural pouches, larynx, flanks, umbilicus, tail, and rectum.[28] Central nervous system infection has also been reported.[28,33] A large area of edema develops in the area of abscess formation. While the abscess matures, the area becomes hard and painful, and some get very large, particularly in the pectoral area. These abscesses typically have a thick capsule measuring up to 10 cm, and can cause severe lameness if located in the axillary or inguinal region.[1,28] Maturation can be slow and drainage difficult to establish if the abscess lies deep to muscle. Once drainage is established by spontaneous rupture or lancing, the majority of cases resolve within 10 to 14 days, however many horses can experience a protracted course of disease lasting months with recurring abscesses. Generally, weight loss is not observed in absence of internal infection. Abscesses may contain from 5 to 400 mL of thick, tan, purulent exudate.[1] The majority of affected horses present with a single abscess rather than multiple abscesses.[28] Fever up to 40° C develops in about 25% of cases. Other signs are nonhealing wounds, lameness, ventral dermatitis, and (less commonly) depression, anorexia, mastitis, and other problems, depending on abscess location.[28] In the majority of horses (91.4%), complete recovery occurred, with no recurrence of infection in subsequent years, implying a long-lasting immunity. However, 8.6% of the horses' infections persisted for longer than 1 year or

recurred as external or internal abscesses.[28] In sheep and goats, humoral and cellular immune responses develop following infection, and macrophages acquire the ability to kill the organism.[6] The case fatality for horses with external abscesses is very low (0.8%).[28] The differential diagnosis for external abscess, particularly pectoral, should include trauma, seroma, hematoma, foreign body, or abscess due to a different organism.

5. In a large study of *C. pseudotuberculosis* infection in the horse, 8% of 538 horses developed internal abscesses.[28] In two different studies, almost half to 63% of horses that had internal abscesses also had concurrent (or a history of) external abscesses.[28,34] In a study of 30 horses with internal abscesses, a female predilection (70%) was apparent.[34] Mean age is 8 years, with a range of 10 months to 23 years.[28,34] The most common clinical signs are anorexia, lethargy, fever (up to 41.1° C), tachycardia, and modest weight loss. Other signs are colic, pale mucous membranes, ventral and/or limb edema, ventral dermatitis, ataxia, hematuria, nasal discharge, and abortion.[28] The most commonly affected anatomic location is the liver, followed by mesentery, mediastinum, lungs, kidneys, diaphragm, spleen, pericardium, blood, and uterus.[1,28,34] A postmortem examination was performed on an aborted fetus from a mare with pneumonia and revealed *C. pseudotuberculosis* abscesses in the liver, lungs, spleen, diaphragm, kidney, and bladder.[34] Bacteremia may also occur. Both single and multiple organ involvement have been documented.[34] The case fatality for horses with internal abscesses ranges from 30% to 40%.[28,34] The differential diagnosis should include other types of abscesses, such as *Streptococcus, Actinomyces, Staphylococcus, R. equi* in foals, *Coccidioides immitis,* anaerobes, neoplasia, and other causes of weight loss. The clinical signs and differential diagnosis will depend on the location of the abscess.

***Humans***

Human infection may result from consumption of unpasteurized infected milk or milk products, continued close contact with infected animals, handling contaminated equipment, and exposure to wounds with exudates.[6,35] Human infection has been reported from strains of small ruminants.[6] Transmission from horses to humans has not been reported, but precautions should be taken when handling infected horses. Infection in humans occurs as a subacute to chronic lymphadenitis and pneumonia.[6]

**CLINICAL PATHOLOGY AND LABORATORY DIAGNOSIS**

Common findings include anemia of chronic disease and an inflammatory leukogram.[28,29,34] Leukocytosis with neutrophilia and increased fibrinogen and Serum Amyloid A are common features of developing bacterial infections, particularly in the case of internal abscesses.[28,29,34] Leukocytosis with neutrophilia was seen in 36% and 76% of horses with external and internal abscesses, respectively.[28] Hyperproteinemia due to increased globulins was observed in 38% and 59% of horses with external and internal abscesses, respectively.[28] Similarly, infected cattle and small ruminants had increases in white blood cell counts.[2,3]

6. Peritoneal fluid from 93% of horses with abdominal abscesses was abnormal.[28] The remaining horses with abdominal abscesses and normal peritoneal fluid had abscesses located retroperitoneally involving the kidneys, without involvement of other abdominal structures. *C. pseudotuberculosis* was isolated by bacterial culture in 32% of the samples of peritoneal fluid in horses with internal abscesses[28], and infection can also be detected by PCR. Failure to detect the organism from peritoneal fluid does not rule out the disease as infection could be located retroperitoneally, sequestered within a thick capsule, or suppressed by local factors or nucleated cells.[36]

The ELISA test for detection of cell wall antigens appears to have some utility for detection and control of infection in sheep.[37-40] The synergistic hemolysis inhibition (SHI) test measures IgG response to the PLD exotoxin in the patient's serum by detecting the highest dilution that will prevent hemolysis of *R. equi* exotoxin–sensitized bovine red cells when mixed with *C. pseudotuberculosis* exotoxin of a known concentration.[19,41] Increasing titers may be seen with exposure, or active external or internal infection and

there exists considerable overlap in values amongst these groups of horses. In a case control study SHI test results had greatest utility for determining internal *C. pseudotuberculosis* infection in horses when there was no evidence of external abscesses.[43] A high probability of internal infection with titers ≥512 was previously reported, however a recent case control study of 171 horses revealed higher titers were more indicative of active external or internal disease rather than internal disease specifically. The SHI test was unable to distinguish the occurrence of internal infection when external abscesses were present. Titers increase with chronicity of infection and bacterial culture is the preferred method of diagnosis for external infection. In horses *without external abscesses*, increased titers >1280 are significantly associated with internal infection. Clinicians are advised against diagnosis of internal infection based upon SHI titer, rather the test should be used in conjunction with other clinical and clinicopathologic evidence of inflammation.

7. The SHI test can be used in sheep and goats to monitor prevalence and exposure of incoming animals and to detect subclinical infections.[4,41] . In horses, a low SHI titer does not rule out the disease as horses that are seronegative at the time an external abscess is drained seroconvert later. The high titers in horses with internal abscesses probably reflect the chronicity of the disease and the resulting prolonged immune stimulation. In summary, high titers can be seen with both internal and external abscesses, and abdominal and thoracic ultrasonography is very useful for confirmation of internal infection in suspect cases.[28,34,43] Exposed herdmates can also have SHI titers in the absence of clinical infection. Prolonged seropositivity has been observed in horses and goats.[28,41,44] Other serodiagnostic tests used in sheep and goats are tube agglutination, complement fixation, and gel immunodiffusion.[17,45]

8. A presumptive diagnosis can be made based on history, local prevalence, time of year, clinical signs, and exudate characteristics.[4] For the diagnosis of internal abscesses, the previous features must be considered as well as the presence of an inflammatory leukogram with elevated fibrinogen, serum chemistry abnormalities, abnormal peritoneal fluid or transtracheal wash, positive blood culture, SHI titer of 512 or higher, and ultrasonographic and/or radiographic evidence of masses.[28,34] A definitive diagnosis is established by isolating the organism from abscesses or draining wounds. The organism is readily isolated and grows well in blood agar in 24 to 48 hours, even when contaminant bacteria are present.[28]

**PATHOPHYSIOLOGY AND EPIDEMIOLOGY**

*C. pseudotuberculosis* is a soil-borne organism that survives for long periods of time, months to years, even in direct sunlight at environmental temperatures.[6,46,47] The incidence of infection in horses varies considerably from year to year. External and internal abscesses in horses can present at any time of the year, but are more commonly observed during the fall and early winter months, with the highest incidence in September, October, and November.[28] However, internal infections are more frequently seen in November through January, 1 to 2 months following the peak number of cases with external abscesses.[34] The largest numbers of equine cases have been observed during the dry months of the year, following heavy rainfall, which may result in optimal breeding conditions for insects.[1,28,30] The seasonal incidence in horses has been associated with the presence of biting insects like *Haematobia irritans* (horn fly); this insect's feeding pattern causes ventral midline dermatitis. Insect vectors involved in transmission of disease in horses (e.g., *H. irritans, Stomoxys calcitrans, Musca domestica*) were identified by detecting the PLD exotoxin gene of *C. pseudotuberculosis* in an endemic area.[48] Disease can be transmitted by horse-to-horse contact via vectors, contact with exudates or contaminated soil.[49] Temporal and spatial analysis indicated an incubation period of 3 to 4 weeks in horses.[50] There is no breed or sex predilection, [28] however, a retrospective study indicated a predilection for internal abscesses in females.[34] A case-control study in an endemic area revealed young adult horses (<5 years of age) had increased risk of infection.[49] Horses housed outside or with access to

an outside paddock or in contact with other horses on pasture appeared to be at higher risk than stabled horses.[49]

9. The disease in cattle from Israel occurred during the spring and summer dry season (March to October) when the housefly population is high.[3] *C. pseudotuberculosis* was isolated from houseflies collected over an Israeli cow lesion.[51] The infection in cattle may spread by direct contact or indirectly by houseflies or fomites.[3] The disease in sheep and goats is not seasonal, and transmission is through contact of exudate from a draining abscess from animal to animal or via contaminated equipment.[1] Lambs born in contaminated surroundings can be infected through the umbilicus, mouth, or inhalation.[4] Sheep that acquire the organism orally or from shearing wounds tend to have parotid, submandibular, prefemoral, or thoracic abscesses.[4] Goats can be infected when wounds are exposed to contaminated milking equipment. The incubation period is long and variable. In experimental infections in small ruminants, the incubation period was from 2 weeks to several months.

