



# Osteosarcoma: Spectrum of Care at Work in Veterinary Oncology

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College of  
Veterinary Medicine  
UNIVERSITY OF GEORGIA



# Disclosure

I have no competing financial or other conflicts of interest to disclose for any of the material to be presented today



# Objectives

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- Review of the basics of canine OSA to ensure you feel comfortable with being able to:
  - ... list the most common canine primary bone tumors
  - ... formulate a diagnostic, staging and treatment plan for a suspected appendicular osteosarcoma
  - ... tailor plans based on client needs and goals (definitive intent vs palliative intent therapy)
- Be able to discuss rationale for immunotherapy in canine osteosarcoma



# Introduction – Canine Osteosarcoma (OSA)

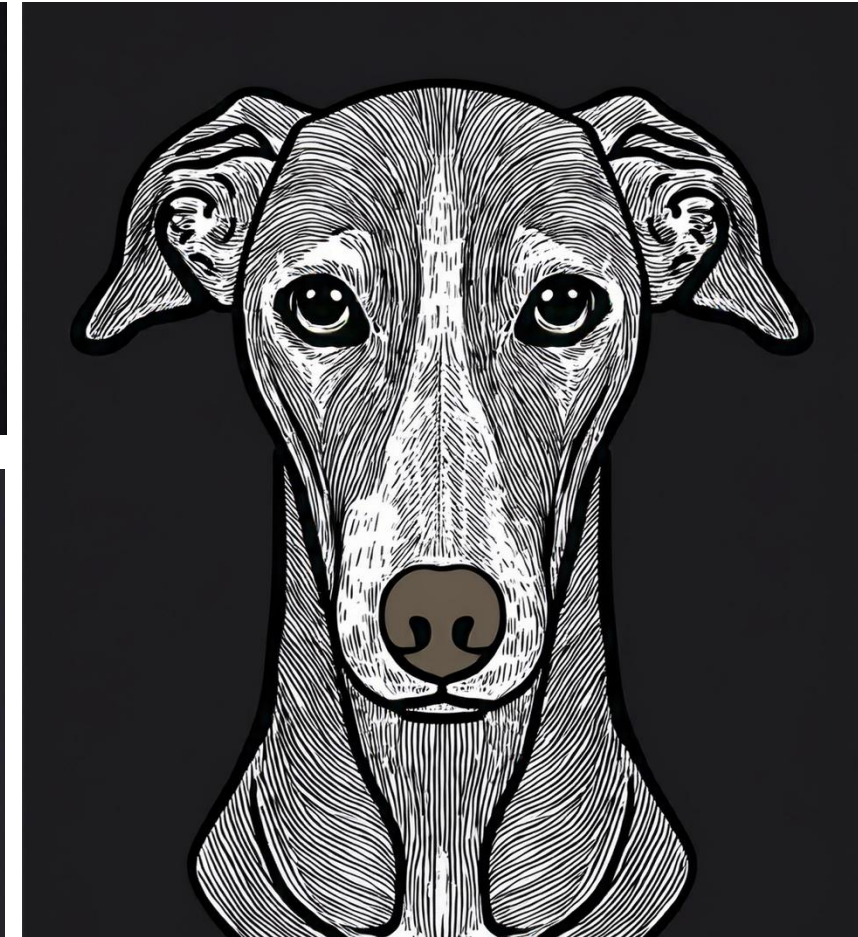
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- Osteosarcoma (OSA) - most common primary bone tumor in the dog and cat
  - >85% of all primary bone tumors
- Other primary bone tumors:
  - Chondrosarcoma
  - Fibrosarcoma
  - Hemangiosarcoma
  - Plasma cell tumor
    - Solitary osseous plasmacytoma
    - Multiple myeloma
  - Lymphoma



# Signalment

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- Most commonly older
  - Small subset in juvenile (< 3y)
- Large to Giant breed
  - 29% of all cases were > 40kg in one study
    - Of these, 95% appendicular
  - St Bernard, Great Dane, Irish Setter, Rottweiler, Doberman, Greyhound, German Shepherd, Golden Retriever, Great Pyrenees, Scottish Deerhound, Leonberger, etc...
- Less common in small breed
  - Smaller dogs have a higher % in the axial skeleton

# Anatomic Location

- Appendicular (75% of all OSA)
  - Most commonly metaphyseal
  - “away from the elbow, toward the knee”
  - Forelimb 2X more than hindlimb
  - Medullary origin most common
  - Surface origin rare, but improved prognosis (periosteal, parosteal)
- Axial (~25% of all OSA)
  - Rib, mandible/maxilla, spine, skull
  - More common in small breed
- Extraskeletal - rare
  - Subcutaneous, spleen, mammary

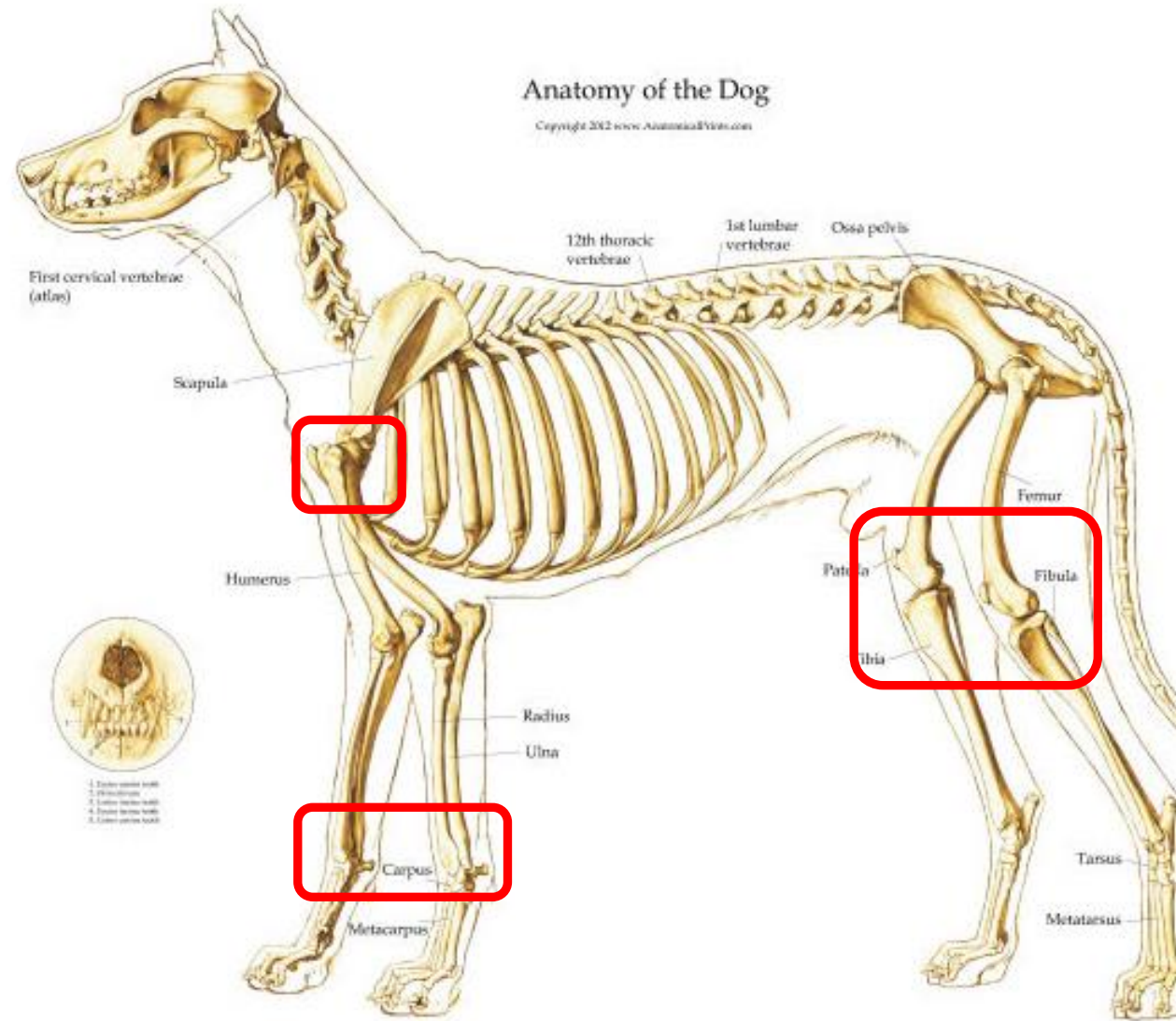
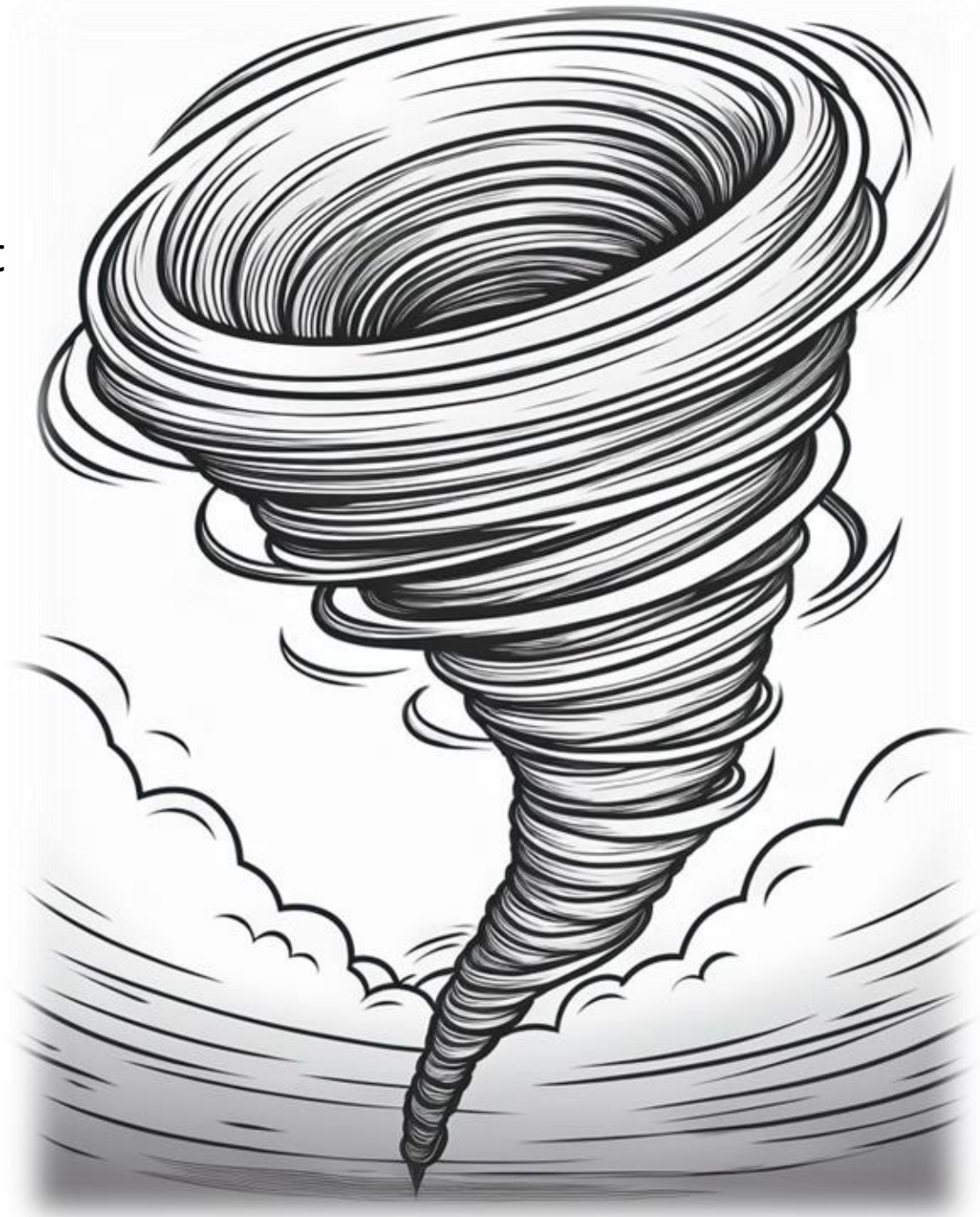


Image Copyright [www.AnatomicalPrints.com](http://www.AnatomicalPrints.com)

# Biological Behavior

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- Malignant cell: mesenchymal stem cell vs osteoblast
- Locally invasive:
  - Destruction of normal bone - lytic
  - Production of new bone matrix - proliferative
- Highly metastatic
  - Hematogenous - primary metastatic site is lung
    - > 85% are negative for mets at diagnosis
    - > 90% will develop metastases → i.e. “micrometastasis”
  - Other metastatic sites:
    - Other bones: < 10% at time of diagnosis
    - Lymph nodes: rare
    - Intra-abdominal organs: rare
    - Subcutaneous: rare





