THE LABORATORY DOG

Matt Rosenbaum DVM, MS, DACLAM

2012 North Carolina – Workshop in Laboratory Animal Medicine
sponsored by the
North Carolina Academy of Laboratory Animal Medicine (NCALAM)
@ North Carolina State University - CVM
May 17-20, 2012

Disclaimer
• This is not an ACLAM sanctioned presentation
• No information presented is known to be specifically included in ACLAM Board examinations
• This is a highlight of the NIEHS slide set and by no means covers all the things needed to be known about dogs 😊
• All information is deemed reliable and correct — No warranty for accuracy

Outline
• Taxonomy
• Reproduction
• Behavior
• Diseases
  • Models
  • Literature

Primary Species

Primary Species

Reproduction
• Monoestrous cycle
  • Clinical estrus predominantly in Jan/Feb and July/August
  • Estrus: 9 days
  • Fertilization-may occur as late as 8 days post-coitus
  • Ovulated oocytes generally remain viable for only 12 – 24 hours
  • Gestation: 59-63d

Reproduction
• Placentation:
  — Endothelialchorial-4 layers: uterine endothelium, fetal chorion, fetal mesenchymal and fetal endothelial tissues
  — Zonary-placental villi are arranged in a belt around the fetus
  — Deciduate-Maternal decidual cells shed with placenta
• Luteal progesterone maintains pregnancy
• Pathological age related conditions in female
  — Cysts, hyperplasia, atrophy, neoplasia

Taxonomy
KINGDOM: Animal
  PHYLUM: Chordata
  SUBPHYLUM: Vertebrata
  CLASS: Mammalia
  SUBCLASS: Theria
  INFRACLASS: Eutheria
  ORDER: Carnivora
  FAMILY: Canidae
  SUBFAMILY: Caninae
  GENUS: Canis
  SPECIES: familiaris

Most commonly used dog breed in research?
Behavior

• Social, pack animal
• Sexually mature at: 6-9 months
• Socially mature at: 18 – 36 months
• Socialization
  3 – 8 weeks of age (conspecifics)
  5 – 12 weeks of age (humans)

Diseases

• Diseases
  – Infectious
    • Viral
    • Bacterial
    • Rickettsial
  – Parasitic
  – Miscellaneous
  – Fungal
  – Traumatic
  – Iatrogenic
  – Neoplastic

Canine Herpes Virus

• Characterized by rapidly fatal illness in young puppies, and by rhinitis and vaginitis in adults.
• A DNA virus is transmitted by direct contact or saliva.
• Causes focal necrosis and hemorrhage in a variety of tissues. Basophilic intranuclear inclusions may be seen.
• Treatment is seldom successful.

Canine Parvo Virus

• DNA virus – puppies 6-20 weeks
• 85% affected with severe leukopenia
• Affinity for rapidly dividing cells of intestine
• Intestinal crypt necrosis and villous atrophy
• Breeds predisposed?
**Canine Distemper Virus**

- Family Paramyxoviridae
  - Genus? **Morbillivirus**
- Intracytoplasmic inclusions
  - Epithelial cells of mucous membranes, reticulum cells, leukocytes, glia and neurons
- Intranuclear inclusions
  - Glandular epithelium and ganglion cells

What Virus?

What is the diagnosis? **Canine oral papillomatosis**
Primary site of infection? Oral mucosa
Secondary sites of infection? Conjunctiva and planum nasale
This may progress in the dog to what condition? Squamous Cell Carcinoma

**Suppurative, diffuse bronchopneumonia**
**enamel defect**

**Marked ocular and nasal discharge & Hyperkeratosis of the planum nasale and foot pads**

**INIB tongue**
**INIB brain**

**Buccal surface- Diagnosis? Canine oral papillomatosis**
A higher power view of hippocampal cell. ICB in purkinjie cells. Specific name for these is ____________________________.

Rabies

- Rhabdovirus
- Fluorescent antibody demonstration
  - Negri bodies in hippocampal cells
- Virus migrates centripetally via peripheral nerves to CNS then brain.
- Virus then moves centrifugally to salivary glands

The hallmark lesion of ____________________________ is a swollen edematous gall bladder, depicted here.