10. The pathogenesis of the disease in horses is unclear, but it has been speculated that the organism enters the equine host through skin or mucous membrane abrasions or wounds, as has been confirmed in sheep.[52, 53] Experimentally induced infections in small ruminants revealed that once *C. pseudotuberculosis* gains access via wounds or abrasions, the organisms spread to subcutaneous or submucosal lymphatics, where they are phagocytosed by macrophages that migrate to the invasion site to engulf them.[54] The organism survives intracellularly because of its high lipid content (corynomycolic acid), resisting the action of lysosomal enzymes.[10] *C. pseudotuberculosis* replicates in the phagolysosome; if large numbers of organisms are engulfed, phagocytic cells die. Experimental inoculation of the organism in sheep revealed a massive infiltration with polymorphonuclear leukocytes, [55] which are believed to carry the bacteria to regional lymph nodes.[4] A PLD toxin of approximately 31.5 kD, produced by all *C. pseudotuberculosis* isolates, increases vascular permeability, causing spread of the organism regionally and systemically.[6, 42,56] Development of abscesses at secondary locations in horses can occur in up to 25% of cases.[28] PLD toxin can cause lymphatic necrosis and thrombosis and may enhance survival and multiplication of the organism via complement depletion and inhibitory effects on phagocytic cells.[6] Corynomycolic acid and PLD toxin contribute to inflammation, edema, and pain during abscess development.[57] The profound reaction of these compounds is probably responsible for the formation a thick abscess capsule that develops as phagocytes accumulate in the abscess core. The abscess eventually matures and drains, but if removal of infected material is incomplete, recurrence may be expected, particularly in small ruminants.[4] The development of internal abscesses in horses is unclear but has been postulated to result from hematogenous or lymphatic spread of bacteria from more superficial sites.[4, 28,34]

**TREATMENT AND PROGNOSIS**

Important features to consider when treating external abscesses are to (1) allow the abscess to mature, (2) establish drainage, (3) collect and properly dispose of the infective exudate, and (4) lavage the wound with an antiseptic solution (5) apply insect repellant ointments and other measures of fly control. In a retrospective study in horses, the majority of external abscesses were incised to establish drainage, then some received antimicrobials after drainage in an effort to decrease cellulitis.[28] Many horses received no treatment; abscesses broke and drained without clinical intervention.[28] Other horses were only treated with antimicrobials.[28] Outcomes were successful for 99% of horses with external abscesses.[28] Horses with abscesses in the axillary region or deep within muscles have considerable pain, necessitating incision and drainage. Ultrasound is useful for localization of deep abscesses.[34]

Antimicrobials for uncomplicated external abscesses are often not indicated. Horses with external abscesses that have systemic illness, recurrent infections, or poor immunity and horses with internal infection or ulcerative lymphangitis require antimicrobials until evidence of infection have completely resolved. If antimicrobials are used, long-term

(minimum 4 - 6 weeks) therapy is necessary for the treatment of internal abscesses and ulcerative lymphangitis. Median resolution time for horses with internal abscesses treated with antimicrobials was 36 to 42 days, with a maximum duration of 97 days.[28, 34] The case fatality for horses with internal abscesses treated with antimicrobials was 30% to 40%, but 100% if not treated.[28, 34] A study describing 35 horses with musculoskeletal infection reported surgical drainage in 60%, antiinflammatories in 97%, and antimicrobials in 86%. [29]

In vitro, *C. pseudotuberculosis* is susceptible to nearly all commonly used antimicrobials and resistance is uncommon.[54] Trimethoprim sulfamethoxazole (30 mg/kg PO q12h), trimethoprim sulfadiazine (24 mg/kg PO q12h), or procaine penicillin (22,000 IU/kg IM q12h) are often effective for external abscesses. Horses with internal abscesses respond well to minocycline (4 mg/kg PO q12h), doxycycline (10 mg/kg PO q12h), enrofloxacin (7.5 mg/kg PO q24h), trimethoprim sulfas (doses above), and potassium penicillin (20,000-40,000 IU/kg IV q4-6h). Rifampin (5 mg/kg PO q12h) is highly effective when added to another antimicrobial (e.g. trimethoprim sulfa or enrofloxacin). Ceftiofur is less effective due to high minimum inhibitory concentrations (MIC) and therefore not recommended. Ulcerative lymphangitis should be treated aggressively with long term antimicrobials (3 – 4 weeks). In horses, colitis is a risk of antimicrobial use. Additionally, enrofloxacin is contraindicated in growing horses due to risk of cartilage damage.

11. Non-steroidal anti-inflammatories (NSAIDs) to control discomfort and inflammation are often used to control the pain and/or fever while waiting for external abscesses maturation.

12. The prognosis for external abscesses is good. Most resolve in 3 weeks from the day of drainage.[4] The prognosis for horses with internal abscesses and ulcerative lymphangitis is guarded but improves if infection is detected early and appropriate long-term therapy is administered. Horses with musculoskeletal infection tend to have a favorable prognosis, but osteomyelitis and septic arthritis can complicate recovery.[29]

13. In a study in cattle, skin lesions on individual cows healed (on average) in 23 days after local or parenteral treatment; 17% of severely affected cattle were culled.[3] Simple drainage in small ruminants does not usually result in resolution of the disease and can become a potential source of infection. Dilute betadine solutions can be used for abscess lavage. Complete excision of the abscess under general anesthesia may be necessary to keep the abscess from draining and prevent spread of the infection to other animals.[4] The treatment of choice in small ruminants is complete surgical removal of affected lymph nodes.

**PREVENTION AND CONTROL**

Even though *C. pseudotuberculosis* infection is one of the most commonly diagnosed infectious diseases in California, little is known about its prevention and control. General recommendations to prevent its spread are isolation of infected animals, fly control, good sanitation, careful shearing practices, disinfection of contaminated fomites, and careful disposal of bedding. On small-ruminant farms, morbidity can reach 100%, with depopulation being the most economic option. Because *C. pseudotuberculosis* can survive in soil and fomites, the potential for environmental contamination is very high.[46,49] Immunization trials utilizing whole cells, cell wall toxoids, and bacterin-toxoid combinations have been used to prevent CLA in small ruminants.[61-65] These vaccines have been shown to provide a high degree of protection, decreasing the number of infected sheep and the number of abscesses per sheep.[61-65] *C. pseudotuberculosis* toxoids are commercially available for sheep and goats (e.g., Caseous D-T [Colorado Serum Co., Denver, Colo.], Glanvac [Australia]). In horses, autogenous bacterin - toxoids have been utilized for many years with anecdotal success.[66] A conditionally licensed bacterin – toxoid (Boerhinger Ingelheim) is available for horses that demonstrates increased SHI titers following 2 infections; however to date conferred protection remains to be established.

14.
15.

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# MEDICINA EN RUMIANTES

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# DOS ESTABLOS LECHEROS: DOS REALIDADES

Se presenta el caso de dos establos lecheros que se ubican en la misma zona geográfica, que cuentan con poblaciones similares de vacas (aproximadamente 450 vacas en ordeño) y que debieran tener desempeños reproductivos y productivos similares, toda vez que cuentan con las mismas fuentes de insumos para la elaboración de alimentos concentrados, y el forraje es adquirido a terceros en el 100% de los casos.

Algunas diferencias encontradas radica en el hecho de que uno de ellos que podemos denominar establo A, tiene un nivel mayor de tecnificación, puesto que cuenta entre otras cosas con collares que permiten medir la actividad diaria de las vacas, lo que da enormes ventajas en la detección de celo si adicionalmente a ello también se realiza una observación visual por personal adiestrado para este fin.

Otra ventaja del establo A es que cuenta con sistema de enfriamiento para las vacas, en la esperanza de mitigar mejor los efectos adversos del estrés de calor, pues cuenta con duchas y sistema de ventilación forzada que le permite mantener frescas a las vacas, especialmente las de alta producción que entran en el sistema de enfriamiento forzado cuatro veces al día, lo que lleva a un mayor consumo de materia seca.

El manejo reproductivo y del establo está a cargo de dos ingenieros zootecnistas a dedicación exclusiva, encargados de realizar las labores propias de la actividad, las que incluyen la inseminación artificial y todo aquello que conlleva a la buena realización de esta actividad de manejo reproductivo, del mismo modo realizan labores de sanidad asesorados por un médico veterinario, que es el mismo para el establo B el que tocaremos más adelante.

El establo B no tiene el nivel de tecnificación que posee el establo A, y para la detección de celos en las vacas y poder realizar de forma adecuada la inseminación artificial, se valen exclusivamente de la detección visual de los celos de las vacas. Para ello cuenta con dos personas: un egresado de la carrera universitaria de administración y otro técnico formado en el establo, quienes tiene a su cargo el manejo de la actividad reproductiva y productiva.

Para mitigar los problemas del estrés de calor en el establo B, se valen de sombras adecuadamente distribuidas, que sirve para paliar los efectos negativos del calor veraniego. Simplemente son sombras hechas de madera como armazón y mala embadurnada con brea a mejorar la durabilidad de la malla rachel con una adecuada orientación.