# History and Clinical Signs

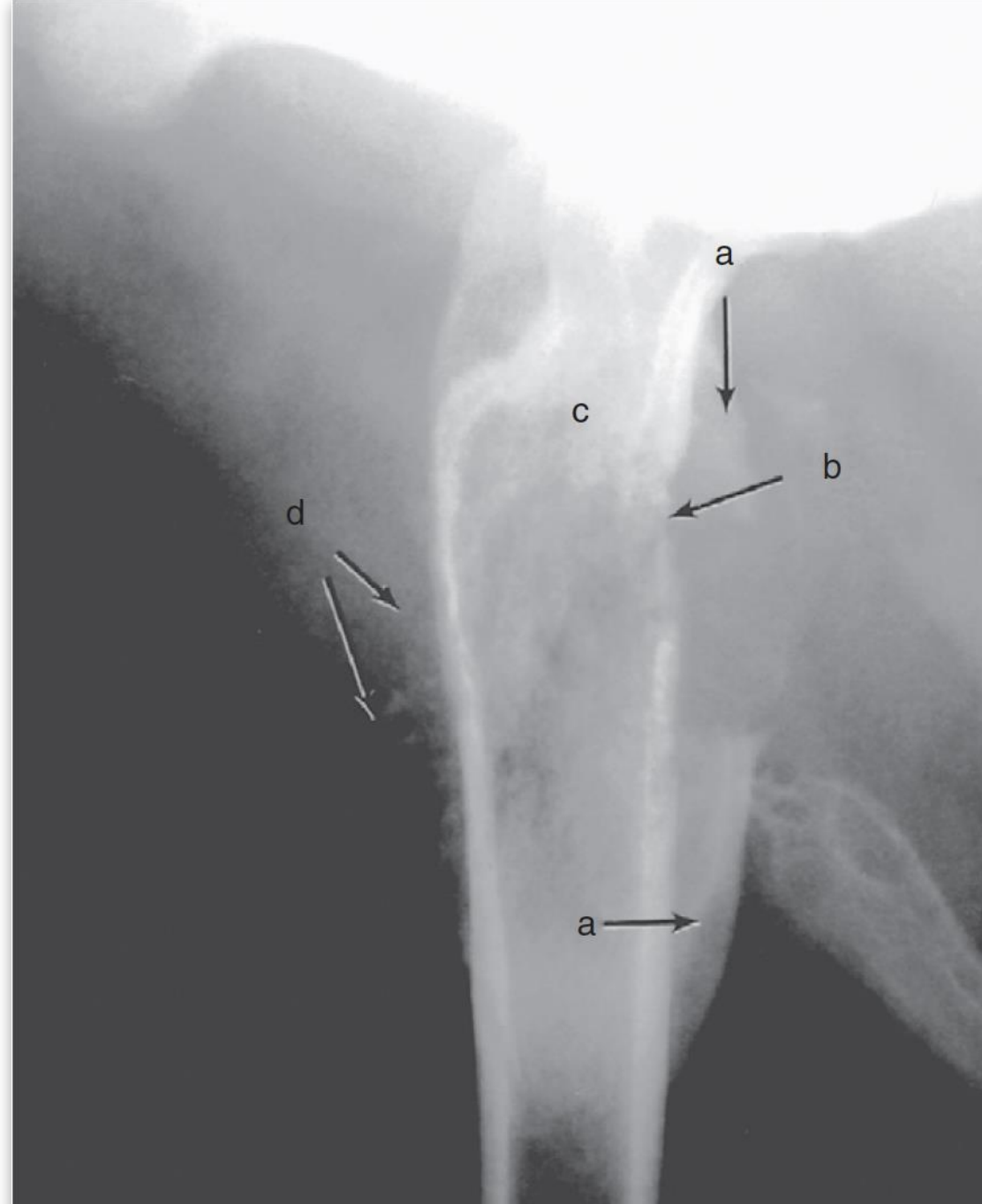
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- Acute to sub-acute onset of lameness of varying severity
  - Degree of pain/lameness is highly variable
  - Frequently responsive to pain medications initially
- Sensitive to palpation of the area
- Firm, painful swelling may be detected (not always)
- Wide variation between patients

# Diagnosis

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- Orthopedic/neurologic exam
  - Localize the pain
- 2 view radiographs of the area
  - Lytic or proliferative, usually both
  - Metaphyseal
  - Radiographic signs (aggressive bone lesion):
  - Radiographic DDx to consider:
    - Primary bone tumor (OSA vs other)
    - Osteomyelitis (esp fungal)
    - Metastatic neoplasia
    - Bone cyst





ROY, DAVID Coco  
280505012Y  
Extremity Left CrCd  
Jun 18, 2019 9:38:40 AM  
Series 1 - Slice 8



RM 2 UGA Veterinary Teaching Hospital  
Canon Inc., CXDI Control Software NE  
70 kV, 2 mAs  
NEWER



ROY, DAVID Coco  
280505012Y  
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Jun 18, 2019 9:41:32 AM  
Series 1 - Slice 8

RM 2 UGA Veterinary Teaching Hospital  
Canon Inc., CXDI Control Software NE  
70 kV, 2 mAs  
NEWER

262093 N/008Y  
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RM 1 UGA Veterinary Teaching Hospital  
Canon Inc., CXDI Control Software NE  
70 kV, 2 mAs  
PRIOR



262093 N/008Y  
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Canon Inc., CXDI Control Software NE  
70 kV, 2 mAs  
PRIOR



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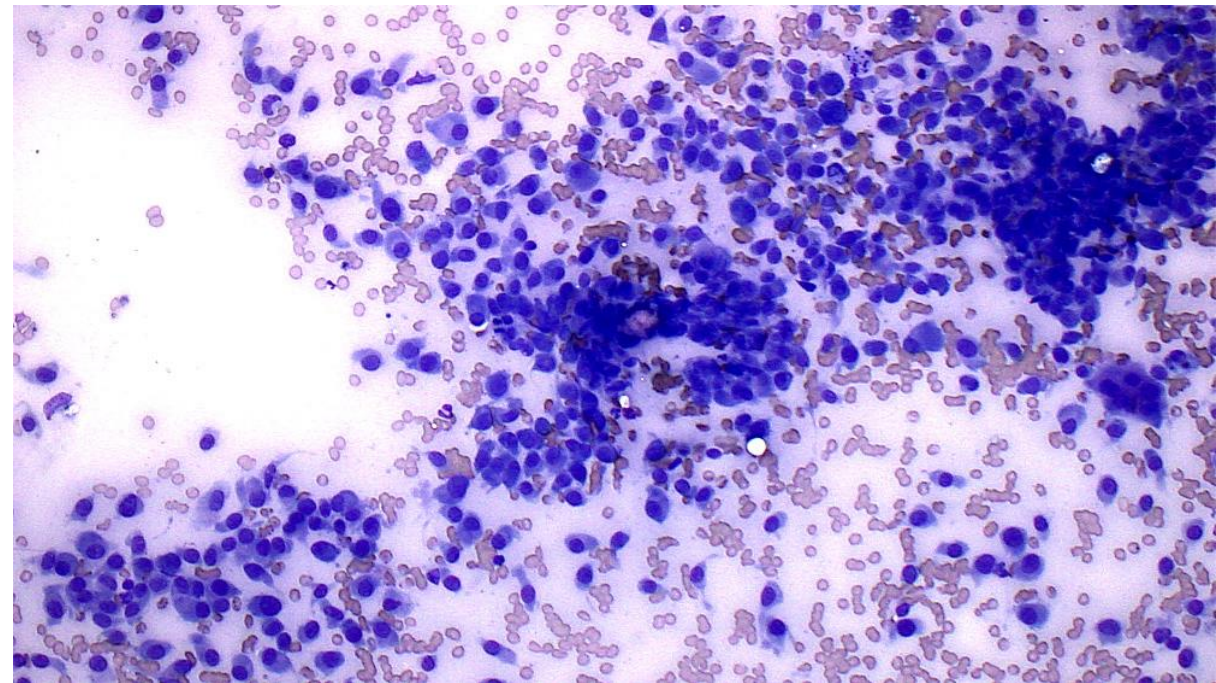
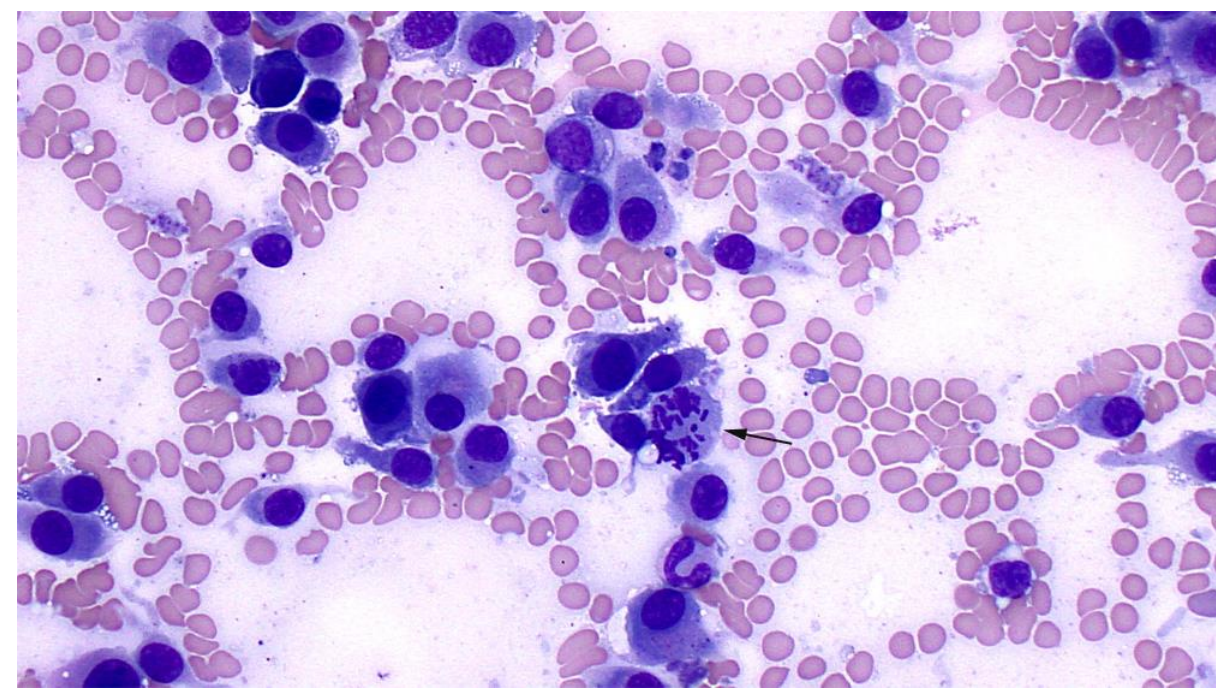




# Tissue Diagnosis - FNA

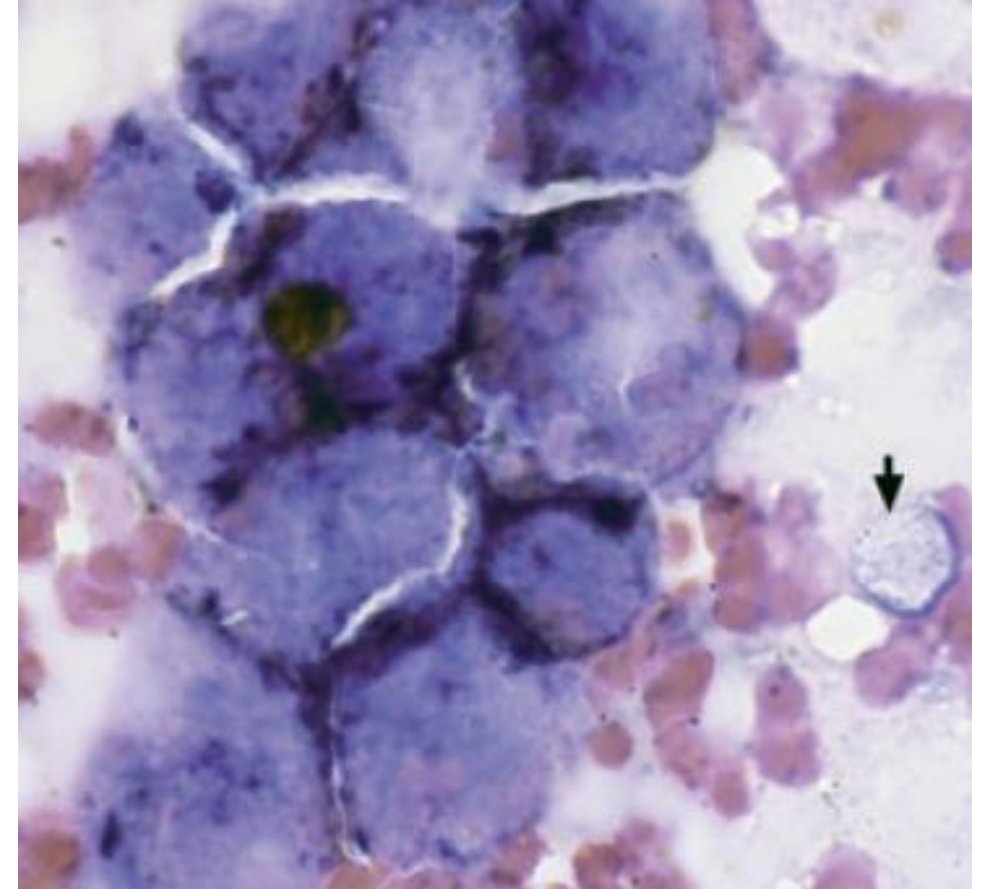
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- Bone Fine Needle Aspirate (FNA)
  - Hitting an area of cortical lysis greatly increases yield
    - Ultrasound guidance helps identify target
  - Up to 85% diagnostic
  - Alkaline phosphatase stain (see in 2 slides)
- FNA of soft tissue swelling can be diagnostic
  - Lower yield, but worth a try



# Alkaline Phosphatase Test

- Differentiate OSA from other sarcomas
- 1 hour incubation w/ BCIP/NBT - substrate for ALP
  - Works on slides previously stained with Wright-Giemsa
- 88% sensitive, 94% specific for detecting OSA
  - False positives (1 of each in study):
    - Melanoma
    - GI stromal tumor (GIST)
    - Anaplastic sarcoma
    - Collision tumor: histiocytic sarcoma + bronchoalveolar carcinoma