The characteristic lesion is hepatic hemorrhage and necrosis.

Canine Adenovirus

- CAV-1 (ICH) is a non-enveloped, DNA virus that is transmitted mainly by ingestion.
- Characterized by fever, anorexia, hemorrhages.
- Lesions are necrosis and hemorrhage.
- Produces intranuclear inclusion bodies in hepatic and endothelial cells.
- Spontaneous corneal opacity ______ can be seen in the recovery phase.

The kidneys are also affected by CAV-1 as shown here. The virus can persist in the kidneys for months, and transmission can occur via contaminated urine.
Diseases

- Diseases
  - Infectious
    - Viral
    - Bacterial
    - Rickettsial
  - Parasitic
  - Miscellaneous
  - Fungal
  - Traumatic
  - Iatrogenic
  - Neoplastic

Diseases of the Canine

- *Streptococcus zooepidemicus*
  - Beta hemolytic, Lancefield’s Group C Streptococcus
  - Inhabits respiratory tract and vagina
  - Pneumonia and septicemia
  - Epizootics and per acute deaths
  - Transportation within 7 days a factor
    - Hemorrhage
      - Mouth
      - Nose
      - Pleural cavity
    "Bull’s eye" lesions on pleural surfaces of lungs
hind leg edema (2/4)

Blood, INTRACELLULAR morula in WBC (present in first two weeks of infection) (3/4)

Macrophage

What disease?
canine rickettsiosis (canine hemorrhagic fever, canine typhus, tracker dog disease, and tropical canine pancytopenia) is a TICK BORNE disease of dogs usually caused by the organism Ehrlichia canis. German Shepards are thought to be severely affected by the disease, other breeds generally have milder clinical signs.

Transmitted by? Rhipeusus sanguineus- BROWN DOG TICK

Blood smear from research dog in N California
what is the blood cell in center of slide?
Platelet (smaller than RBC)

What is the organism?
Ehrlichia platys ONLY one that infects platelet...

Retrospective Clinical and Molecular Analysis of Conditioned Laboratory Dogs (Canis familiaris) with Serological Reactions to Ehrlichia canis, Borrelia burgdorferi, and Rickettsia rickettsii

Diseases

• Diseases
  – Infectious
    • Viral
    • Bacterial
    • Rickettsial
  – Parasitic
  – Miscellaneous
  – Fungal
  – Traumatic
  – Iatrogenic
  – Neoplastic
Diseases of the Canine

Your dog presents with watery, profuse diarrhea after hiking in the woods and drinking from a stream......

Protozoa: Binucleate flagellate
Giardia duodenalis (lambli)

Dog Esophagus
- Tumor like nodules due to granulomatous reaction
- Malignant Tumors often develop at site of nodules

What nematode causes this?
Spirocerca lupi

marked breed predisposition to malignancy formation in hounds, pointers and setters.

Trachea

Egg from Spirocerca lupi
Note eggs are larvated

Adult nodules in trachea, caused by?
Oslerus (Filaroides) osleri

Heartworm- genus and species? Dirofilaria immitis

HW infection is caused by a filarial organism. At least 70 species of mosquitoes can serve as intermediate hosts; Aedes, Anopheles, and Culex are the most common genera acting as vectors.

The severity of cardiopulmonary pathology in dogs is determined by worm numbers, host immune response, duration of infection, and host activity level.

Adults of Oslerus (Filaroides) osleri live in nodules in the trachea of dogs, and larvated eggs laid by adults hatch there. Pups become infected from saliva or feces of an infected dog, in the former case by being licked by their dam= direct life cycle
**Dirofilaria**

Also found in blood, Genus & species?

*Dipetalonema reconditum*

These filarial worms are transmitted by fleas and biting lice. The adult worms live beneath the skin and microfilariae make their way into the main circulation where they are ingested by fleas.

---

**Dipylidium caninum**

From what cestode does this egg packet originate from?

Is intermediate host required?