El balanceo de las raciones y el manejo del alimento en los comederos es similar en ambos establos, vale decir que no hay diferencias marcadas. Ambos establos

cuentan con forraje o ensilado picado y mezclado con el concentrado, labor que se realiza en carros mezcladores y cuya distribución es automatizada.

El desempeño reproductivo en ambos es similar, con tasas de concepción mejores en el establo B. Se hubiera esperado que el establo A tenga mejores rendimientos en cuanto a tasas de concepción, por el hecho de manejar mejor la detección de celos. El aspecto que más resalta es que a lo largo del año el establo B registra mejores {índices de no retorno, es decir que de las vacas destinadas a diagnóstico de preñez, exceptuando tres meses de verano, el establo B siempre ha tenido mejores tasas de concepción que el establo A, lo que significa que el personal del establo B, está detectando mejor los retornos tras un servicio que el establo A. En cuanto a niveles de rendimiento lechero, el establo A si obtiene mejores rendimientos, producto de un mejor manejo de la distribución de alimento probablemente, y apoyado con el sistema de enfriamiento de las vacas.

Se resalta el efecto que puede tener el factor humano como elemento contribuyente al mejor desempeño reproductivo de las vacas, lo que debe quedar como una recomendación en la obtención del concurso del capital humano, en labores tan especiales como son los relacionados a manejo del desempeño reproductivo.

# SÍNDROME DE HÍGADO GRASO EN VACAS LECHERAS Y SU IMPACTO EN LA PRODUCCIÓN Y REPRODUCCIÓN

**INTRODUCCIÓN**

El hígado graso o la esteatosis hepática es un desorden metabólico que se desarrolla entre la primera semana y el primer mes posparto, su incidencia generalmente se asocia a otros desórdenes metabólicos y a la ineficiencia reproductiva, siendo uno de los problemas de salud animal que tiene mayor impacto en la producción y reproducción, especialmente en su forma subclínica, ya que su identificación es difícil para el ganadero (Contreras, 1998). Las vacas de alta producción suelen disminuir bruscamente la ingesta de alimentos por la reducción del apetito debido a cambios hormonales en el parto e inicio de la lactancia, generando un balance energético negativo (BEN) que obliga a la movilización de las grasas desde los depósitos del cuerpo al hígado y se acumula en forma de triglicéridos (Andresen, 2001).

El hígado graso aparece preferentemente cuando hay una excesiva movilización grasa hacia el torrente sanguíneo que va acompañado de elevadas concentraciones de ácidos grasos no esterificados (NEFA) en sangre. El origen de este cuadro apunta a causas como dieta inadecuada durante el periodo de transición, déficit de Vitamina A, obesidad durante el periodo de seca, distocias durante el parto, retención de placenta, entre otros (Contreras, 1998). Los signos clínicos de mayor importancia son la letargia, atonía ruminal, condición corporal igual a 5 con pérdida rápida subsecuente, hiperestesia (Radostits *et al*., 1999). Para el diagnóstico adecuado se requiere de pruebas histoquímicas (Jorritsma *et al.,* 2001).

La presentación subclínica usualmente desatendida por los ganaderos y profesionales involucrados en la ganadería, debe tomar importancia, puesto que usualmente estamos frente a vacas aparentemente sanas, con un buen consumo de alimento que no se nota en el hato, pero que al tener el hígado infiltrado, no lleva a cabo debidamente las funciones como para mantener un organismo normal y con capacidad de producción de leche, o con capacidad de síntesis de hormonas que la hagan apta para el inicio de los programas reproductivos a tiempo, generando vacas de baja producción y con problemas reproductivos que golpean con fuerza al ganadero (Radostits *et al*., 1999).

Puesto que su etiología es multifactorial se deben establecer estrategias preventivas que reduzcan la movilización de grasa durante el periodo de transición por lo que es importante minimizar las grandes caídas en el consumo de alimentos antes del parto y mantener un nivel de consumo adecuado después del parto. Una de las estrategias es evitar el estrés así como cambios bruscos frecuentes en las raciones (Contreras, 1998).

## ETIOLOGÍA

El síndrome de hígado graso se produce por la movilización excesiva y rápida de grasa desde las reservas corporales, lo cual concuerda con la alta oferta de este elemento por acumulación

especialmente en la etapa final de la lactación o primeras semanas de seca, este hecho –como veremos más adelante- bloquea la función hepática, haciendo que este órgano no pueda cumplir con la función normal a la que se expone a una vaca de alta producción (Andresen. 2001).

La causa más frecuente de deficiencias de energía se encuentra asociada a una ingesta insuficiente de alimentos ya sea por falta de aporte de nutrientes o limitaciones del consumo voluntario. Esta situación se suele presentar en la etapa de transición, al emplear forrajes con escaso nivel de nutrientes y materia seca sin cubrir los requerimientos, trastornos digestivos que alteren la absorción, disminución del apetito o alimentos de mala calidad; también el estrés del parto, los desbalances hormonales y una combinación de estos factores pueden provocar un déficit de energía. La caída en el consumo de materia seca es típico de la etapa de transición de las vacas lecheras de altas producción, dado a las alteraciones hormonales que ocurren en el periparto (Contreras, 1998).

## FACTORES DE RIESGO

### Factores nutricionales

El principal factor es la obesidad. En vacas obesas con una condición corporal superior a 4, la lipolisis del tejido adiposo en situaciones de BEN o de estrés metabólico o inmunológico es mayor que en vacas con una condición corporal óptima. En estas situaciones suele disminuir bruscamente la ingesta de alimentos lo que desencadena un balance energético negativo más acentuado. Sin embargo, la obesidad no produce necesariamente hígado graso, sobre todo cuando el estado sanitario es correcto o cuando la ingestión de alimentos se acomoda a las necesidades para la producción de leche, pero la alta oferta de grasa de fácil movilización constituye un factor de riesgo alto (Herdt, 1988).

### Factores de manejo

Los cambios bruscos de dieta y las dietas con gran proporción de concentrados incrementan el riesgo de acidosis ruminal y endotoxemia bacteriana, ambas involucradas en la aparición del hígado graso, porque las situaciones patológicas acentúan la depresión el consumo de materia seca. Restricciones de alimentación de un 30-50% durante solo 4 ó 6 días previos o posteriores al parto pueden inducir la aparición de esta patología. El hígado graso también se desarrolla frente a determinadas hormonas, alimentos o toxinas que alteren el metabolismo hepático (Herdt, 1988).

## FISIOPATOLOGÍA

Debe indicarse que la movilización de grasa corporal desde las reservas, ens un proceso que ocurre en el 100% de vacas de reciente parto, de modo que si el hígado está en la posibilidad de metabolizar esta grasa, hará que se provea de energía para la síntesis de la leche y la grasa de la misma, dando como resultado final CO2 y agua. (Andresen, 2001)
Durante el periodo de transición y equilibrio de energía negativa y antes de la lactación, la glucemia puede disminuir ligeramente, la relación insulina/glucagón disminuye y estas y otras hormonas (catecolaminas) activan las lipasas sensibles a hormonas que convierten la grasa tisular en NEFA y glicerol. En el hígado el glicerol puede utilizarse para producir glucosa o puede recombinarse con los NEFA para formar TG. Además, los NEFA pueden degradarse a través de la oxidación β, y los dos ácidos grasos carbonados convertirse en acetil coenzima A

(CoA).El acetil CoA se combina con el oxalacetato para entrar en el ciclo de los ácidos tricarboxílicos para producir energía. Si no se dispone de suficiente oxalacetato, la acetil CoA se convierte en cuerpos cetónicos, que en concentraciones altas puede reducir el consumo de alimentos y perpetuar el equilibrio energético negativo. Los triglicéridos formados pueden seguir dos vías: pueden ser exportados a la sangre nuevamente como lipoproteínas de muy baja densidad, que es como se transportan las grasas por la sangre o se acumulan en el tejido hepático (Dufval, 1983). Esta acumulación de grasa en el hígado disminuye la capacidad de este para sintetizar glucosa y detoxificar amonio en urea; todos estos eventos producen en el animal una toxemia grave que lo llevara a la muerte. En suma se generan compuestos nitrogenados y estos circulan y llegan al SNC en donde causan daños estructurales (Bobe *et al.,* 2004).

## SIGNOS CLINICOS

Los signos clínicos que manifiesta el animal son útiles para el diagnóstico, pero no definitivos. Siendo los de mayor importancia: la inapetencia, atonía ruminal, letargo, cc = 5, debilidad, depresión o hiperestesia, Temperatura corporal normal o subnormal, mucosas pueden mostrar ictericia, en fases terminales hay coma y taquicardia se vuelven totalmente recumbentes y mueren en 7-10 días (Radostits *et al*., 1999).