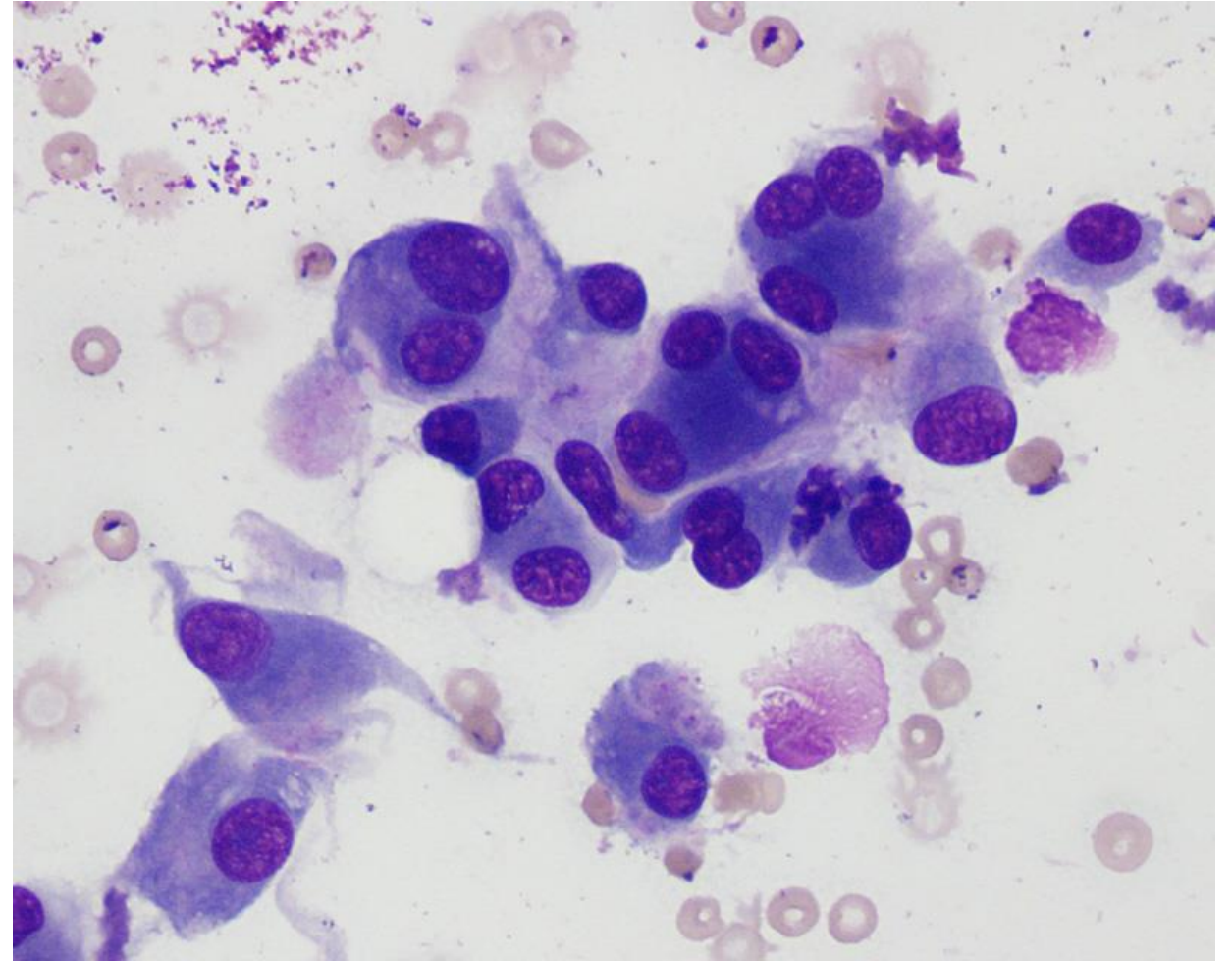
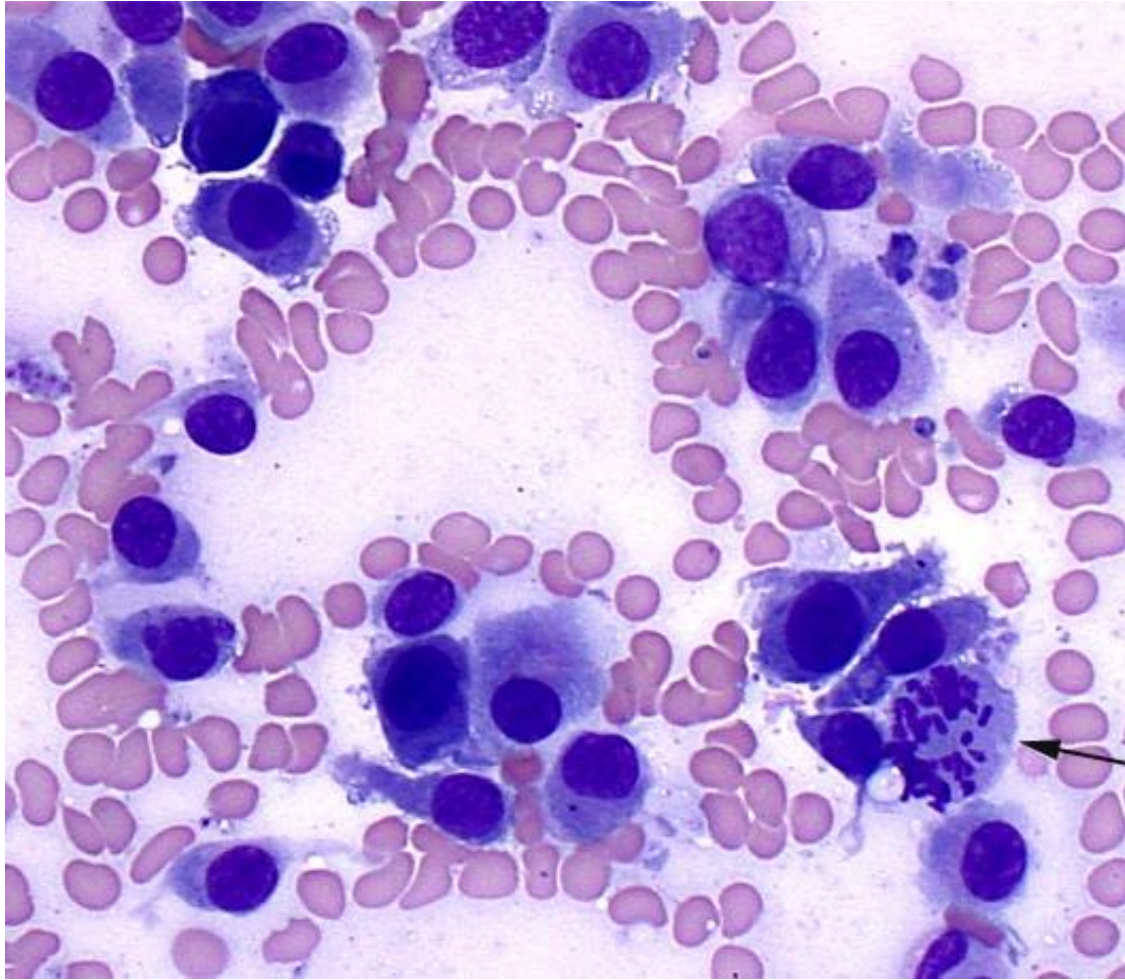


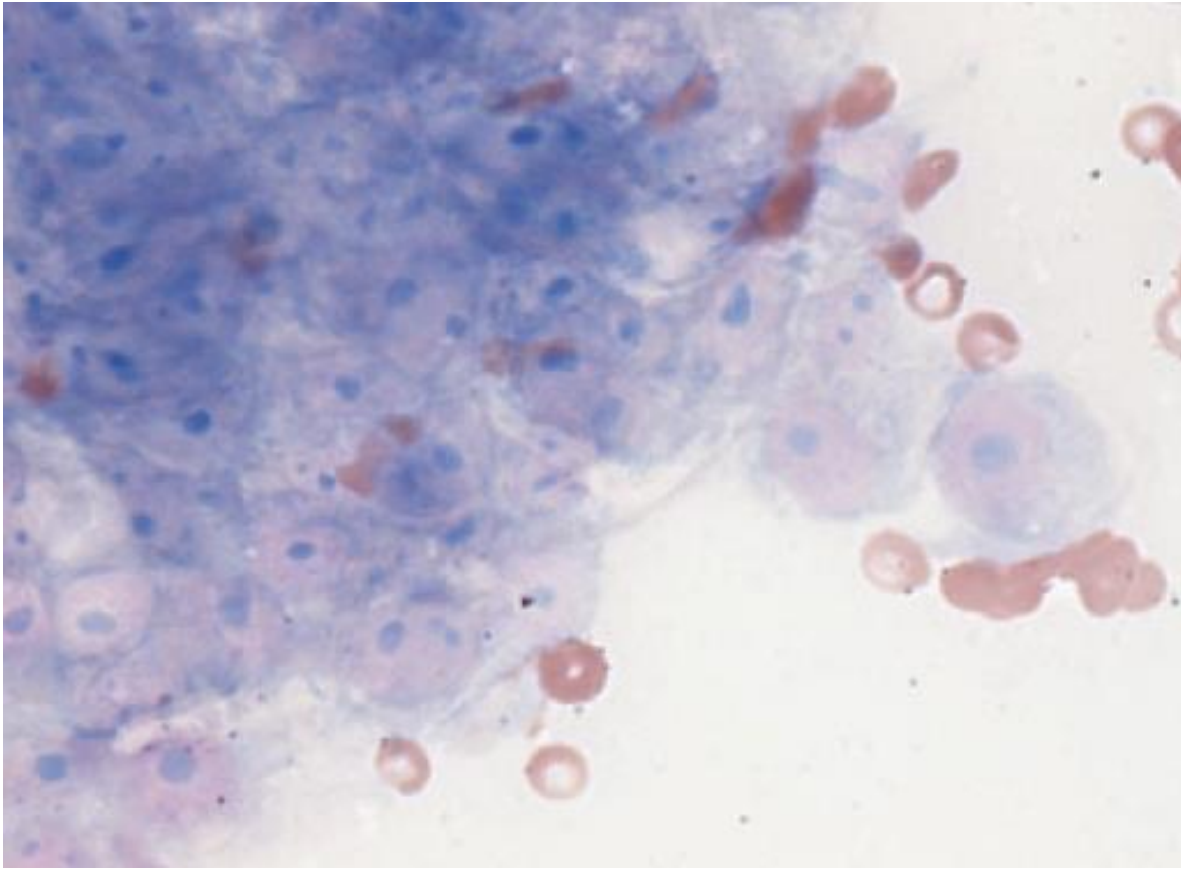
**Detection of alkaline phosphatase in canine cells previously stained with Wright–Giemsa and its utility in differentiating osteosarcoma from other mesenchymal tumors**

Julia K. Ryseff, Andrea A. Bohn

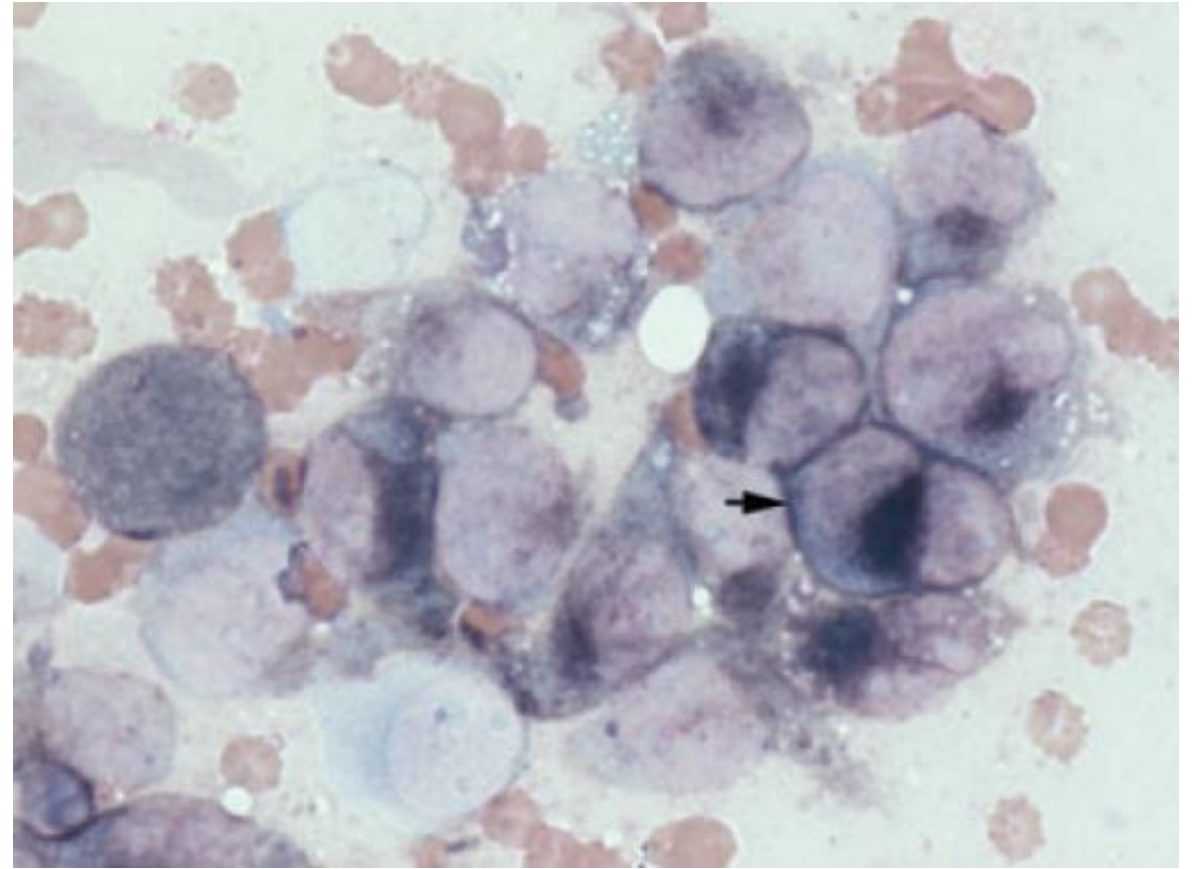
# Which Sample is Osteosarcoma?