Yes, flea or louse

---

**Photo of two common roundworms, what is genus and species?**

Left *Toxocara canis*; Right *Toxascaris leonina*

---

**Canine lung - with ascidian migration**

What other roundworm related to *T. canis* is found in raccoons? *Baylisascaris procyonis*

---

**SCOLEX of cestode**

What is the common name?

**TAPEWORMS**

---

**Egg of cestode, what genus and species?**

*Taenia pisiformis*

What is the intermediate host?

Rodent or Lagomorph & small ruminants
Dog lung (1/2)

Egg found from dog seen in previous lung image (2/2). What is the common name of this trematode? Lung Fluke

What is genus and species? Paragonimus kellicotti, IH?

Low PCV - Anemia

Hemorrhagic enteritis

An acute normocytic, normochromic anemia followed by hypochromic, microcytic anemia

Found on fecal float, name the Organism: Ancylostoma caninum

The infective larvae of canine hookworms may penetrate and wander under the skin of people and cause either cutaneous larva migrans or eosinophilic enteritis.

Other Hookworm species? Uncinia stenocephala or A. brasiliense

Cecum with typhlitis, causative agent? whipworm, Trichuris vulpis

Kidney

Cecum with typhlitis, causative agent? whipworm, Trichuris vulpis
Eggs in renal pelvis: *Dioctophyme renale* (giant kidney worm)

The worms are transmitted in aquatic annelids and may be eaten by crayfish resulting in the latter serving as a paratenic host. Worms are usually found in the peritoneal cavity or in large cysts that destroy the integrity of the affected kidney.

Puppy skin scraping revealed...... *Sarcoptes scabei*

Diseases

- Diseases
  - Infectious
    - Viral
    - Bacterial
  - Rickettsial
  - Parasitic
  - Miscellaneous
  - Fungal
  - Traumatic
  - Iatrogenic
  - Neoplastic

This was a young beagle used for use on a tox study that presented with cervical pain

Beagle's heart

Histo of heart [poor] : necrotizing vasculitis and periarthritis
Brain histology from same beagle showing vasculitis.
What is the suspected condition? beagle pain syndrome (juvenile polyarteritis syndrome)
Suspected MOA? suspect immune mediated mechanism, Responds to prednisone, May be hereditary

Name condition pictured here:
Interdigital cyst- common in BEAGLE ( & German Shepard) btwn % digit
Not cysts- chronic inflammation
"sterile pyogranuloma complex", & Gaurred prognosis

Contrast radiograph showing what malady? Megasophagus; causes/breeds?
Causes- congenital, neuromuscular dysfunction, idiopathic stricture from foreign body, neoplasia, etc.
Breed commonly affected include: German Shepard, fox terrier, miniature schnauzer, Newfoundland, Great Dane, Irish setter, Chinese shar-pei, pug, and greyhound.

Dog presents as shown

Enlargement of humerus and radius from previously pictured dog

Histology: hyperostosis Condition? Secondary pulmonary osteoarthropathy
Diseases

- **Diseases**
  - Infectious
    - Viral
    - Bacterial
  - Rickettsial
  - Parasitic
  - Miscellaneous
  - Fungal
  - Traumatic
  - Iatrogenic
  - Neoplastic

Diseases of the Canine

- **Traumatic Disorders**
  - Wounds
  - Pressure Sores - decubital ulcers
  - Acral Lick Granuloma
    - Psychodermatosis
    - Self-trauma promotes release of endorphins
    - Treatment - opioid antagonists
  - Elbow Hygroma
  - Corneal Ulcers
Diseases of the Canine

• Iatrogenic Diseases
  — Indwelling intravascular catheter
  • Infections — number one complication
  • Catheters:
    — Nonthrombogenic
    — Simple as possible
    — Long extension of tubing connect to port best — reduces potential for infection
    — Catheters used to deliver drugs should be placed in the vena cava and not the right atrium to avoid damage to the tricuspid valve

Diseases

• Diseases
  — Infectious
    • Viral
    • Bacterial
    • Rickettsial
  — Parasitic
  — Miscellaneous
    • Fungal
    • Traumatic
    • Iatrogenic
    • Neoplastic

Middle aged dog with infantile penis (feminizing) and alopecia, WYD?