## LESIONES

Las lesiones que se evidencia en esta enfermedad son: excicosis de la piel, marcada hepatomegalia, el hígado está muy hipertrofiado y de color amarillo pálido, friable y graso. A nivel histológicos se observa la aparición de quistes grasos o lipogranulomas, hipertrofia de los hepatocitos, compresión de las sinusoides hepáticas, disminución del volumen del retículo endoplásmico rugoso y signos de lesión mitocondrial (Herdt, 1988).

| % de infiltración | Signos clínicos |
|---|---|
| **Más de 35%** | Severas lesiones de hígado y signos clínicos de hepatopatía. |
| **25-35%** | Generalmente se observan signos clínicos de enfermedad. |
| **13-25%** | Generalmente no se observan signos de hepatopatía.<br>Son las vacas de mayor riesgo y provocan las mayores pérdidas productivas. |
| **13% o menos** | Se considera normal. |

***Cuadro 1. Porcentaje de grasa en el parénquima hepático y su relación con los signos clínicos en las vacas* (Herdt, 1988).**

## DIAGNÓSTICO CLÍNICO

El diagnóstico de esta enfermedad se puede realizar a través de las manifestaciones clínicas, curso de la enfermedad y la historia clínica. El diagnóstico preciso de "hígado graso" requiere de pruebas histoquímicas, para lo cual se tiene que realizar una biopsia hepática. Los exámenes de laboratorio clínico proporcionan datos útiles, adicionales al examen clínico y antecedentes epidemiológicos; sin embargo, no son exactos, especialmente para establecer el grado del compromiso hepático. Los más útiles son la determinación de las enzimas hepáticas AST, AGNE y secundariamente el cuerpo cetónico B-Hidroxibutirato (Jorritsma *et al.,* 2001), (Weijers *et al.,* 2012)

PARÁMETROS BIOQUÍMICOS EN VACAS DE LECHE

Fuente: M. Sevinc et al., 2001.

| Parámetros | Control (n:12) | HÍGADO GRASO Leve (n:17) | Moderado (n:17) | Severo (n:20) |
|---|---|---|---|---|
| Ácido biliar (µmol/L) | 34.9±8.3 | 51.6±8.2 | 72.5±8.6 | 97.8±9.0 |
| Glucosa (mg/dl) | 82.3±5.1 | 53.4±2.5 | 58.8±5.6 | 53.7±4.0 |
| Proteína de celulas T | 7.9±0.1 | 8.1±0.2 | 7.1±0.2 | 7.7±0.2 |
| Albúmina (g/dl) | 3.4±0.1 | 3.3±0.1 | 2.7±0.1 | 2.1±0.1 |
| Globulina (g/dl) | 4.5±0.1 | 4.9±0.2 | 3.8±0.3 | 4.4±0.2 |
| T. Bilirrubina (mg/dl) | 0.3±0.1 | 0.3±0.1 | 0.5±0.1 | 0.6±0.1 |
| D. Bilirrubina (mg/dl) | 0.1±0.3 | 0.1±0.3 | 0.1±0.3 | 0.2±0.3 |
| I. Bilirrubina (mg/dl) | 0.2±0.1 | 0.2±0.1 | 0.3±0.1 | 0.4±0.1 |
| Urea (mg/dl) | 18±1.2 | 19.4±1.3 | 31.4±4.4 | 26.8±3 |
| ALP (U/L) | 99.8±8.2 | 64.4±7.6 | 71.5±77.1 | 79.4±5 |
| CK (U/L) | 121.2±12.3 | 112.2±9.6 | 197.9±22 | 228.4±4 |
| GGT (U/L) | 22.3±2.1 | 24.6±2.6 | 73.7±7.5 | 6.7±1.1 |
| AST (U/L) | 65.1±4 | 82.6±7.3 | 96.0±6.7 | 154.6±23 |
| ALT (U/L) | 29.1±1.7 | 24.9±1.3 | 27.0±1.6 | 29.3±1.5 |

*Cuadro 2 Parámetros bioquímicos en vacas de leche (Savine et al.,2001)*

## DIAGNÓSTICO DIFERENCIAL

| ENFERMEDAD | SIGNOS SIMILARES | DIAGNÓSTICO |
|---|---|---|
| **DESPLAZAMIENTO DE ABOMASO A LA IZQUIERDA** | Caquexia, disminución de producción láctea, heces escasas y blandas, constantes fisiológicas normales. | A la auscultación y percusión resonancia metálica en el flanco izquierdo. |
| **RETÍCULOPERITONITIS A CUERPO EXTRAÑO** | Pérdida de peso, dorso arqueado, anorexia, producción de leche disminuida. | Taquicardia, respiraciones aceleradas, y también fiebre (39.4 a 40.5 °C). Positivo a la prueba de pellizco. |
| **METRITIS** | Pérdida de apetito, deshidratación, letargo, disminución de la producción láctea. | Secreción vaginal es de un olor pútrido y se acompaña de fiebre. |

| | | |
|---|---|---|
| **MASTITIS HIPERAGUDA** | Anorexia, debilidad, ojos hundidos, pulso débil y rápido, fiebre, depresión. | Calor, rubor, dolor y secreción anormal en la glándula mamaria. |

*Cuadro 3. Diagnóstico diferencial*(Bobe *et al.,* 2004,)(Katoh, 2002)

## TRATAMIENTO

Probablemente es la enfermedad que de presentarse en su forma aguda no responde a los esquemas de tratamiento estándar, puesto que la toxemia grave y el daño al SNC, sean suficiente como para llevarlo a la muerte. Sin embargo se instaura tratamiento que en algunos casos ha resultado eficaz, consistente en el goteo IV lento de glucosa al 5% con insulina o sucedáneos de ella como la zinc protamina. El tratamiento de soporte incluye la administración de una variedad de alimentos agradables al gusto y el ejercicio para fomentar la combustión de los cuerpos cetónicos (Bobe *et al.,* 2004)

El tratamiento recomendado de infusión IV de glucosa (Dextrosa) y soluciones de múltiples electrólitos, debe ser lenta, debido a que la glucosa exógena y la endógena pueden llevar al animal a que tenga hiperglucemia lo cual es contraproducente. Medidas adicionales constituyen de ayuda en el problema, como la administración oral de líquido ruminal (5-10 L) procedente de vacas normales, en un intento por estimular el apetito de las vacas afectadas. También se han empleado los corticosteroides, como, por ejemplo, la dexametasona a dosis

de 20 mg cada dos días IM, hasta la recuperación, incluso hay intentos de trabajar con carnitina con resultados no publicados (Bobe *et al.*, 2004).

## PREVENCIÓN Y CONTROL

Un adecuado programa de transición puede disminuir la presentación de casos clínicos, manteniendo el consumo de materia seca por encima de los 10 kg en rpomedio, podemos hacer que la movilización de la grasa sea brusca. El suministro de nutrientes suficientes y un medio ambiente limpio y saludable en el periodo del periparto podría reducir las pérdidas de producción más que cualquier otro tratamiento, el centro de atención del control del balance energético negativo debe estar en aportar el máximo de energía ingerida y reducir la movilización de grasa en el periparto (Grum *et al.,* 1996)

Es fundamental proporcionar alimentos de buena calidad, con una adecuada cantidad de proteína degradable y no degradable a nivel ruminal, para permitir una adecuada actividad microbiana y absorción de aminoácidos esenciales a nivel del intestino. El aporte total diario de concentrados debería distribuirse en pequeñas fracciones durante el día, para mejorar su utilización, promover el apetito y evitar la acidez ruminal, siendo necesario en algunos casos utilizar alcalinizantes como bicarbonato de sodio en la ración. La administración de glucemientes como propilenglicol o propionatos ayudan a mantener la glucemia, especialmente antes del parto, contribuyendo con ello a que la movilización de grasa desde las reservas corporales, no sea abrupta y que la vaca pueda hacer un puerperio en mejores condiciones (Grum *et al.,* 1996).

Por último, es necesario considerar el uso de estrategias de apoyo que disminuyan los efectos negativos del balance energético negativo. Entre ellas, el manejo de un programa de transición en donde se maneje dietas altamente energéticas y muy palatables, siempre ayudan a controlar y prevenir la presentación del hígado graso que disminuye las concentraciones de BHB y NEFA en plasma. Se han probado otras alternativas como la administración de colina protegida que favorece la exportación de los triglicéridos como lipoprotínas de muy baja densidad, disminuyendo así la infiltración de triglicéridos en los hepatocitos, es una alternativa que está tomando fuerza en los últimos años. Los elementos lipotrópicos sin protección de la degradación ruminal tienen limitado efecto en la prevención del hígado graso. Por otro lado se sigue promocionando otros elementos que se suponene lipotrópicos sin éxito comprbado, como la suplementación con grasa en el periparto, el uso de niacina o ácido nicotínico o la administración de compuestos involucrados en el metabolismo lipídico (Grum *et al.,* 1996).

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# MASTITIS BOVINA

## INTRODUCCIÓN

La primera reflexión que viene a la mente es cuál de los ganaderos de nuestro medio o de otras latitudes está libre de mastitis, y la respuesta es que ninguno está libre. Lo que pueden tener son niveles de mastitis más altos o más bajos comparados con otras explotaciones, pero que en suma "no hay establo lechero que no tenga mastitis". Esto hace que sea un reto para médicos veterinarios y personal que labora en un establecimiento ganadero, puesto que todos apuntan a que la enfermedad se mantenga en los niveles más bajos, y ese va a ser el objetivo de la lucha contra esta enfermedad.