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Soft Tissue Sarcoma



Osteosarcoma

# Tissue Diagnosis Options – Bone Biopsy

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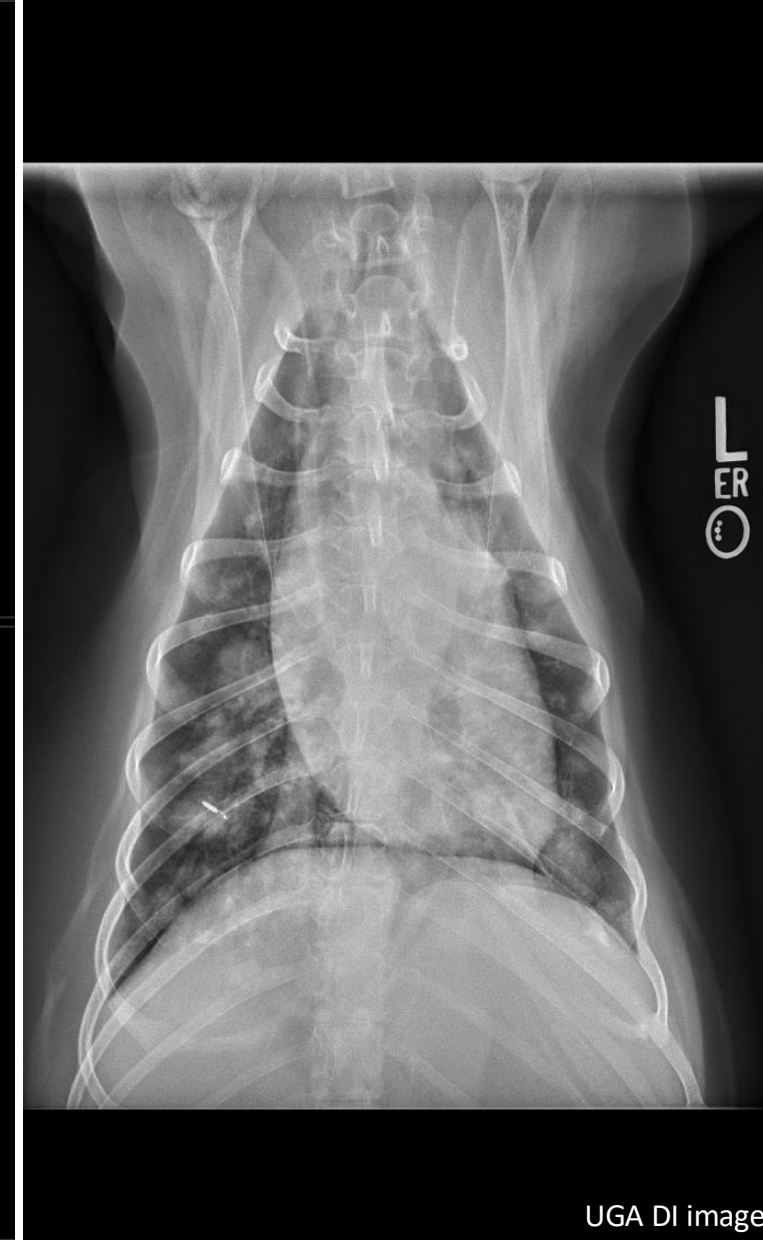
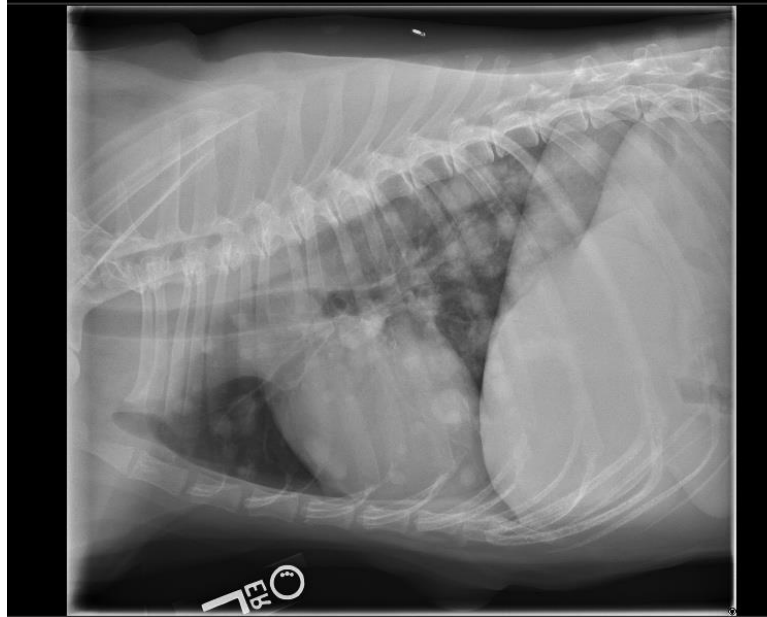
- Options:
  - Open
  - Core (Michele trephine, Jamshidi)
- Fluoroscopy guidance can increase yield
- Infrequently pursued due to:
  - Fracture risk – further weaken compromised cortex
  - Non-diagnostic samples are common
  - Delays intervention waiting for dx - DECALCIFICATION
- Consult oncologist if considering options beyond amp
  - Further increase risk of fracture in RT treated cases (see later)



# Staging

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- Minimum: thoracic evaluation
  - 3-view chest radiographs v. CT
- Others (less commonly pursued):
  - Nuclear scintigraphy
  - Abdominal ultrasound (case-dependent)
  - Full body CT scan
  - Full body PET-CT

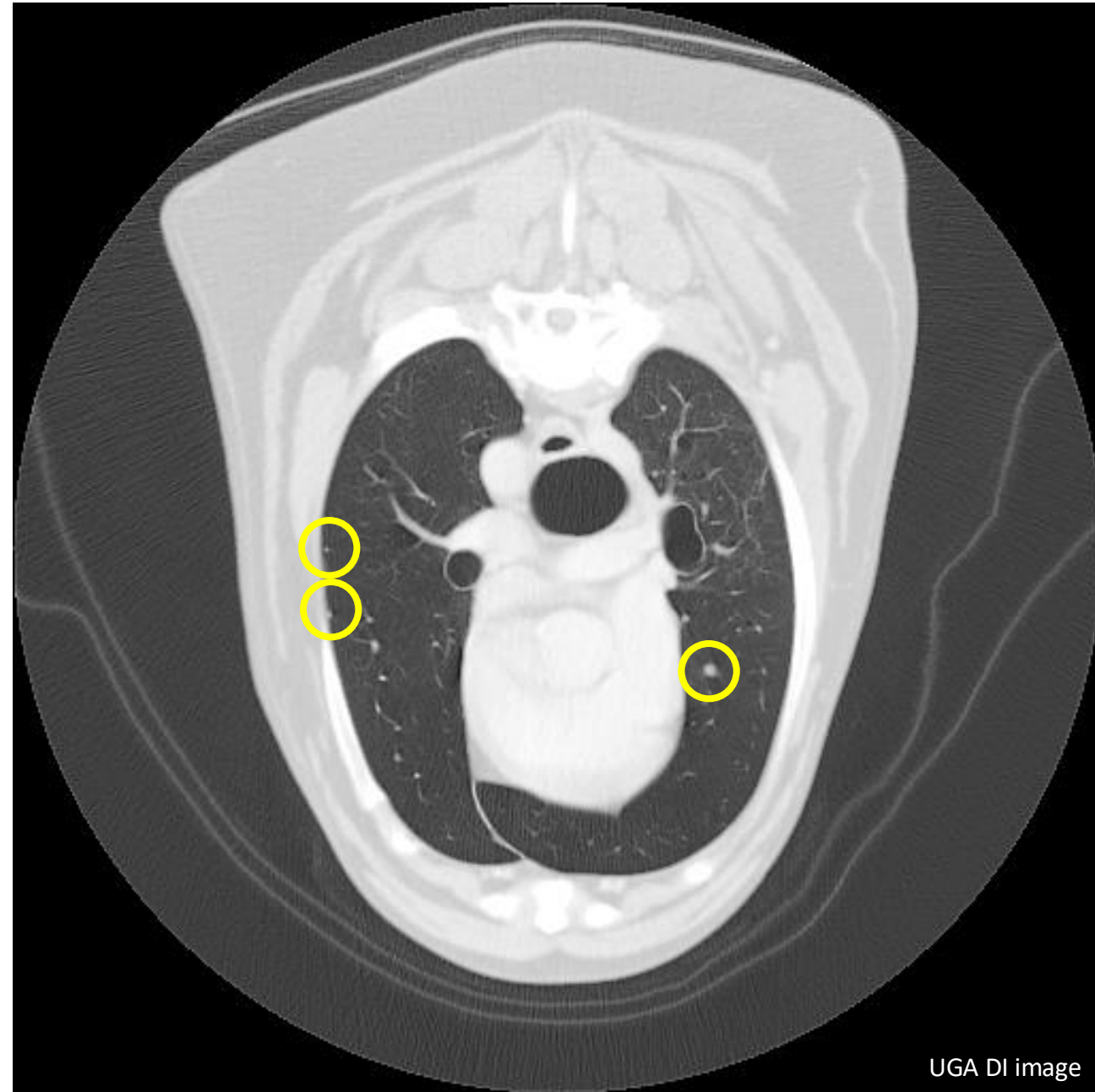


# Comparison of examination of thoracic radiographs and thoracic computed tomography in dogs with appendicular osteosarcoma

N. Eberle, M. Fork, V. von Babo, I. Nolte and D. Simon

Small Animal Hospital, University of Veterinary Medicine Hannover, Hannover, Germany

- 39 dogs w both CXR and CT
- Radiographic metastatic rate: 5%
- CT metastatic rate: 28%
- Stage drift
  - Increased sensitivity → detect smaller lesions → prognostic impact??



# Summary of CT Staging Studies

- Radiographs relatively sensitive for determining presence or absence
- CT better at total #
- CT detects smaller nodules
- CT more sensitive in large to giant breed dogs

## **Comparison of three-view thoracic radiography and computed tomography for detection of pulmonary nodules in dogs with neoplasia**

Laura J. Armbrust, DVM, DACVR; David S. Biller, DVM, DACVR; Aubrey Bamford, BS; Ruthanne Chun, DVM, DACVIM; Laura D. Garrett, DVM, DACVIM; Michael W. Sanderson, DVM, MS, DACVMP

JAVMA, Vol 240, No. 9, May 1, 2012

## A COMPARISON OF COMPUTED TOMOGRAPHY, COMPUTED RADIOGRAPHY, AND FILM-SCREEN RADIOGRAPHY FOR THE DETECTION OF CANINE PULMONARY NODULES

KATE ALEXANDER, HUGO JOLY, LAURENT BLOND, MARC-ANDRÉ D'ANJOU, MARIE-ÈVE NADEAU, JULIEN OLIVE, GUY BEAUCHAMP

*Vet Radiol Ultrasound, Vol. 53, No. 3, 2012, pp 258–265.*

# Osteosarcoma Treatment Options

## Definitive intent

Pick one

- 
- Amputation
  - Limb-sparing surgery
  - Stereotactic radiation therapy

+ Carboplatin for best outcome  
(see later)

## Quality of life (palliative) intent

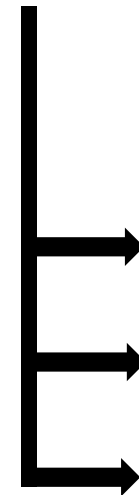
Combine, if possible

- 
- Medical pain management
  - Bisphosphonate
  - Palliative radiation therapy

If path fracture:  
palliative amputation v euthanasia

# Definitive intent

Pick one

- 
- Amputation
  - Limb-sparing surgery
  - Stereotactic radiation therapy

+ Carboplatin for best outcome  
(see later)