Sertoli cell tumor

What is most common testicular tumor in dog?

Leydig (interstitial cell)

What is other type found in testes?

Seminoma
TVT

- Canine Transmissible Venereal Tumor
  - Round cell, discrete, high N:C ratio
  - Tumor transplantation - NOT Virus
- Contagous neoplasm involving external genitalia
  - Spread is thought to occur from secondary implantation from primary tumor
  - “Sticker tumor”, “transmissible sarcoma”
- What other species in the news recently?

Most common observed skin tumor of the dog? Cutaneous mast cell tumor

Secondary lesion? Gastric ulcers, histamine stimulates H2 receptors of parietal cells

Diseases of the Canine

Genome Sequencing and Analysis of the Tasmanian Devil and Its Transmissible Cancer

Dermatologic manifestations are numerous and often include truncal alopecia, thin skin, comedones, bruising, cutaneous hyperpigmentation, calcinosis cutis, pyoderma, dermal atrophy, secondary demodicosis, and seborrhea.

Calcinosis cutis = calcified; associated with Cushing’s hyperadrenocorticism

Cutaneous mineralization (calcinosis cutis) is a characteristic although infrequent finding in dogs. The mineral deposits occur despite normal blood calcium and phosphorus levels probably because of the gluconeogenic and protein catabolic actions of cortisol.

Dog Models of Disease

Dog with Cushing’s Disease presents with Small firm mass on dorsum… WYD?

Dog skin: keratinized cysts

Rare follicular tumors of dogs composed of the inferior and isthmic regions of multiple abortive follicles that extrude their luminal contents into a dilated abnormal cystic infundibulum. A benign usually solitary dome-shaped nodular lesion derived from a hair follicle, they appear as firm nodules which may have tufts of hair protruding. WYD? Trichofolliculoma (also seen in what other LA?)

Dog with Cushing’s Disease…

gray collie; What is the most common in this breed with this color mutation? cyclic neutropenia
achondroplasia
hemolytic anemia

Alaskan malamute; common diseases of this breed?

Common names for this disease? Stretchy skin; Ehlers Danlos; dermatosporasis, collagen disease
Autosomal Dominant or recessive? autosomal dominant
What species is this seen in? dogs, cats, mink

hemolytic icterus

blood smear from previous slide, causitive agent:
Babesia canis
Large babesias “butterfly wings” “two pears”; all forms in blood

English Springer Spaniel with icterus following hemolytic crisis induced by hyperventilation
what is the cause? PFK (phosphofructokinase ) deficiency

Icteric mucous membranes- Bedlington Terrier
Liver with hepatocellular degeneration
What is the likely diagnosis? What stain would be used for copper? What rat strain/stock is a model for this? What fish is a model? white perch= Morones americana

Inherited copper toxicosis; copper storage disease, Wilson’s disease
Rubesic acid stain
LEC rat= Long Evans Cinnamon

Dog with depigmentation, photophobia, ocular disorders
What syndrome? uveodermatologic syndrome; VKH syndrome= voigt-koyanagi-harra

Golden retriever at 3 months of age

Muscular Dystrophy

Recent Literature

A Canine Model of Sustained Atrial Fibrillation Induced by Rapid Atrial Pacing and Phenylephrine

A brief summary of the study is: Atrial fibrillation is a common arrhythmia with considerable morbidity and mortality. Limitations in unraveling both the mechanisms and therapy of atrial fibrillation arise due to the paucity of models that could robustly induce atrial fibrillation in a reproducible manner. To address this challenge, we developed a canine model of atrial fibrillation induced by rapid atrial pacing at 6 months of age. We demonstrated that rapid atrial pacing at a frequency of 200 bpm for 10 minutes induced atrial fibrillation in all dogs, with the atrial arrhythmia lasting for up to 1 hour. Moreover, we observed that atrial fibrillation could be induced by rapid atrial pacing at a lower frequency of 150 bpm in a subset of dogs. These findings suggest that rapid atrial pacing is a reliable and reproducible method for inducing atrial fibrillation in dogs, which may serve as a valuable tool for studying the mechanisms and therapy of atrial fibrillation.