Sabemos que es una enfermedad muy costosa y genera serios problemas en la industria lechera en todo el mundo debido a que induce a la disminución de la producción de leche, afecta en forma negativa a la calidad de la misma e incrementa los costos del cuidado de la salud del hato (Santivañez *et al.,* 2014). El impacto económico de la mastitis clínica y subclínica requiere ser revisado continuamente y se sabe que no es evidente sin un análisis de niveles de producción en un período largo, razón por la cual es difícil de comprometer a los ganaderos en la decisión de tomar medidas de control (Andresen H. 2001)

Está claro que la leche proveniente de cuartos afectados con mastitis presenta un menor porcentaje de sólidos totales, proteínas, grasas y calcio; mientras que el recuento total de bacterias, así como el riesgo de encontrar residuos de antibióticos se incrementan, afectando su calidad constituyendo un peligro potencial para la salud de los consumidores. Hoy en día especialmente en países en desarrollo para muchos no es claro aún y en relación al público consumidor, quien entraña más riesgo, la leche proveniente de una ubre con mastitis o los residuos de antibióticos que se genera con los tratamiento que se sigue, especialmente en las mastitis clínica (Velásquez y Vega, 2012).

## ETIOLOGIA

Es una infección causada en un alto porcentaje (cercano al 100%) por bacterias y en donde la infección ascendente desde el medio que rodea a la vaca es algo que ya no admite discusión, sea durante el ordeño cuando la infección pasa de vaca a vaca y de teta a teta, o cuando la vaca que ha salido de la sala de ordeño y tiene los esfínteres relajados y al echarse en los corrales, está sumamente expuesto a los microorganismos ambientales. La invasión del sistema de conductos y el tejido glandular mamario por parte de microorganismos además puede involucrar a otros elementos, como hongos, levadura, algas, y estas conducen al desarrollo de una infección del tejido mamario, condición que tiene dos modalidades: contagiosa y medioambiental (Mendoza *et al*., 2017)

Los patógenos contagiosos pueden considerarse como organismos adaptados para sobrevivir dentro del huésped, en particular dentro de la glándula mamaria. Son capaces de establecer infecciones subclínicas, que normalmente se manifiestan como una elevación en el recuento de células somáticas (leucocitos predominantemente neutrófilos y células epiteliales) de la leche del barrio afectado;

por lo general, se propagan de vaca a vaca en el momento del ordeño (Smith, 2010)

Los principales patógenos contagiosos comprenden *Staphylococcus aureus (S. aureus), Streptococcus agalactiae (S. agalactiae), y Mycoplasma bovis (M. bovis),* los cuales residen dentro de la glándula mamaria *(S. agalactiae)*, piel de la glándula mamaria y cuya transmisión tiene lugar en el momento del ordeño. (Mendoza *et al.*, 2017). En contraste, los patógenos ambientales se describen mejor como invasores oportunistas de la glándula mamaria, no dependen de la presencia en la ubre de la vaca; típicamente ellos pueden 'Invadir', dividirse y generar una respuesta inmune del hospedero y se elimina rápidamente (Bradley, 2002)

Los principales patógenos ambientales comprenden la Enterobacteriaceae, como *Escherichia coli* (*E. coli*), *Streptococcus uberis (S. uberis), Streptococcus dysgalactiae (S. dysgalactiae), Pseudomonas aeruginosa (P. aeruginosa), Kelbsiella pneumoniae (K. pneumoniae), Arcanobacterium bovis (A. bovis).* (Mendoza J. *et al.* 2017). Por otro lado existen patógenos menores, son aquellos que se aíslan esporádicamente de leches mastíticas y dentro de ellos se encuentran *Stahylococcus* coagulasa negativos (SCN), *Bacillus cerius, Nocardia farcinicus, Prototheca zopfii.* La frecuencia de la infección por estos patógenos es variable y depende del nivel de prevención, los métodos de ordeño y las condiciones de manejo de los animales.(Mendoza J. *et al*. 2017)

**FACTORES DE RIESGO**

**Manejo**

Muchos de los microorganismos pueden vivir en la piel de la glándula mamaria y su transmisión puede ocurrir en el momento del ordeño por prácticas que constituyen factores de riesgo para la presentación de la enfermedad, como la carencia de limpieza de las ubres y pezones, el uso compartido de toallas para secado las ubres, mediante las manos contaminadas de los ordeñadores o por el uso de pezoneras no desinfectadas entre vacas en los ordeños mecánicos. En general los estudios referentes a factores de riesgo en nuestro medio se relacionan con deficiencias en la rutina de ordeño. Probablemente el manejo a la hora del ordeño sea uno de los factores de riesgo más importantes, pues muchos ganaderos no prestan la debida atención a la separación de vacas por número de partos y etapa de lactación, y en la sal de ordeño prestan poca importancia al protocolo que se debe seguir para realizar el correcto ordeño (Mendoza *et al*. 2017)

**Medio Ambiente**

Factor importante en la generación de infecciones, especialmente en el diseño y construcción de corrales en donde se descuida el área que deben tener los animales el que no debiera de ser menor a 40 m2, de suerte que la vaca tenga área suficiente como para el descanso en los corrales. El mantener corrales con lodo producto de fugas de agua o desagüe, convierten al lugar donde las vacas toman el descanso en lodazales con una lata carga bacteriana que termina por vencer las capacidades de defensa que posee la glándula mamaria. (Acuña y Rivadeneira 2008)

**Máquina de Ordeño**

Se trata de todo el sistema y el equipo de ordeño; a su vez de la construcción de la sala de ordeño e instalación de los equipos, como su ubicación en armonía con las demás instalaciones del establo y del mejor acceso a fuentes de energía eléctrica, disponibilidad de abundante agua de buena calidad y baja dureza y red de desagüe (Andresen, 2001). Cuando el funcionamiento del equipo es ineficiente así como el nivel de vacío en las diferentes partes de la máquina no es el adecuado, se constituye en un

factor de riesgo y en muchos casos es causante de brotes de mastitis. Hoy en día se trabaja mucho en actividades de evaluación de máquinas de ordeño, dado que se ha comprobado que su participación en la generación de mastitis es crucial para el ganadero (Acuña y Rivadeneira, 2008)

**Características del animal**

Las vacas con características indeseables y especialmente en lo concerniente a la ubre, son un factor de riesgo para mastitis, simplemente debemos tomar en cuenta una vaca con ubre pendulosa la que constantemente está sometiendo a trauma la glándula mamaria, va a generar mastitis recurrente, constituyéndose en diseminadora de bacteria generadoras del problema y constituyéndose en vacas difusoras de la enfermedad. (Smith, 2010). La estructura del canal del pezón es importante en la regulación de la entrada de microorganismos. Algunos autores afirman que si el tono de las estructuras anatómicas de la apertura del pezón es reducido, lo que es un carácter heredable, la resistencia a la entrada de los microorganismos será menor (Acuña y Rivadeneira 2008).

**Microorganismos**

Patógenos contagiosos comprenden *Staphylococcus aureus (S. aureus), Streptococcus agalactiae (S. agalactiae), y Mycoplasma bovis (M. bovis),* los cuales residen dentro de la glándula mamaria *(S. agalactiae)*, piel de la glándula mamaria y cuya transmisión tiene lugar en el momento del ordeño. (Mendoza *et al.*, 2017). Los principales patógenos ambientales comprenden la Enterobacteriaceae, como *Escherichia coli* (*E. coli*), *Streptococcus uberis (S. uberis), Streptococcus dysgalactiae (S. dysgalactiae), Pseudomonas aeruginosa (P. aeruginosa), Kelbsiella pneumoniae (K. pneumoniae), Arcanobacterium bovis (A. bovis).* (Mendoza J. *et al.* 2017). Por otro lado existen patógenos menores, son aquellos que se aíslan esporádicamente de leches mastíticas y dentro de ellos se encuentran *Stahylococcus* coagulasa negativos (SCN), *Bacillus cerius, Nocardia farcinicus, Prototheca zopfii.* (Mendoza J. *et al*. 2017)

**EPIDEMIOLOGIA**

La mastitis por su naturaleza de ser una enfermedad y una infección dinámica, no permite con facilidad determinar la prevalencia en determinadas áreas de nuestro medio, sumamos a ello la poca importancia que el ganadero y los profesionales brindan a su determinación, la dificultad de acceder a los laboratorios de manera adecuada por cuestiones de distancia, falta de cultura en la toma de muestras. Estas situaciones y otras más no permiten determinar con facilidad la prevalencia o un diagnóstico situacional de la mastitis bovina.

En un estudio que se realizó en la provincia de Huaura, Lima entre 2009 y 2010 se evaluó la frecuencia de mastitis subclínica por efecto del tamaño del establo, número de partos y momento de lactancia (Velásquez y Vega 2012).

En el valle de Huaura, el 92% de los establos son pequeños (promedio de seis vacas), con sistemas de crianza semiintensivos y bajo estas condiciones, el estrés a que son sometidos los animales en producción es inferior al de establos medianos y grandes, lo que influiría en una menor presentación de mastitis subclínica. La mastitis subclínica se presentó con menor frecuencia en establos pequeños. Se encontró además, una mayor presentación de mastitis subclínica en vacas de dos o más partos, ya que tienen mayores probabilidades de infección por

su mayor tiempo de permanencia en el establo y de exposición a los patógenos. Además, algunas infecciones se vuelven crónicas y el sistema inmunológico de las vacas adultas y de edad avanzada no es tan eficiente como en las vacas jóvenes (Velásquez y Vega 2012).