# Amputation

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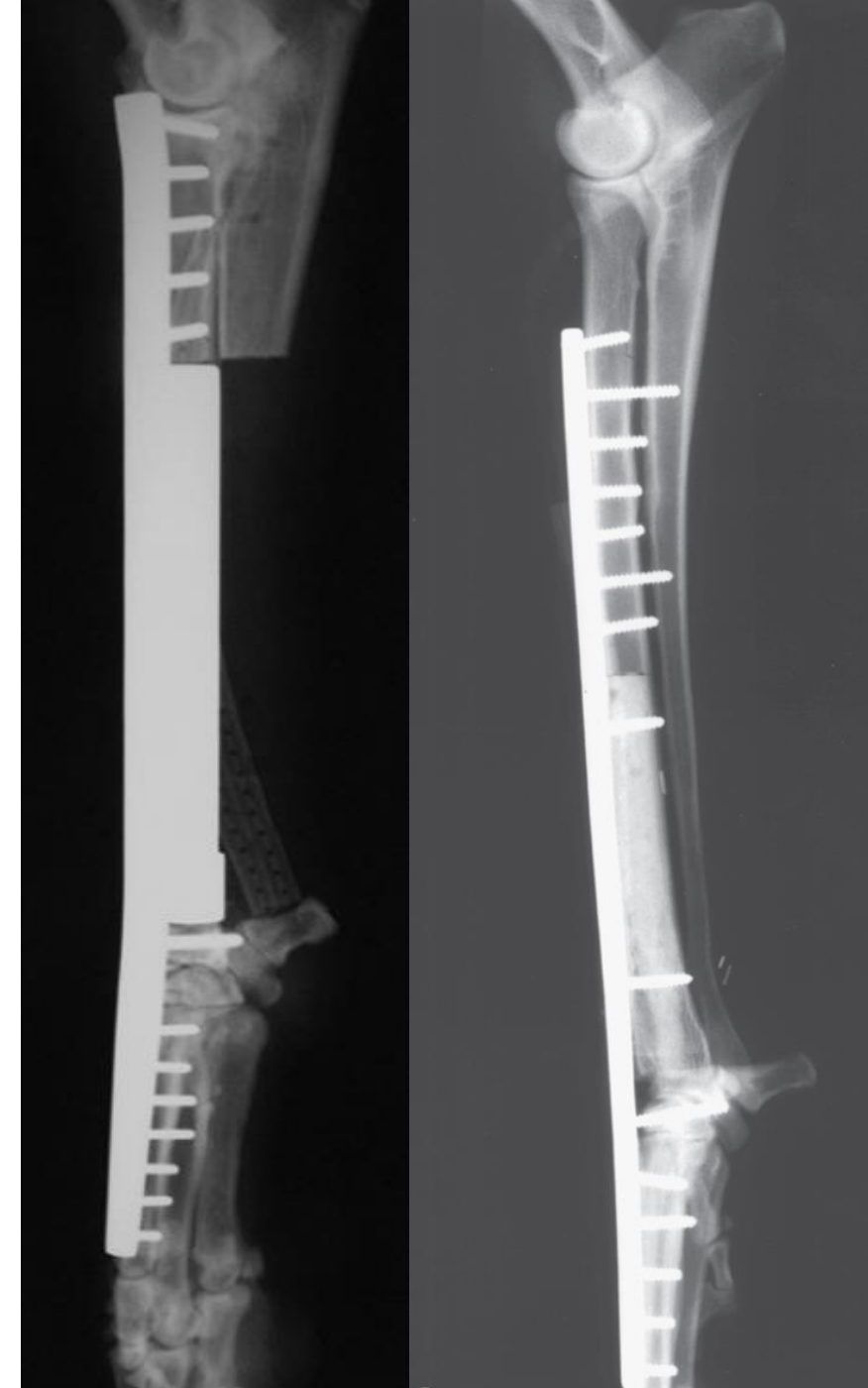
- Current “standard of care”
- Removes tumor and source of pain
- Most dogs do well with appropriate evaluation prior to amputation (orthopedic and neurological)



# Limb Sparing Surgery

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- Options limited by:
  - Lesion location (distal radius, ulna)
  - Lesion size (must be <50% of affected bone)
  - Surgeon availability (very few offer this procedure)
- Ulna: ulnectomy if less than half affected and radius normal
- Radius: Surgical removal of affected bone with a margin followed by reconstruction (hardware v. allograft)
- Positives:
  - Avoids amputation
  - Similar long-term outcome as amputation
- Drawbacks:
  - High post-operative infection rate (hardware) - Silver lining?
  - Post-operative hardware failure possible
  - Expense/availability



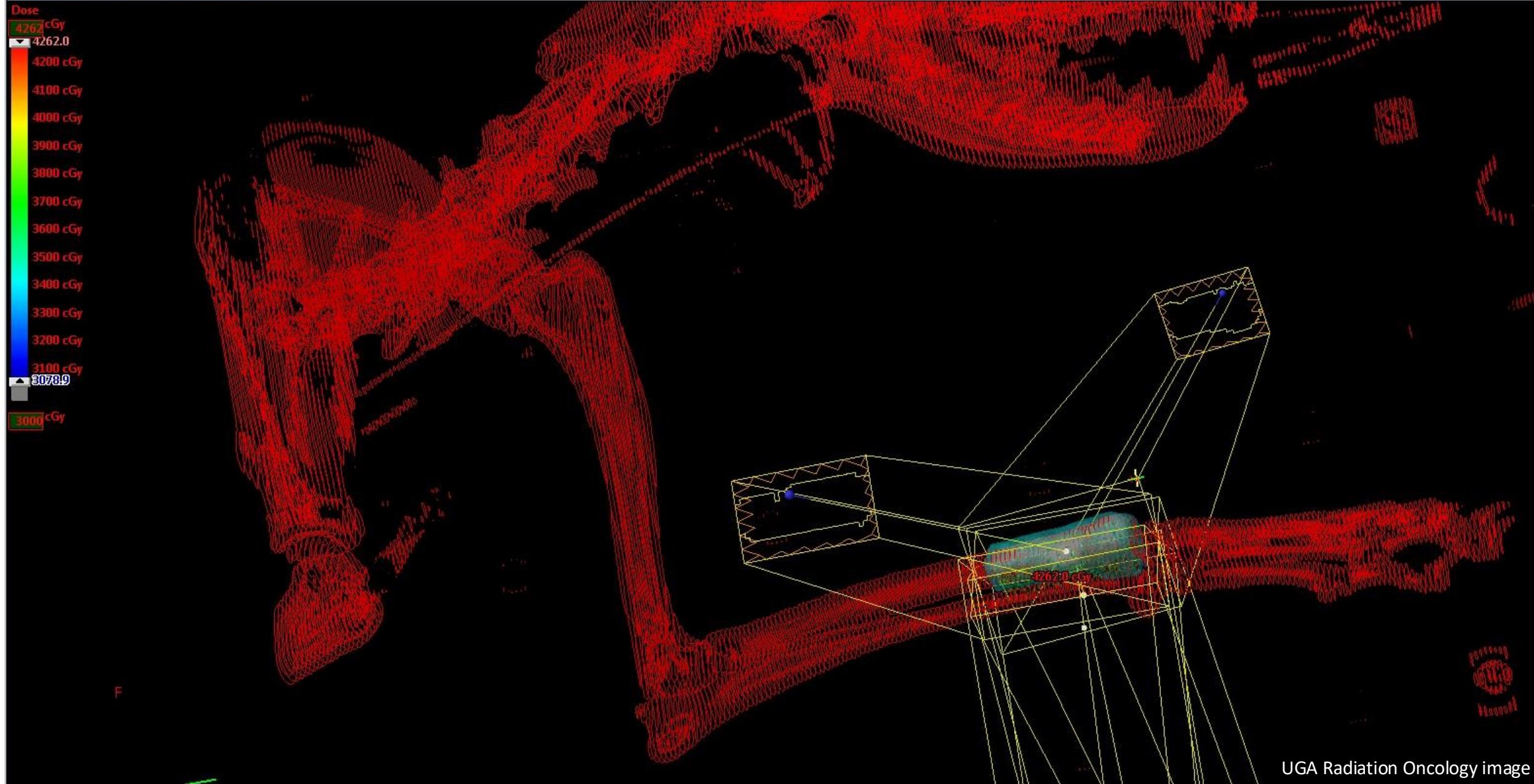
# Stereotactic Radiation Therapy (SRT)

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- High dose, highly targeted radiation
- Usually 3-5 treatments, once daily
- Positives:
  - Avoid amputation
  - Similar long-term outcome compared with amputation
- Drawbacks
  - Post-RT fracture rate is high (40% in largest study)
    - CT needed to determine fracture risk
  - Requires state of the art machine (\$\$)
  - Multiple anesthetic episodes
  - Risk of skin toxicity, especially in distal radius







# Adjuvant Chemotherapy

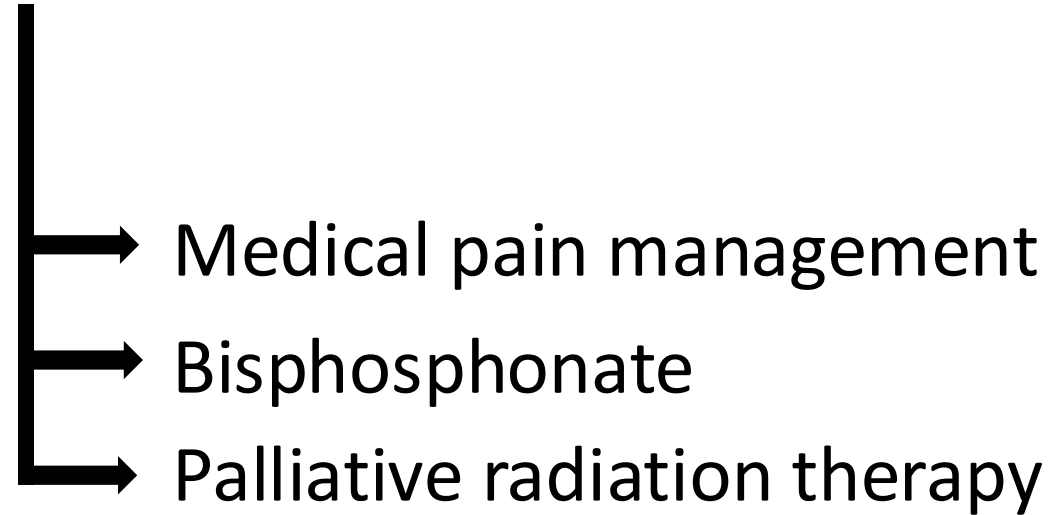
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- Median Survival Time (MST):
  - Definitive local control alone = 4-6 months
    - Most eventually develop/succumb to metastatic disease
  - Definitive local control + chemotherapy - MST 9-12 months
    - Statistically proven survival advantage
- Most commonly carboplatin
  - Generally well-tolerated
  - Most common adverse event bone marrow suppression, mostly sub-clinical
- Early chemo (< 5 days post-amputation) probably better than traditional (~14 days post-amputation)



# Quality of life (palliative) intent

Combine, if possible



If path fracture:

palliative amputation v euthanasia

# Medical Pain Management

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- Options (combine, if possible)
  - NSAIDs
  - Gabapentin
  - Tramadol, amantadine, tylenol codeine
  - Will eventually fail to control pain



# Palliative RT

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- Many protocols:
  - 1 treatment/day for 2 consecutive days most common (“boom-boom”)
- At least 75% response (reduction in pain)
  - Recent studies: 90%+ response rate is possible
- Lasts 2-4 months
- If effective, can be repeated





# Bisphosphonates

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- Zoledronate
- Inhibit osteoclasts = reduced bone destruction
- 30-50% response rate (improved pain management)
- IV q4 weeks until no longer effective
- May be synergistic with RT
- Nephrotoxic and renal clearance:
  - Check renal values prior to **every** dose
  - Don't use in patients with renal compromise
  - Long-term use - risk of bone density decrease, especially in mandible

# Palliative Amputation

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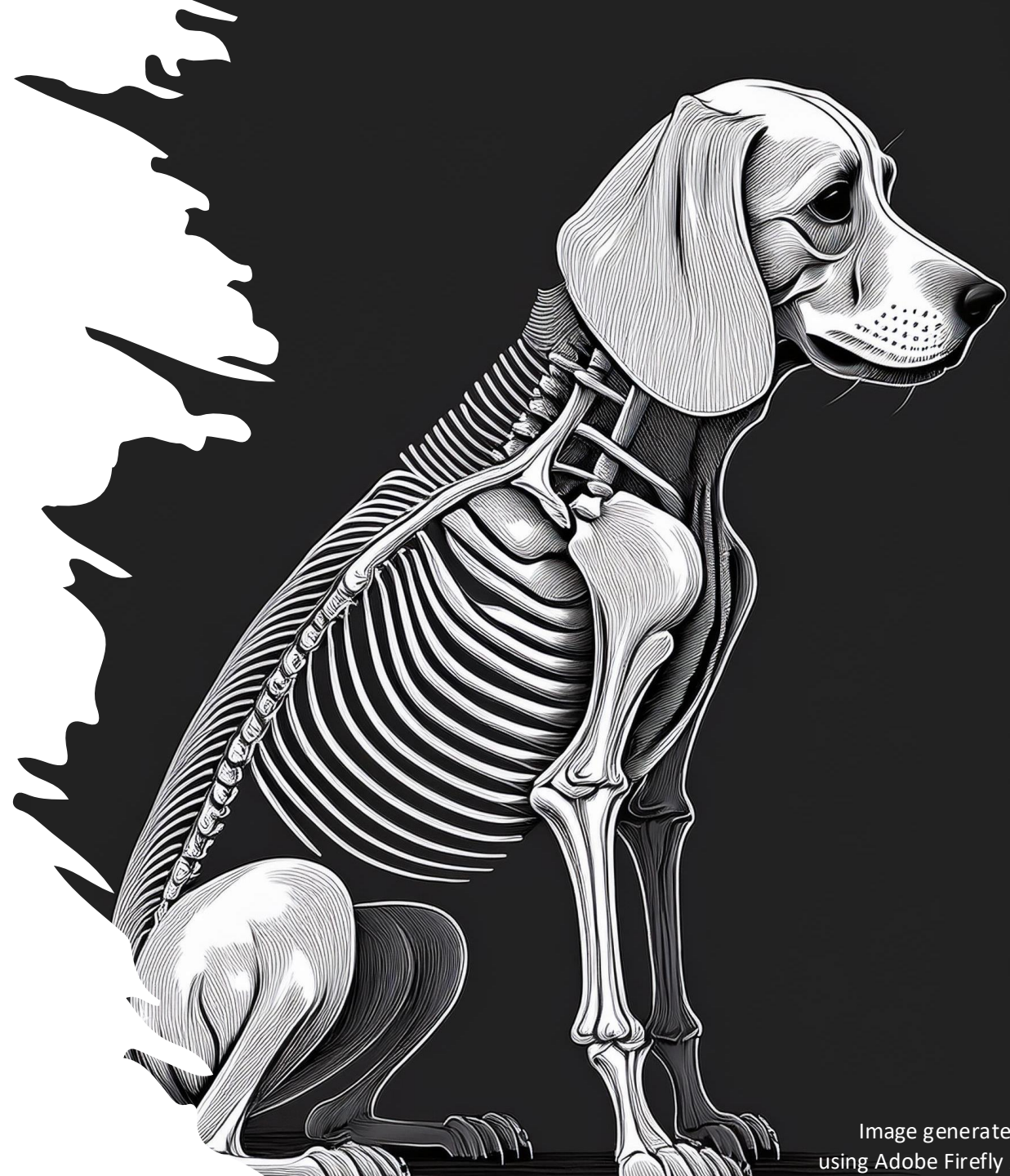
- In cases of pathologic fracture or uncontrolled pain