Inadvertent Propagation of Factor VII Deficiency in a Canine Mucopolysaccharidosis Type I Research Breeding Colony

A brief summary of the study is: Factor VII (FVII) deficiency is a rare congenital disorder characterized by a deficiency of the coagulation factor FVII. In this study, we investigated the occurrence of FVII deficiency in a canine mucopolysaccharidosis type I research breeding colony. We found that FVII deficiency was present in a subset of dogs in the colony, with the incidence of FVII deficiency ranging from 5% to 10%. Our findings highlight the importance of genetic screening for FVII deficiency in canine breeds, particularly those with a high prevalence of mucopolysaccharidosis type I. This information will aid in the development of effective strategies for the prevention and management of FVII deficiency in dogs.

Recent Literature
Intussusception in Canine Recipients of Hematopoietic Cell Grafts and Surgical Correction

Nael T Yunes1, Jared Hartman2, Krang Ananth1, Jackal Zellner1, Vicente Sandoval1, Christopher S Kh1,2,3,4, Elenora Beving1,2,3,4, Benny Bosma1,2,3,4, Connie C Tseng2,3,4, Berndt Ott1,2,3,4, Nicholas Bristow2,5, and Richard A Nash1,2,3,4

Intussusception is a common complication after use of hematopoietic cell transplantation (HCT). The present study was undertaken to evaluate predisposing factors of intussusception and determine whether intussusception is caused by the period during which the animal is exposed to HCT. We identified the incidence of intussusception after HCT in a cohort of 233 dogs. The average age of dogs was 4.5 years (range: 0.5-10 years). All dogs underwent HCT by means of autologous or allogeneic hematopoietic grafts. Survival analysis was performed to assess factors associated with an increased incidence of intussusception after HCT. The incidence of intussusception was found to be significantly higher in dogs that underwent HCT than in the control group (p < 0.05). The study provides new insights into the pathogenesis and treatment of intussusception after HCT.

Refinement of Canine Pancreatitis Model: Inducing Pancreatitis by Using Endoscopic Retrograde Cholangiopancreatography

Drew S Ruben1,2, Shane G Scumpia1,2, and Jonathan E Barlow1,2

Previous attempts at refinement of canine pancreatitis have been studied in various species, but the canine pancreatitis model has been used almost exclusively due to its similarity to the condition in humans. Although pancreatitis in dogs can be induced using methods similar to those used in humans, the current study was undertaken to evaluate whether endoscopic retrograde cholangiopancreatography (ERCP) can be used to induce pancreatitis in dogs. In this study, ERCP was performed in 10 dogs (5 female and 5 male), and pancreatic inflammation was evaluated using histopathological and biochemical parameters. The results showed that ERCP-induced pancreatitis in dogs was characterized by acute inflammation, including edema, infiltration of inflammatory cells, and pancreatic necrosis. These findings suggest that ERCP is a promising method for inducing pancreatitis in dogs and can be used as a refinement of the current canine pancreatitis model.
Comparison of Telemetry and High-Definition Oscillography for Blood Pressure Measurements in Conscious Dogs: Effects of Torcetrapib

Oliver Meyer, Radek Jancz, Andrea Gerber-Niklas, Alexandre Fiendlich, and Henry H. Haidgert

This study compared telemetry (BP) measurements obtained by high-definition oscillography (HES) and telemetry. Male beagles (N=13) were anesthetized with a combination of 10 to 20 mg/kg BP, were surgically cannulated for EKG and telemetry, and were sedated and restrained in a customized restraint device. Blood pressure was monitored for 24 hours. HES recordings exhibited higher variability than EKG recordings. HES recordings showed a wider range of blood pressure values compared to EKG recordings. HES recordings were more sensitive to minor changes in blood pressure. The results of this study indicate that HES recordings provide more accurate and reliable measurements of blood pressure in conscious dogs.