Existe una relación de dependencia entre el momento de la lactancia y la presentación de mastitis subclínica. El mayor porcentaje de cuartos afectados en los estadios finales de la lactancia se debería al incremento de la cantidad normal de células somáticas que se concentran en un menor volumen de leche, por efecto de una menor producción a medida que avanza la lactancia (Velásquez y Vega 2012).

Cuadro 2. Frecuencia de mastitis subclínica en vacas lecheras en producción, en relación al tamaño del establo, número de partos y momento de lactancia, en establos lecheros del valle de Huaura. 2009-2010

| Factores | N.° de cuartos mamarios | | | |
|---|---|---|---|---|
| | Total | Positivos a CMT[1] | | |
| | (n) | n | % | IC (95%)[2] |
| Tamaño del establo[3] | | | | |
| Grande | 6,823 | 3,403 | 49.9[a] | 48.9 - 50.9 |
| Mediano | 565 | 297 | 52.6[a] | 48.6 - 56.6 |
| Pequeño | 1,006 | 299 | 29.8[b] | 26.8 - 32.8 |
| Número de partos | | | | |
| 1 | 262 | 86 | 32.8[ab] | 26.8 - 38.8 |
| 2 | 113 | 28 | 24.8[a] | 16.8 - 32.8 |
| >2 | 248 | 101 | 40.8[b] | 34.8 - 46.8 |
| Momento de lactancia[4] | | | | |
| Inicio | 220 | 51 | 23.2[a] | 17.2 - 29.2 |
| Medio | 199 | 76 | 38.2[b] | 31.2 - 46.2 |
| Final | 238 | 96 | 40.3[b] | 34.3 - 46.3 |

[1] California Mastitis Test
[2] Intervalo de confianza de 95%
[3] Pequeño: ≤25; Mediano: 26-100; Grande: ≥100 vacas en producción
[4] Inicio: ≤100; Media: 101-180; Final: >180 días
[a,b] Superíndices diferentes dentro de factores indican diferencias significativas (p<0.05)

En la región litoral occidental en Uruguay, se utilizó una submuestra que incluye 1077 vacas lecheras de granjas seleccionadas al azar para determinar la prevalencia de mastitis subclínicas que fue 52.4% en base a las vacas y los patógenos aislados de los casos subclínicos y sus frecuencias relativas fueron: *Staphylococcus aureus* 62.8%, *Streptococcus agalactiae* 11.3%, *Enterococcus sp*. 8%, estafilococos coagulasa negativos 7,4%, *Streptococus uberis* 6,4%, *Streptococcus dysgalactiae* 1,8%, *Escherichia coli* 1,5% y *Staphylococcus hyicus* coagulasa-positiva al 0,6%. (Gianneechini *et al.*, 2002)

**FISIOPATOLOGÍA**

Su desarrollo se puede explicar en tres etapas: invasión, infección e inflamación del área dañada (Constable *et al.* 2017)

**Invasión**

*Las bacterias causantes de la mastitis penetran a la glándula mamaria a través del canal del pezón.*

El conducto del pezón y el tejido musculoelástico que lo rodea constituyen la barrera física primaria a la invasión microbiana y también impiden la fuga de leche entre los ordeños. La forma tortuosa del conducto proporciona protección física frente a la infección, como su riqueza en queratina, que producen continuamente las c é lulas epiteliales y que recubre el conducto. Este conducto o canal del pezón al terminar el ordeño y por efecto del trabajo al que es sometido, termina relajado y sin la capacidad de recobrar el tono hasta un periodo de 20 a 30 minutos del ordeño, este hecho es aprovechado por las bacterias medioambientales para vencer el esfínter del pezón y ubicarse en la glándula mamaria especialmente en la porción glandular (Smith, 2010).

La queratina tapona físicamente el conducto y atrapa a los microorganismos invasores, que después son expelidos con la queratina desprendida en el momento del ordeño. La queratina también contiene ácidos grasos y proteínas que tienen efectos bacteriostáticos o bactericidas. Se une a los microorganismos, la cual altera la pared celular, lo que los hace más susceptibles a la presión osmótica, esto provoca la muerte bacteriana, de igual manera, la queratina previene la migración de los microorganismos a la cisterna de la glándula. Esta queratina prácticamente desaparece con el ordeño lo que incrementa la susceptibilidad del canal de pezón a la invasión y colonización bacteriana (Smith, 2010).

Cuando tenemos microrganismos infecciosos, la invasión del pezón ocurre durante el ordeño. Los organismos presentes en la leche o en el la máquina de ordeño son impulsados hacia el canal y la cisterna cuando hay admisión de aire no deseado en la unidad de ordeño. Después del ordeño, el canal del pezón permanece dilatado por una o dos horas (las fibras elásticas que rodean al conducto se retraen y la queratina comienza a renovarse); sin embargo, el canal de un pezón dañado puede permanecer parcialmente o permanentemente abierto y los organismos del medio ambiente o los que se encuentran en la piel lesionada en la punta del pezón pueden invadir fácilmente un canal de esta condición (Wattiaux, 2010)

**Infección**

*Los patógenos colonizan y están listos para la división binaria e invasión del tejido mamario.*

La población de patógenos puede establecerse en el canal del pezón y producirse una serie de dividiones y extensiones generando una infección del tejido mamario que ocurre con frecuencia u ocasionalmente dependiendo del hospedador y patogenicidad del microorganismo, pero lo usual es que invadan la porción alveolar de la glándula mamaria y es ahí que con la ayuda de sus factores de virulencia y patogenicidad, se establecen. El tipo de bacteria determina su capacidad de hacer división binaria en la leche y adherirse al epitelio mamario. La virulencia de especies bacterianas individuales se debe a esta capacidad de adherencia. La infección se produce más fácilmente en el período de secado, debido a la ausencia de flujo (Constable *et al*., 2017)

**Inflamación**

*La presencia de los microorganismos y la generación de toxinas dan lugar a la respuesta inflamatoria que es la causante del inicio de las alteraciones en las características organolépticas de la leche*.

Una vez que el microorganismo infecta el tejido mamario, empieza la división binaria y la generación de toxinas, las que generan a su vez daño tisular con la consecuente liberación de sustancias quimiotácticas. Las toxinas bacterianas generan daño, pero a su vez y a través de las sustancias quimiotácticas, promueven a la migración de las células blancas desde la circulación, y fundamentalmente migran leucocitos polimorfonucleares, que a la llegada a la glándula mamaria reciben el nombre de células somáticas que en adelante serán los que marquen la pauta sobre el grado de inflamación. (Smith, 2010).

Los neutrófilos sanguíneos deben adherirse al endotelio vascular antes de migrar a la leche mediante una molécula de adhesión de superficie llamada CD62L (L-selectina). Una vez unidos, los neutrófilos migran entre las células endoteliales y epiteliales mamarias hacia la leche (diapédesis), viajando a lo largo de un gradiente quimiotáctico hasta la zona de la infección ( Smith, 2010)

Una vez en esta zona de infección, los neutrófilos fagocitan y destruyen a los microorganismos patógenos, pero a la vez dejan libre sus enzimas y estos también causan daño tisular en la glándula mamaria, incrementando la respuesta inflamatoria. Ejercen su efecto bactericida a través de una explosión respiratoria que produce radicales hidroxilo y oxígeno, que son componentes importantes del mecanismo de eliminación dependiente del oxígeno (Constable *et al*., 2017)

Las sustancias liberadas por los leucocitos conducen a la destrucción completa de las estructuras alveolares, que son reemplazadas por tejidos conjuntivos y cicatrices generando así la tercera línea de defensa de la vaca para controlar la infección (Wattiaux M., 2010)

La intensidad de la respuesta inflamatoria determina si la mastitis es clínica o subclínica. En una mastitis subclínica, la respuesta inflamatoria no es preponderante, el patógeno puede infectar uno o más cuartos, pero no causa mayor daño en el alveolo mamario como para dar de resultado leche visiblemente anormal. En estos casos el sistema inmune de la vaca responde a la invasión bacteriana enviando glóbulos blancos al cuarto inflamado para combatir a la bacteria invasora (Rueg, 2001)

**SIGNOS**

Los signos clínicos varían, pueden netamente locales o ser infecciones generalizadas. En las afecciones locales, lo primero que se observa es el cambio en las características de la leche, se puede ver presencia de grumos, flóculos en su gran mayoría, pero con la vaca aparentemente normal. Cuando el problema involucra un problema sistémico, es probable que se pueda detectar hinchazón o edema en la glándula mamaria, con cambio marcado en las características de la leche, pero paralelamente a esto es posible detectar fiebre, anorexia y depresión de sensorio, todo esto dependerá de las características del microorganismo involucrado, ya que algunas cepas muy selectas de coliformes o esfilococos, generan las formas hiperagudas de mastitis que en algunos casos pueden acabar cion la vida de la vaca.

En la mastitis subclínica (MSC), el proceso inflamatorio no da lugar a alteraciones visibles ya que la vaca parece sana, la ubre no muestra signos de inflamación y la leche

tiene apariencia normal; pero existe una disminución en la producción de leche y se altera su composición por el incremento en el número de células somáticas (SCC) (Acuña y Rivadeneira, 2008)

**DIAGNÓSTICO**

El hallazgo de los signos clínicos enumerados da el diagnóstico de mastitis clínica, la que debe ser corroborada por métodos de laboratorio, como el aislamiento y la tipificación de los microorganismos involucrados, y para ello se tiene que tener un protocolo de toma de muestras de leche, a fin de que el laboratorio nos pueda dar un diagnóstico certero. Hoy en día en los países donde la lechería está desarrollada, los métodos de diagnóstico basados en la determinación de ADN bacteriano ya se encuentran en uso.