# Axial Skeleton OSA

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- Often more difficult to obtain adequate local control
  - e.g. spine, pelvis
  - May have to rely on RT (palliative or SRT)
- Variable prognosis
  - Clinical signs may be hard to control
    - eg compressive spinal cord lesions
  - Flat bones of the skull:
    - Lower metastatic rate
    - Improved prognosis vs appendicular w local control
    - Ex: mandibular OSA + hemimandibulectomy – survival times of 1.5 to 2+ years reported
  - Rib does much worse - frequent metastasis at time of diagnosis



# Prognostic Factors in Canine OSA

Better  
prognosis



Worse  
prognosis



Location	-Mandible -Digit, metacarpal, metatarsal	-Rib -Prox. humerus
Age at Diagnosis		< 3 years old (juvenile OSA)
Serum ALP		Elevated
Grade		High (most are high)
Peripheral Monocyte Count		Above 0.4 (this is WNL at most labs)
Metastatic Disease		Presence of metastasis



# Immunotherapy: The Next Frontier for Canine Osteosarcoma



# Why Immunotherapy in K9 Osteosarcoma?

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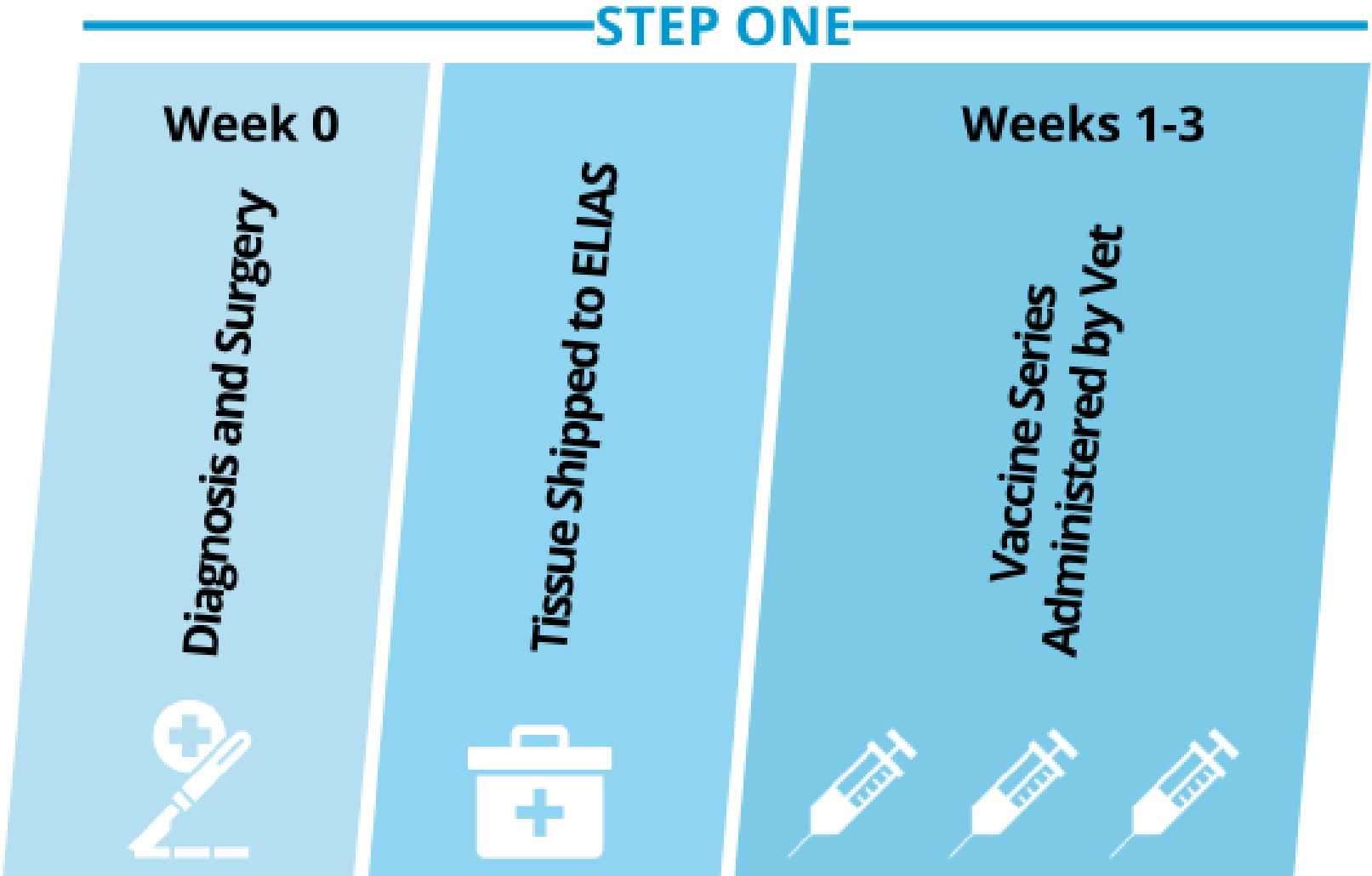
- Survival rates with surgery and chemo are stagnant and have been for a long time
- Surgical limb-spare patients (human and canine) that develop post-op infections are long-term survivors at higher rates than other populations
- OSA has a high mutation burden, a marker for improved immunotherapy response
  - Simply, mutated proteins are antigenic
- Non-specific immunostimulatory molecules such as L-MTP-PE (a synthetic bacterial cell wall component) demonstrate survival advantages (human and canine)

# Immunotherapy Strategies

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- HER2-listeria vaccine – data says it might work, but some dogs culture for listeria... on hold due to biosafety concerns
  - Uses listeria to stimulate an immune response to a protein commonly mutated in OSA
- Simple autologous vaccine – eg take patient tumor tissue, mash it up, inject
  - Stimulates response, but duration of response is limited → limited efficacy
  - Immunosuppressive tumor microenvironment and other complex immunology to blame
- Conditioned effector cytotoxic t-cells (CAR-T) being developed
  - Genetically modified T-cells that have antigen receptors specific for tumor antigens
  - Complicated, expensive, still experimental (for now)
- Autologous Adoptive T-cell Cancer Vaccine
  - Harvest tumor
  - Create autologous vaccine
  - Inject into patient, allow patient to mount immune response
  - Harvest T-cells, expand ex-vivo
  - Inject patient with T-cells + low-dose T-cell growth factor (IL-2)

# Example of an Autologous Activated Cell Therapy (ACT) Vaccine



This part is no different than any other autologous vaccine

## STEP TWO

**Week 5**

**T cells Collected via  
Apheresis**



**T cells Shipped to ELIAS**



**Population of Killer  
T Cells Produced**



**Week 6**

**Infusion of Activated  
Killer T cells**



**Weeks 7-8**

**IL-2 Injections**



# Recap: K9 OSA

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- Appendicular, metaphyseal most common
- Appendicular has a high rate of metastasis (> 90%)
  - → to lungs most commonly
- Definitive intent treatments include amputation, limb sparing surgery or SRT
  - MST with any of above alone ~4-6 months
  - MST with any of above + adjuvant carboplatin chemotherapy ~9-12 months
- Palliative intent treatments can be very effects and include: palliative radiation therapy (boom-boom), pain medications, bisphosphonate and amputation
- Prognostic factors: anatomic location, stage, age at diagnosis, serum ALP, peripheral monocyte count and grade
- Immunotherapy is likely our next big step (in many veterinary cancers)

## **Livestock Emergency Response Planning (LERP) for First Responders & Veterinarians**

On any given day in the United States, there are several hundred thousand head of livestock and equine being transported over the roads to multiple destinations, with most of these being moved via semi-truck and trailer. As the number of animals being transported via motor vehicle has significantly increased over the years, so has the number of accidents involving large animals. Currently in the United States, standard operating procedures for addressing such accidents do not exist. This need was realized by multiple groups concerned with animal welfare in such accidents, mostly beginning in the western US. The United States Department of Agriculture, the Department of Transportation, emergency & law enforcement entities, extension services, and cooperating universities have developed a framework for local emergency responders to more appropriately address accidents involving animal transport vehicles, deemed "Livestock / Bovine Emergency Response Planning" or LERP / BERP.

This training targets first responder protocols, public safety, and animal care & well-being in multiple types of accident situations in order for competent decision-making involving individuals who may provide support or assistance in dealing with these emergencies (including emergency management personnel, public safety communicators, governmental administrators, and veterinarians). It provides agricultural and traditional responders with an introduction, some performance skills, and understanding of some of the unique situations involving motor vehicle incidents with livestock and equine carriers. The knowledge and skills gained will assist in effective preparation and response to these type of unique emergency situations. This is designed as a one day course providing an overview of background and response actions, biosecurity, proper animal care & handling, triage & containment, humane euthanasia, and mortality handling & disposal.

Several years ago after realizing the increase in multiple traffic incidents in Georgia involving animals, leaders in public safety and animal industries here began organizing LERP sessions by inviting such training experts from Tennessee, West Virginia, Iowa, North Dakota, and Ohio. Currently, this training is being presented / sponsored by the GA Department of Transportation, Georgia Traffic Incident Management Enhancement (TIME) Task Force, GA Department of Agriculture, UGA Animal & Dairy Science, UGA College of Veterinary Medicine, Georgia Beef Commission, and the UGA Extension Service. The sessions offered include continuing education credits for participation. The information presented is divided into partial classroom / powerpoint presentations of real incident scenarios & lessons learned, and partial hands-on instruction demonstrating trailer specifications for extrication and animal handling techniques. Aspects of humane euthanasia scenarios are discussed in the veterinary presentations. At this time, there have been 30 training sessions completed within the state in the past 6 years, with approximately 900 individuals trained.

The GVMA is assisting in this effort by requesting veterinarians in different regions of the state to volunteer to be a point of contact in case of such an incident in the local area. The goal is to have a strategic plan / communication tree predetermined in order for efficient, rapid responses between knowledgeable individuals as a key to a timely, successful outcome. Other key members of a regional team include producers with access to trailers & portable panels, stockyard employees, Animal Control, towing professionals, Fire / EMS / Sheriff, and local DOT personnel. If veterinary assistance is needed at the site of an accident, financial compensation for veterinary time and supplies used in such incident responses is provided.

## Livestock Roadside Emergency Response Check List

### Contact List

1. Containment – if a livestock trailer has rolled over or in an accident of any kind, prepare an animal containment area before letting the cattle or other animals out of the trailer.

Panels and barricades – Containment for cattle can be quickly set up using portable panels (Figure 1). Dimensions are typically 10 to 12 foot in length by 5 ft. tall, approximately. Hogs, sheep and goats will need containment panels and or boards that are flush to the ground.



Figure 1: Cattle Panel for Temporary Containment

2. Cattle Handlers and Trailers for animal relocation  
Contact people with cattle handling experience and cattle trailers that can relocate animals to a local sale barn or other facility with good containment, water and hay.
3. Scene Security – Traffic control in areas where there may be loose livestock.
4. Provide information for scene access – all responders
  - a. Consider escorts by law enforcement
  - b. Have dispatch communicate best access
5. Contact Ga. Department of Agriculture
6. Veterinarian on Site (if at all possible)  
The attending veterinarian will need a proper method of euthanasia. A 22 magnum or larger is needed for most cattle to be humanly euthanized. Analgesics or sedatives such as xylazine may be needed. Drug delivery poles may be necessary for delivery.
7. Dead Animal Disposal / Rolloff Dumpsters  
Cattle or other animals found dead at the accident scene will need to be discreetly transported to a landfill. Call GA Dept. of Agriculture in this process to ensure proper disposal is necessary.
8. Relocation of Animals
  - a. Stockyard or other location – Disease Control is imperative
9. Get insurance information for carrier – contact early as possible; verify payment of resources used.
10. Track resources that are used for scene
  - a. Initial contact time.
  - b. Scene arrival time.
  - c. Scene Departure time.
11. Incident Debrief
  - a. After Incident Review
  - b. Critical Stress debriefs





# Appendix B: Animal Transport Incident Assessment

Responding law enforcement \_\_\_\_\_ Department \_\_\_\_\_

Phone \_\_\_\_\_ Email \_\_\_\_\_

Location of incident \_\_\_\_\_

Date/time of incident \_\_\_\_\_

**Transportation Company** \_\_\_\_\_

- Contacted
- Phone number \_\_\_\_\_

**Insurance Company** \_\_\_\_\_

- Contacted
- Phone number \_\_\_\_\_

**Driver name** \_\_\_\_\_

- Functional
- Nonfunctional

**Vehicle type**

- Farm trailer (bumper hitch)
- Gooseneck trailer
- Pickup with stock racks
- Bobtail truck
- Semitrailer (straight load)
- Semitrailer (potbelly)

**Vehicle condition**

- Operable
- Nonoperable

**Vehicle accident result**

- Upright
- On its side    Left    Right

**Accident site**

- Urban
- Rural
- On road
- Shoulder
- Ditch
- Other \_\_\_\_\_

**Animal type**

- Cattle
- Horses
- Pigs
- Sheep
- Poultry
- Deer
- Bison
- Llama
- Ostrich/Emu
- Other \_\_\_\_\_

**Emergency Contact** \_\_\_\_\_

**Comments** \_\_\_\_\_

**Age group**

- Young
- Intermediate
- Mature

**Quantity**

- Known    Number \_\_\_\_\_
- Unknown    Estimate \_\_\_\_\_

**Classification**

- Slaughter
- Feeder
- Replacement
- Biosecurity concern (sealed trucks, etc.)