La mastitis subclínica es sutil y más difícil de detectar. Se puede demostrar usando varias pruebas como la Prueba de Mastitis de California (CMT) dentro de lo más conocido, como también otras como la Prueba de Whiteside (WST), Prueba de mastitis del campo de surf (SFMT), Prueba de lauril sulfato de sodio (SLST). El recuento de células somáticas (RCS) probablemente sea el método más aceptado en el diagnóstico de la mastitis y la valoración de la calidad de la leche, y esto se puede aplicar por dispositivos que tiene celdas fotoeléctricas aun cuando la observación de frotices de leche coloreados también tiene aceptación. Otras pruebas como la prueba de conductividad eléctrica (CE) han sido evaluadas y utilizadas en el diagnóstico de la mastitis subclínica. En la mastitis subclínica también están indicadas el aislamiento y la identificación de los microorganismos que causan la mastitis, los procedimientos de cultivo microbiológico siguen siendo el estándar de oro (Mpatswenumugabo *et al.,* 2017)

Sin embargo, una de las técnicas empleadas para evaluar la afección de las glándulas mamarias es el California Mastitis Test (CMT) dado su practicidad, bajo costo, simplicidad, rapidez en la obtención de resultados diagnósticos, aplicabilidad y efectividad (Santivañez *et al*., 2014)

**TRATAMIENTO**

Lo que universalmente van a hacer tanto profesionales como ganaderos es utilizar los antibióticos, estos irán de acuerdo a la gravedad y lo avanzado sea el proceso. Muchos profesionales piensan que el tratamiento debe hacerse por vía intracisternal y otros piensan que debe ser parenteral. En ello siempre habrá controversias. Pero cualquiera que fuera la vía de administración, lo que debe quedar claro es que la antibioterapia, debe ser racional, de manera que cubra la etapa clínica y vaya a dos ordeños más después de desaparecido los signos clínicos. También se puede realizar ordeños frecuentes y masajes de los cuartos por cada 4 horas por 3 a 4 días para bajar la carga bacteriana, esto ayuda mucho en la disminución de la eliminación de toxinas y disminución de carga bacteriana (Andresen, 2001)

A diferencia de la mastitis clínica que deben tratarse de inmediato, la mayoría de los casos de mastitis subclínica no deben tratarse durante la lactancia, sino al momento de la seca; salvo que el hato tenga una alta prevalencia de infecciones por *S. agalactiae*, en cuyo caso sí existe una justificación económica para hacerlo. Este vive solo en la ubre de la vaca y el 80-90% de las vacas infectadas generalmente se curan con un tratamiento intramamario con medicamentos a base de penicilina (Rueg, 2001)

Por tanto cuando su infección es alta se puede usar el tratamiento "blitz", que consiste en tratar una vez todas las vacas (o sólo las infectadas detectadas mediante cultivo) con penicilina procaínica, de preferencia en una base de larga acción. Este método obliga a no ordeñar los cuartos a las vacas tratadas durante 48 horas y luego eliminar la leche ordeñada por lo menos durante los siguientes 4 ordeños para eliminar los residuos del antibiótico (Andresen, 2001)

No es rentable tratar a la mayoría de las vacas que están infectadas subclínicamente con *Staphylococcus aureus* porque las tasas de curación durante la lactancia son generalmente inferiores al 20%. Sin embargo, puede haber algunos casos en los que se deba intentar el tratamiento de la mastitis clínica (Rueg, 2001). En estos casos se puede administrar antiinflamatorios como:

- Flunixine, mínimo 1.3 g IM cada 24 horas por 3-5 días
- Dexametasona, 250 mg EV cada 24 horas por 3-5 días
- Ketoprofeno, 2 g IM cada 24 horas por 3-5 días

A su vez administrar un antibiótico

- Sulfa + Trimetroprim (24%), 50 ml EV cada 24 horas por 3-5 días
- (Norfloxacina) o Enrofloxacina (Baytril 5% iny, 30 ml EV cada 24 horas por 3-5 días)
- Amoxicilina + Ac. Clavulánico (Augmentin, 8 viales de 1.2 g EV, cada 12 horas por 3-5 días)

**CONTROL Y PREVENCIÓN**

Esta enfermedad no se puede eliminar por completo del hato, pero la incidencia se puede llevar al mínimo, el control de la enfermedad se hace a través de buenas prácticas de manejo que pueden incluir: el tratamiento temprano y eficaz de los casos clínicos, una adecuada higiene en el ordeño, el uso de equipos de ordeño que funcionen correctamente, el suministro de áreas de alojamiento limpia y seca, programas nutricionales adecuados y la identificación y el tratamiento adecuados de las vacas infectadas con mastitis clínica y subclínica. (Rueg, 2001).

La evaluación y corrección de las fallas que se detectara en la máquina de ordeño deben ser corregidas con prontitud, y un programa de evaluación de la máquina de ordeño que cubra por lo menos semestral contribuirá a mantener un buen estado sanitario en relación a mastitis. Ordenar las vacas en función al ingreso a la sala de ordeño es uno de los factores que ayuda mucho a controlar el problema, de ahí que deben ingresar primero las vacas primerizas frescas, luego las primerizas con periodo de lactación medias y tardías, luego irán las vacas multíparas frescas seguidas de las que tiene periodos de lactación más prolongadas, para que al final vayan las vacas enfermas y en tratamiento.

El protocolo de rutina de ordeño debe ser respetado, de manera que el presellado o desinfección preordeño, debe ser realizado de manera adecuada, y luego el despunte y la limpieza de los pezones debe ser individual y seguida de la colocación de las unidades de ordeño para cosechar la leche, para luego pasar a la desinfección posordeño o sellado. Estas simples recomendaciones han logrado disminuir la mastitis significativamente en algunos hatos que aplican de manera sistemática.

Durante el periodo seco, varios autores recomiendan el uso de antibióticos para eliminar infecciones que se hayan presentado durante la última etapa de la lactación y prevenir nuevas infecciones durante el inicio del periodo seco justo cuando la glándula

mamaria es más susceptible a infectarse, de esta manera se controla la mastitis durante el periodo seco (Acuña y Rivadeneira, 2008)

Los procedimientos de higiene durante el ordeño como el lavado de manos, entre otros (limpieza de pezones y ubre en seco de preferencia), uso de desinfectantes, secado con toallas desechables individuales antes de cada ordeño, higiene de la unidad de ordeño y utensilios, y desinfección o sellado de los pezones con materiales que tengan la capacidad desbloquear o inhibir el crecimiento y desarrollo microbiano), previenen la transmisión de microorganismos a través del ordeñador a las vacas, disminuyendo la población microbiana sobre la piel del pezón (Constable *et al.,* 2017)

Sacrificio de los animales con enfermedad crónica es una medida que se debe considerar para disminuir la incidencia de mastitis subclínica (Rueg, 2001)

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# RAUL GUERRERO

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# LA SOMATOTROPINA BOVINA EN PRODUCCIÓN DE LECHE

La hormona del crecimiento o somatotropina es esencial para el desarrollo normal de los humanos y animales. Una de las características de la somatotropina en mamíferos, que se encontró hace muchos años, es la de participar en el proceso de producción de leche. Antiguamente para obtener la somatotropina había que extraerla directamente de la hipófisis de las especies a estudiar por ser específicas para cada especie animal. El proceso de obtención de hipófisis adecuadas en cantidades suficientes para la extracción, aislamiento y purificación de la somatotropina se hacía muy complicado y caro por la cantidad de hipófisis a usar para obtener unos pocos miligramos de hormona pura. Con el advenimiento de la biotecnología se facilito la posibilidad de producir grandes cantidades de somatotropina en forma eficiente y económica. Así se iniciaron estudios para administrar pequeñas cantidades adicionales de somatotropina bovina a vacas lecheras para inducir la mayor producción de leche siempre y cuando las vacas tengan condiciones adecuadas para recibir el tratamiento y sean mantenidas en buenas condiciones nutricionales y de salud

La somatotropina bovina puede constituir una herramienta efectiva en el manejo de las vacas lecheras para mejorar la producción de leche.

# ANABÓLICOS EN LA PRODUCCIÓN DE CARNE

Uno de los mayores objetivos de los médicos veterinarios es contribuir a la producción de alimentos de origen animal para satisfacer las necesidades de una población humana en crecimiento constante, se calcula que en 25 años se tendrá que producir por lo menos un 30% más de la producción actual de alimentos a nivel mundial para cubrir las necesidades de entonces con alimentos en suficiente cantidad, nutritivos, sanos y particularmente asequibles a las de poblaciones de pocos recursos económicos.

A través del tiempo se han usado conocimientos técnicos para incrementar la producción de alimentos de origen animal para hacerlo en forma más eficiente (vitaminas, minerales, hormonas, suplementos nutricionales, antibióticos y productos químicos entre otros).

Recientemente se introdujeron en el mercado productos anabólicos tanto naturales como sintéticos para mejorar la eficiencia en producción de carne en bovinos, algunos de ellos son objetados por su naturaleza o por dejar residuos de ellos o metabolitos en algunos órganos y en carne que al ser consumida por humanos podrían tener efectos no deseables. En algunos países hay restricciones establecidas para limitar o prohibir el uso de ellos, habiendo otros países que permiten su uso cumpliendo con las recomendaciones de organizaciones internacionales y de los fabricantes de esos productos para obtener los resultados esperados en inocuidad y mejoramiento de eficiencia en producción.

# USO RACIONAL Y PROFESIONAL DE ANTIBIÓTICOS

Desde que se descubrieron los antibióticos y se usaron para combatir infecciones producidas por bacterias en humanos y animales se formularon algunos temores sobre la posibilidad de perder la eficacia de los mismos por la aparición de cepas resistentes a los antibióticos que con el tiempo podrían hacer inútil su uso en terapia de infecciones bacterianas.

En los últimos años se han incrementado reportes de identificación de cepas de bacterias, causantes de infecciones particularmente en humanos que muestran resistencia a algunos antibióticos que hacen pensar que estamos confrontando una disminución de la eficacia de algunos antibióticos.

Estos hechos han motivado preocupación y organización de reuniones internacionales de especialistas en la materia para compartir experiencias y tratar de establecer actividades comunes para enfrentar el problema.

Grupos como la Organización Mundial de la Salud (OMS/WHO), Organización de Agricultura y Alimento (FAO), Organización Mundial de Sanidad Animal (OIE), Asociacion Mundial de Medicos Veterinarios y otros más se reúnen regularmente para examinar y compartir los progresos logrados y coordinar acciones.

También en forma regional instituciones y grupos profesionales están tratando de establecer metas y programar actividades.

Es conveniente hacer énfasis en la importancia de participar en estas actividades para contribuir a hacer frente a este problema y difundir recomendaciones y procedimientos a fin de controlar el avance de la resistencia a los antibióticos. Los médicos veterinarios en su actividad de profesionales de salud pública deben tener un rol preponderante en contribuir eficazmente para evitar el progreso de la aparición de resistencia bacteriana a los antibióticos usados en terapia de enfermedades infecciosas.

# POSTERS

# ESTENOSIS INTESTINAL EN YEYUNO POR CUERPO EXTRAÑO EN CANINO SCHNAUZER DE 8 AÑOS

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**INTRODUCCION**

**La estenosis refiere a la constricción/estrechamiento de un orificio/conducto corporal, congénito o adquirido. Puede ocurrir por cuerpos extraños, intususcepción y menos comúnmente por adhesión. La ingestión de cuerpos extraños en caninos se atribuye a hábitos alimenticios indiscriminados, dando como resultado desequilibrio de electrolitos, hipovolemia y toxemia que también se suman a mala digestión y mala absorción de nutrientes (Stagnant loop Syndrome o Síndrome de Asa Estancada).**

**OBJETIVOS**

**Obtener casuística no muy común en nuestro medio, para mejorar el diagnóstico de pacientes con procesos crónicos y así seguir los casos posteriores de la mejor manera posible.**

**METODOLOGIA**

**Presentación del caso: Paciente canino de raza Schnauzer de 8 años de edad de nombre George, con historial de anorexia, emesis y diarrea intermitente además de pérdida progresiva de peso de noviembre de 2016 a Junio de 2017. Tiempo en el cual se realizaron exámenes complementarios como hemograma, coproparasitológico, bioquímica sanguínea y examen completo de orina con resultados no concluyentes.**

**En junio de 2017 se realizó ecografía abdominal donde lo más resaltante fue la evidencia de líquido libre en abdomen y presencia de líquido en asas intestinales, además de congestión de las mismas y a la par se realizó estudio radiográfico de abdomen donde se evidencia gran cantidad de gases en asas intestinales.**

**RESULTADOS**

**Se programó al paciente para cirugía, previa transfusión de sangre completa. En la laparotomía se observó estenosis intestinal a nivel de yeyuno, se realizó enterectomía de la zona afectada, el resto de órganos no presentaban alteraciones macroscópicos. En la muestra retirada se encontró material de textura dura y color negro insertado en las paredes del intestino.**

**CONCLUSIONES**

**Se concluye que muchas veces en el diagnóstico de cuerpos extraños ninguna prueba es concluyente al 100%, debiendo realizarse diferentes pruebas antes de llegar a un diagnóstico definitivo.**

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# REPORTE DE 100 CASOS EN TOMOGRAFIAS COMPUTARIZADAS

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**INTRODUCCION**

**La tomografía computarizada es una técnica de diagnóstico por imagen no invasiva, tecnología de exploración de rayos X que produce imágenes detalladas de cortes axiales del cuerpo, cada vez más usada en medicina veterinaria. Es utilizada en patologías de cavidad nasal y senos paranasales, medula espinal, fracturas y pacientes oncológicos.**

**OBJETIVO Mejorar el diagnóstico veterinario mediante el uso de pruebas complementarias como es el diagnostico por tomografía en diferentes áreas del organismo.**

**METODOLOGÍA**

**VENTAJAS**

**1. Mayor resolución de contraste siendo superior a la radiografía convencional, mediante la toma de imágenes transversales, evita la superposición de estructuras. 2. Permite el uso de medios de contraste que servirán para aumentar la cantidad de información, mejorando la calidad y aumentando la disponibilidad de información morfológica. 3. Método de diagnóstico de elección en medicina veterinaria, debido a su rapidez, fiabilidad y versatilidad, para poder definir con precisión las situaciones y optimizar el tratamiento.**

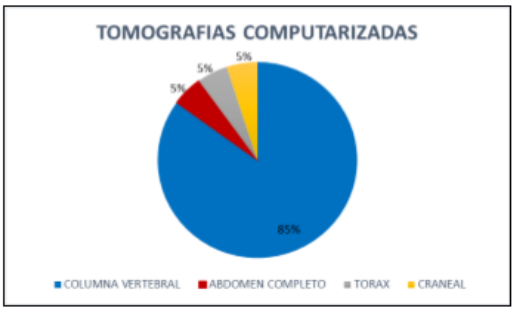
**DESVENTAJAS**

**1. Requiere que los pacientes permanezcan quietos, lo cual quiere decir que deben permanecer sedados para la realización del examen. 2. El riesgo que conlleva este examen ya que, se ven relacionados con el uso de radiaciones ionizantes. 3. Los medios económicos con lo que se cuenta no son favorables.**

**El presente estudio se basa en el resultado de 100 pacientes caninos, de diferentes edades, raza y sexo, logrando obtener resultados en el 99% de casos y solo un fracaso del 1%, siendo 12 de columna lumbosacra, 52 de columna lumbar, 16 de columna dorso lumbar, 8 de abdomen completo, 8 de cráneo, 4 de tórax.**

**RESULTADOS**






**CONCLUSIONES**

**1. Cada vez más se toma en consideración la tomografía como prueba diagnóstica no solo en afecciones de columna. 2. El elevado costo de una sola prueba, en este caso la tomografía, no permite que esté al alcance de todos. 3. Hacen falta especialistas veterinarios en interpretación de imágenes tomográficas en nuestro medio, siendo muy útil como prueba diagnóstica.**

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# USO DE LA TOMOGRAFÍA COMO APOYO DIAGNÓSTICO EN UN CASO DE TUMOR VENÉREO TRANSMISIBLE (TVT) EN CAVIDAD NASAL DE CANINO SCHNAUZER MACHO DE 3 AÑOS

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**Introducción**

**El tumor venéreo transmisible (TVT) es un tumor de células redondas de origen histiocítico que afecta a perros y otros cánidos como el lobo y coyote. Con mayor frecuencia en perros de 2 a 5 años sin raza o predisposición sexual. El tumor se transmite principalmente mediante la inoculación de células neoplásicas intactas en la membrana mucosa lesionada o en la piel durante el apareamiento, pero también se han reportado otras formas, morder, oler y lamerse. La enfermedad generalmente se considera benigna con predilección por los genitales externos (prepucio, pene y vagina), pero también hay informes de metástasis en otros órganos del cuerpo (piel, cavidad oral y nasal, conjuntiva, recto e hígado).**

**Objetivos**

**Identificar la signología poco común en nuestro medio, para poder compartir los alances y así seguir los casos posteriores mejorando la tánica diagnóstica en la clínica particular.**

**Metodología**

**Presentación del caso: se presenta al Hospital de Mascotas para consulta y segunda opinión un macho canina de raza Schnauzer de 3 años de edad, llamado Tato. Reporte de vacunas y desparasitación al día. Al examen clínico presentó condición corporal 3/5, peso de 15 kg. Temperatura 38.6ºC. Reporta secreción nasal unilateral derecha hace 5 meses, durante los cuales estuvo en tratamiento con distintos antibióticos sin mayor éxito, además se observa en área afectada inflamación.**

**Resultados**

**Se procedió a realizar una PAAF (punción aspiración con aguja fina) del área afectada y realizar tomografía. El resultado final de la PAAF fue TVT canino y la tomografía evidencia masa en cavidad nasal unilateral derecha. Se procedió a tratamiento endovenoso con Vincristina, una dosis semanal con recuperación favorable en un mes de tratamiento.**

**Conclusiones**

**La poca presencia de TVT canino en lugares poco comunes como cavidad nasal pueden llevar al error diagnóstico, se debe obtener la mayor y mejor información de una buena anamnesis y realizar los exámenes auxiliares necesarios para determinar la patología final. Bibliografía**

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