**Destination**

- Farm                       Auction market
- Slaughter plant    Feedlot
- Other \_\_\_\_\_

**Scene Security Status**

- Contained
  - Number tied \_\_\_\_\_
  - Number loose \_\_\_\_\_
- Escaped \_\_\_\_\_

**Health Status**

- Uninjured \_\_\_\_\_
- Injured \_\_\_\_\_
- Dead \_\_\_\_\_
- Unknown \_\_\_\_\_

**Extrication**

- Yes    No

**Support required**

- Live animal transport/relocation
- Personnel
  - Veterinarian
  - Euthanasia specialist
  - County Extension agent
- Equipment
  - Fencing
  - Gates
  - Lighting
  - Tow truck


IOWA STATE UNIVERSITY  
College of Veterinary Medicine

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## Pet Pig Medicine

Justin Brown DVM, PhD  
Assistant Professor of Swine Production Medicine  
Iowa State University College of Veterinary Medicine

Slides adapted from Dr. Jessica Bonnema



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### Why does a pet pig need to see a veterinarian?

- Yearly exams and health check
- Routine vaccinations
- Maintenance procedures
  - Tusk/hoof trimming
  - Spay/neuter
- Illness

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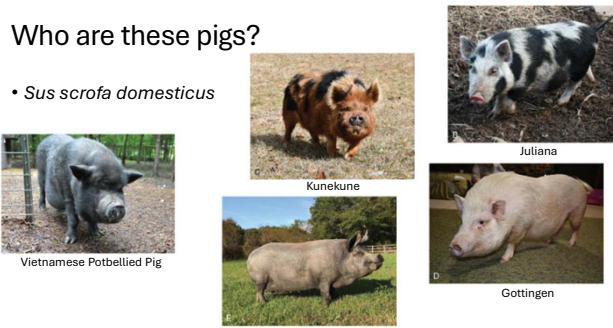
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### Who are these pigs?

- *Sus scrofa domesticus*



Photos courtesy of Mezzachio

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### Not to be confused with these pigs

- Also *Sus scrofa domesticus*



Commercial Crossbred Pig

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### Handling and Restraint

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### How does the pig come to the clinic?



- Some pigs are leash trained
- Some pigs may ride in a carrier
- Some pigs may ride in a lap (as safety allows)
- Some clinics will encourage in-home exams, which allows for the pig to be in its comfort zone

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### Behavior Review

- Pigs are highly intelligent animals, but they're also naturally a prey animal, so any perceived threats escalate stress quickly
- Pigs explore their surroundings using their nose and mouth
  - Rooting is instinctive –will chew and ingest almost anything
  - Stimulation and enrichments are necessary
- Socially: herd animal with hierarchy
  - Adjustments may be necessary in household settings



Photo courtesy of Mazzachio

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### Handling and Restraint

- Basic animal handling techniques apply:
  - Quiet
  - Calm
  - Efficient
  - Less is more (as much as possible)
  - Safety for humans and animals
- Hearing protection is highly recommended
- Muzzle? Soft tie piece for biters

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### Manual Restraint

- Extremely docile pigs: belly rub is all that is needed
- Smaller pigs may sit in laps
- Held close to body
  - Arms (smaller pigs)
  - Vertical Flip (larger pigs)



Photo courtesy of Mazzachio

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### Pig Flip: Dorsal Recumbancy

- Pigs become quite calm when laid on back
- Variety of methods to get pigs there
  - Lay on ground, then roll over
  - Grab opposite leg quickly, pull towards you, and flip pig
- Larger pigs may require support/padding on the sides to remain stable
- The use of treats is not recommended just prior to the technique
  - Aspiration risk




Photo courtesy of Mozzachio

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### Pig Handling: Equipment

- Sorting boards
- Dog kennels for transportation and holding
- Slings
- Use of snares is not recommended in pet pigs
  - Reaction very different from commercial pigs
    - Locking in place vs. thrashing and extreme stress




Photo courtesy of Mozzachio





Photo courtesy Panepinto sling



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### Pig Restraint: Chemical Calming/Light Sedation

Drug Name(s)	Dose	Route	Frequency	Withdrawal
Gabapentin/Trazadone	G: 20 mg/kg T: 10 mg/kg	PO	Night before procedure, then ~30 minutes prior to procedure	30 days
Midazolam	0.1-0.2 mg/kg	IN	~15-30 minutes prior to procedure	14 days
Acepromazine	0.1-0.2 mg/kg	IM	~15-30 minutes prior to procedure	7 days

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### Pig Restraint: Chemical Heavier Sedation for Longer Procedures

Drug Name(s)	Dose	Route	Frequency	Withdrawal
TKX (Telazol/Ketamine/Xylazine) *1 bottle of tiletamine/zolazepam mixed with 250 mg xylazine and 250 mg ketamine	1 mL/75-100 pounds	IM	~15-30 minutes prior to procedure	<b>T: 40 days</b> K: 2 days X: 30 days
Xylazine 1 mg/kg Midazolam 0.2 mg/kg Ketamine 5-10 mg/kg	X: 1 mg/kg M: 0.2 mg/kg K: 5-10 mg/kg	IM	~15-30 minutes prior to procedure	<b>X: 18 days</b> M: 14 days K: 2 days
Xylazine Butorphanol Ketamine	X: 1 mg/kg B: 0.1 mg/kg K: 5 mg/kg	IM	~15-30 minutes prior to procedure	<b>X: 18 days</b> B: 7 days K: 2 days

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## Physical Exam

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### Performing a physical exam on a pig

- Overall mentation and activity
- Body condition score
  - <https://www.minipiginfo.com/minipig-body-scoring.html>
- Locomotion
  - Hoof conformation



Images courtesy of American Mini Pig Association



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### Physical Exam

- TPR
  - Temperature: 102.5°F (99.5-103.0)
  - Pulse 70-100 bpm
  - Respiration 12-24 breaths/minute
- Skin
  - Many pet pigs some degree have dry, flaky skin as they age
  - Dark brown ear wax is normal
  - Evaluate mange potential
  - Pigs will shed hair when stressed, and many pigs have seasonal shedding patterns
- Eyes
  - Environmental irritation or entropion?
- Oral Cavity
  - Tusks
- Urination/Defecation
  - Urolithiasis
  - Constipation or diarrhea



Photos courtesy of Mozzachio

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### Vaccine Protocols

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### Vaccination protocol basics

- As with any animal, there is not a one-size-fits-all protocol, but there are strong, consistent recommendations
- Swine vaccines are licensed with the commercial pig in mind but work well for pet pigs
  - Keep in mind that dose adjustments are off label and remove any claims of efficacy from the company
  - Use of vaccines from other species is also off label and must be done with strong scientific foundations
- Must be evaluated in light of
  - Age
  - Environment
  - Breeding Status
  - Geography

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### Foundational Vaccine Protocol: Must-Haves

Disease	Timing/Frequency	Swine-Approved Vaccine Available?	Zoonotic Potential	Notes
Rabies	Yearly	No	Yes	Labeled dose considered efficacious, induces adequate titers
Erysipelas	Yearly or bi-yearly	Yes	Yes	Injectable or water vaccine
Leptospirosis	Yearly	Yes	Yes	Vaccine often in combination with parvovirus, sometimes erysipelas

**\*\*Vaccines generally have a 21 day meat withdrawal**

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### Situation-Dependent Vaccines

- Respiratory disease
  - Primary issue in commercial herds; not as worrisome in pet pig situations
    - *Actinobacillus pleuropneumoniae*
    - Atrophic rhinitis (*Bordatella bronchiseptica* and *Pasteurella multocida*)
    - *Mycoplasma hyopneumoniae*
    - Porcine Circovirus Type 2 (PCV2)
  - Take into consideration how close this pet pig may be to a commercial herd
- Tetanus
  - Pigs are generally more tetanus resistant than other species
  - However, recommended administration with surgery or large wound repair

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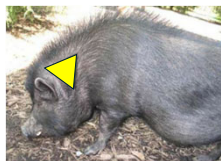
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### Vaccine Administration: Location



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Photos courtesy of Mezzachio

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# Parasites

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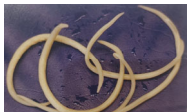
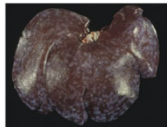
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### Internal Parasites

- **Ascarids (*Ascaris suum*)**
  - Large adult worms → physical damage and competition with host for nutrients
  - Clinically: weight loss, rough hair coat, cough
  - Larval migration causes organ damage
    - Liver, lungs

Diseases of Swine, 11<sup>th</sup> Edition

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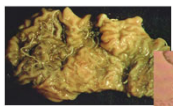
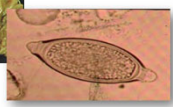
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### Internal Parasites

- **Whipworms (*Trichuris suis*)**
  - Large bowel diarrhea +/- blood
  - Pigs at least 6-7 weeks of age
- **Strongyles (*Strongyloides ransomi*)**
  - Affects suckling piglets more severely
  - Infective larvae shed in colostrum after hypobiotic state in mammary fat

Diseases of Swine, 11<sup>th</sup> Edition

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## External Parasites

- Common offenders
  - Sarcoptic mange (*Sarcoptes scabiei* var. *suis*)
  - Lice (*Hematopinus suis*)
  - Fleas, ticks, other insects are generally not host specific, but will bite pigs
    - Main reactions are hypersensitivity and erythematous papules
    - Preventative often not needed
    - Sanitation, remove from infected environment

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## External Parasites: Sarcoptic mange

- Host specific and transmitted via direct contact
- Short lived (3 days) in environment
- Eggs and adults live in the epidermis
- Clinical signs:
  - Intense pruritis
  - Erythema, papules
  - Hyperkeratosis
- Diagnosis:
  - skin scraping: crusts from pinnae of ear (negative skin scrapes are bo
- Tx:
  - Injectable avermectins every 2-3 weeks
  - OP topically
- **Zoonotic**



Photos courtesy of Mozzachio

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## External Parasites: Lice

- Blood-sucking adults are easily visible, small white nits seen on lower hair shaft
- Transmitted by direct contact, do not survive long in environment
- Clinical signs:
  - Pruritis and self trauma
  - Severe infestations: anemia, weakness, and lethargy
- Dx: ID adults and/or nits
- Tx:
  - Injectable ivermectins
  - Topicals: Prolate for pigs (OP)
  - Clean environment (this is where you can use a Frontline spray?)

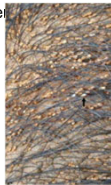


Photo courtesy of Mozzachio

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### Parasite Control Recommendations

Drug	Example Products	Dose	Notes	Withdrawal
Febendazole	Safeguard pellets	2 oz/day q 3 d	Activity vs. most internal parasites, including whipworms	0 days
Avermectins	Dectomax, various generics	1 mL/75 pounds IM	Roundworms, lungworms, sucking lice, and mange mites *Resistance patterns noted	24 days
Phosmet (OP)***	Prolate	Topical spray daily PRN	Lice and sarcoptic mange	1 day
Permethrin***	Swine Guard	Pour/Spray	Flies, mosquitoes (needs retreatment in 14 days)	5 days

\*\*\*EPA vs. FDA regulated products

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## Venipuncture

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- ### Venipuncture
- Why?
    - Assess overall health
      - CBC, Chem Panel
    - Survey for specific diseases
    - Sedation
    - IV fluids
    - Euthanasia
  - Where can you send these blood samples for diagnosis?
    - In house
    - Reference Laboratory
    - ISU Clin Path has a large (relatively) swine database
    - ISU VDL has excellent testing for disease status
  - Keep in mind hematologic ranges for swine have been compiled with a relatively small database

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### Venipuncture locations

Prewean and Nursery pigs (<40 pounds)

Growing/finishing pigs (>40 pounds)

- Juglar furrow allows access to
  - Anterior vena cava
  - Jugular vein
- Blind stick in the deepest part of the jugular furrow
- Try to stay on the pig's right side
  - Vagus nerve

Diagrams courtesy of Certified Swine Sample Collector Training

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### Venipuncture locations

Auricular Vein

Saphenous Vein

Coccygeal (tail) Vein

Also Orbital Venous Sinus

Photos courtesy of Mozzachio

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## Maintenance Procedures

Hoof trimming and dentals

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### Before and After

Photos courtesy of Mozzachio

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### Dentals

- Adult pigs have 44 permanent teeth
- Dental issues are common in pet pigs
  - Periodontitis
  - Abscesses
  - Cavities (caries)
  - Malocclusions/crowding
  - Very convoluted root structure (radiographs are a must)
  - Tusk trimming (males)
- Difficult to completely examine a pig's mouth without sedation due to
  - Excitable state
  - Narrow mouth

Photo courtesy of Mozzachio

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### Tusk trimming

- 4 canine tusks that erupt around 5-7 months
  - Males have four permanent canines that grow continuously
  - Females stop growing around 2 years
- Trim ~ 1-2x per year and as needed
  - Why? Excessive length, points, catching/hooks, malocclusion, SAFETY
- Special tusk considerations
  - Pulp cavity (nerves) extends above the gumline (will hurt when trimming)
  - Long, multiple, lower tusk roots in male extend back through the body of the mandible

Photo courtesy of American Mini Pig Association

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### Tusk trimming



- Sedation and inhalant anesthesia are necessary
- Use Gigli (OB) wire and/or rotary grinding tool like a Dremel
  - NO cutting tools, as the force may → cracks or tooth breakage
- Cut about two feet of wire, attach to handles
  - Keep in mind both these and the Dremel may get hot
- Take breaks, keep soft tissues (gums, lips) out of the way.
- Start with short strokes to get a groove in the tooth, then go for longer strokes
- Leave about a half an inch above gumline, check occlusion

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### Surgical Procedures

Spay, neuter, and pain control

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### General Surgical Considerations

- 12 hour fast prior to surgery
- +/- Tetanus prior to surgery
  - CDT vaccine?
  - Antitoxin prior to surgery?
- IV fluids (LRS) are a great idea
- Gastroprotectants highly recommended
- Ondansetron
- Are antibiotics indicated perioperatively?

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### Spay (OHE)

- Importance
  - Population control
  - Behavioral effects seen with estrus (every 21 days!)
- Uterine neoplasia
  - 75% of intact female pigs >10 years old will have some type (Large Animal CE)
    - Leiomyoma, leiomyosarcoma, endometrial adenocarcinoma
  - Always keep on your differential list of ADR intact female pigs

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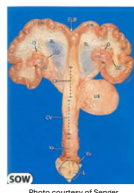
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### Spay Considerations

- Ideal age is 3-6 months/40-60 pounds
- NOT in heat (do a physical exam to confirm yourself)
- Obesity increases challenge level




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### Spay Considerations

- Uterus is very easy to find and exteriorize
  - A more caudal incision may be helpful
  - Remember the horns are quite long
- Broad ligament is very thick and vascular
  - Several bites will be needed to properly apply hemostasis
  - Ligate, ligate, ligate...and then ligate some more
  - Cautery is also a good option
- Ovary will have multiple follicles—a bumpy appearance is normal
- For in-depth procedural discussion see Large Animal Consulting and Education ([largeanimalce.com](http://largeanimalce.com))




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## Neuter Considerations

- Ideally done at 2-6 months of age
- Prevention of
  - Unplanned pregnancies
  - Testicular cancer
  - Behavioral changes
- Very similar procedure to dogs
  - Prescrotal incision, closed castration is ideal
  - Intra-dermal closure

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## Pain: What does it look like?

- Hunched posture
- Grinding teeth, smacking lips
- High pitched vocalizations (acute, intense pain)
- Shifting positions (chronic pain)
- Occasionally dog-sitting
- Decreased activity and appetite
- Drooping ears



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## Pain Management

- Banamine-S (flunixin meglumine, 50mg/mL)
  - Withdrawal 12 days
- Meloxicam 0.4 mg/kg PO q 24h
  - Withdrawal 28 days
  - Extra label
- Gabapentin 15 mg/kg PO once, then 8.5 mg/kg q 8 hours PO (Hampton et al, 2021)
  - Withdrawal 30 days
  - Extra label

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# Survey of Commonly Seen Conditions

Gastrointestinal, Integumentary, Behavioral

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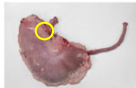
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## Gastrointestinal: Gastric Ulcers



- Found in the pars esophagea (non-glandular region) of the stomach
- Clinical Signs
  - Anorexia, teeth grinding, tarry, black stools
  - Generally ADR (may be a sequel to other conditions)



- Treatment
  - Medications
    - Sucralfate (1 g PO q 6 h)
      - Withdrawal 4 days
    - Omeprazole (10-20 mg q 24 h)
      - Withdrawal 21 days
    - Famotidine (0.1-0.2 mg/kg PO/SQ/IM)
      - Withdrawal 12 days
  - Remove stressors
  - Check diet and nutrition
  - Always do a full exam and investigate other underlying disease

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## Gastrointestinal: Foreign Body

- Pigs are orally oriented, and a variety of items may enter their GI system
- Clinical Signs
  - Anorexia, reluctance to eat, weight loss (chronic)
  - +/- Vomiting, constipation
- Dx:
  - Radiograph and/or endoscopy
- Tx:
  - Surgical removal
  - Ulcer care afterward

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## Integumentary: Erythema multiforme AKA Dippity Pig

- Clinical signs—seen more in younger pigs (less than 3)
  - Pig will dip back (flatten/arch alternatively) +/- vocalization → pain response
  - Reddened, serosanguinous lesions, sometimes horizontally like grill marks appear on dorsum soon after
  - Cause has not been identified
- Dx: R/O other causes (esp. sunburn)
- Tx:
  - Usually self-resolving in 2-4 days
  - Analgesic
  - Topicals for secondary infections as needed



Photo courtesy of the American Mini Pig Association

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## Integumentary/Systemic: Erysipelas AKA Diamond Skin Disease

- Etiology: *Erysipelothrix rhusiopathiae*
- Clinical Signs:
  - Characteristic reddened, rhomboid shapes on the pig's skin
  - Lethargy, fever, pain
  - Long term: arthritis and heart failure (VVE)
- Dx:
  - Clinical presentation
  - Necropsy: Culture, histopathology, PCR, IHC
- Tx: Usually empirical
  - Procaine penicillin G is **labeled** for treating this!
  - 1 mL/100 pounds IM q 3-5 days; 7 day withdrawal
  - 5 mL/100 pounds IM q 3-5 days; 17 day withdrawal (**extra label**)
- Preventative: vaccine is efficacious and highly recommended



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## Integumentary: Pityriasis rosea

- Clinical signs: younger pigs: 4-16 weeks of age
  - Reddened, raised circular lesions, usually starting on ventral abdomen
  - Erythematous borders, with paler center
  - Lesions spread and coalesce
  - Not contagious
  - Cause is unknown
- Tx: None
  - Lesions are self-resolving in a few weeks



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### Musculoskeletal/Lameness

- Main issues
  - Arthritis
  - OBESITY + age
  - Nutritional deficiencies
  - OCD
  - Improper hoof trimming
- Proper diagnostic workup—determine the root cause
  - Radiology
  - Bloodwork
  - Address pain/welfare issues

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### Systemic/Neurologic: Salt toxicity/water deprivation

- Limited access to water through a variety of causes
- Clinical signs:
  - Disorientation
  - Ataxia
  - Recumbency with paddling
- Tx:
  - **Gradual** rehydration
  - Address neurologic issues as needed

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### Behavioral

- >95% of pet pigs get rehomed at some point (Large Animal CE)
  - Behavioral issues have much to do with this
- Investigate the underlying cause: Is there a deficiency in their environment?
- Reproductively intact animals are naturally more aggressive
- Pigs are naturally herd animals, so having a buddy around sometimes helps curb bad behavior
- Pigs are very intelligent animals and will try to push the boundaries often
  - Signs: Biting, charging, throwing head around
  - Usually not as much of a problem in multi-pig households

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### Swine Antimicrobial Toolbox

Drug Name	Dose/Route/Duration	Withdrawal	Labeled Use	Notes
Lincomycin (Ex: Lincomix 300)	1 mL/60 pounds IM SID q 5 d	5 days	Indicated for use of arthritis caused by susceptible organisms and for <i>Mycoplasma pneumonia</i>	
Ceftiofur (Excede for Swine)	1 mL/44 pounds IM once	14 days	Indicated for the treatment of swine respiratory disease (SRD) associated with <i>Actinobacillus pleuropneumoniae</i> , <i>Pasteurella multocida</i> , <i>Glaeseria</i> <i>parvula</i> , and <i>Streptococcus suis</i> , where SRD has been diagnosed.	Do not inject >2 mL per site <b>**NO ELDU</b> for prevention, or change in dose, frequency, duration, route
Enrofloxacin (Baytril 100)	3.4 mL/100 pounds SQ once	5 days	For the treatment and control of swine respiratory disease (SRD) associated with <i>Actinobacillus pleuropneumoniae</i> , <i>Pasteurella multocida</i> , <i>Glaeseria</i> <i>parvula</i> , <i>Streptococcus suis</i> , <i>Bordetella</i> <i>bronchiseptica</i> , and <i>Mycoplasma</i> <i>hyopneumoniae</i> . For the control of colibacillosis in groups or pens of weaned pigs where colibacillosis associated with <i>Escherichia coli</i> has been diagnosed	Do not inject >5 mL per site <b>**NO ELDU</b>

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### Take Home Ideas

- A pig is a pig is a pig
  - Physiologically, anatomically, mentally, behaviorally unique
  - Use swine-labeled and approved treatments
- You cannot get too basic when educating your pig clients
  - Remember animal husbandry (water, feed, floor, air)
- Review of swine anatomy, physiology, and disease processes is helpful



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### Take Home Ideas

- We have resources to help!
  - Swine Medicine Education Center
    - [www.smec.iastate.edu](http://www.smec.iastate.edu)
  - Large Animal Medicine Consulting and Education
    - [www.largeanimalce.com/product/this-little-piggy-course-series](http://www.largeanimalce.com/product/this-little-piggy-course-series)
  - Potbellied Pig Veterinary Medicine* by Kristie Mozzachio
  - Pathways to Pregnancy and Parturition*. P.L Senger
  - American Mini Pig Association
    - [www.americanminipigassociation.com](http://www.americanminipigassociation.com)



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IOWA STATE UNIVERSITY  
College of Veterinary Medicine

# Swine Diseases: Current Trends

*Justin Brown DVM, PhD*



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## Overview

- Coronavirus
- IAV-S
- PRRSV

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## SDRS

- 6 diagnostic labs
  - ISU
  - SDSU
  - Minnesota
  - Kansas State
  - Ohio
  - Purdue



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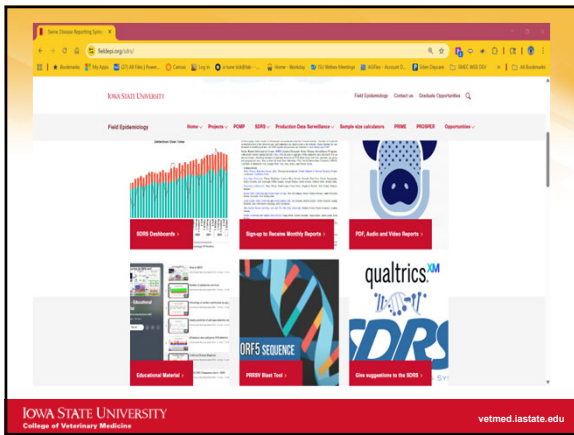
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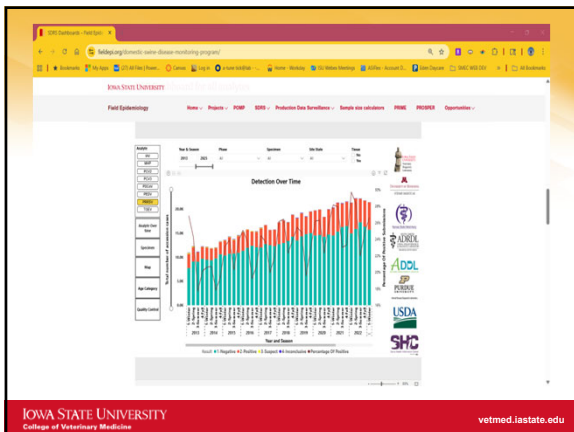
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The screenshot shows the Iowa State University website with a navigation menu and a main content area. A prominent QR code is labeled "Sign-up". Below the QR code, there are several text-based announcements regarding webinars and events, including dates and topics related to "Enteric Coronavirus".

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## Enteric Coronavirus - PEDV

- 2013
- Villus atrophy
- 100% morbidity
- Up to 100% mortality in neonates

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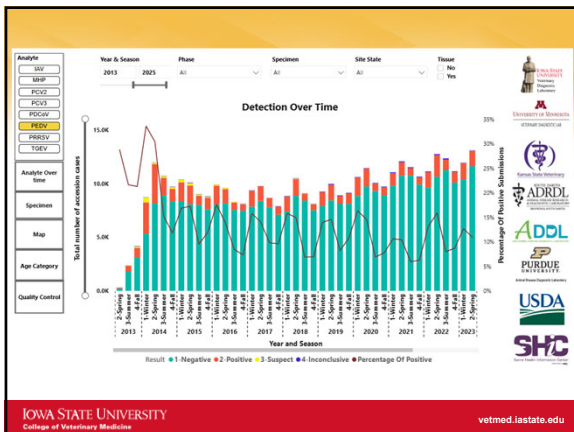
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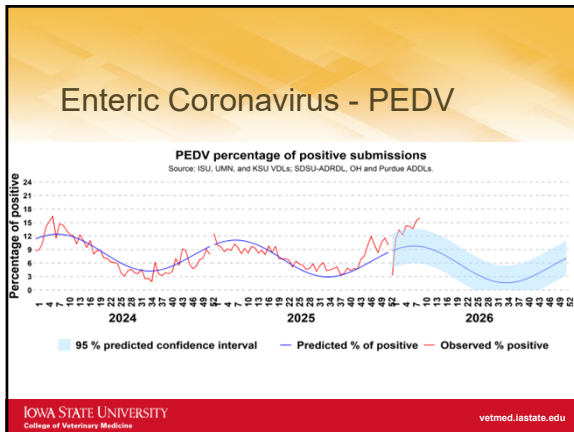
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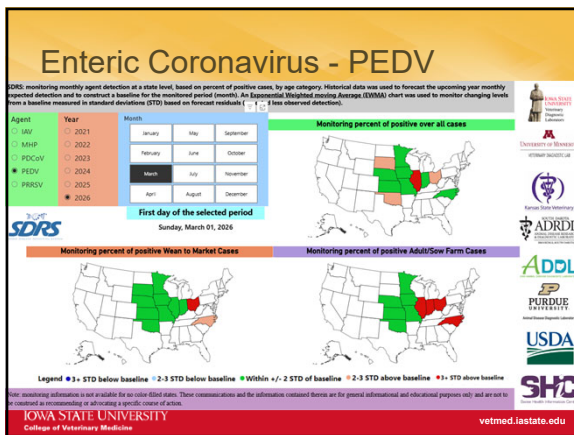
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### Enteric Coronavirus - PDCoV

- Porcine Deltacoronavirus
  - Similar clinically to PEDV
  - Usually less severe

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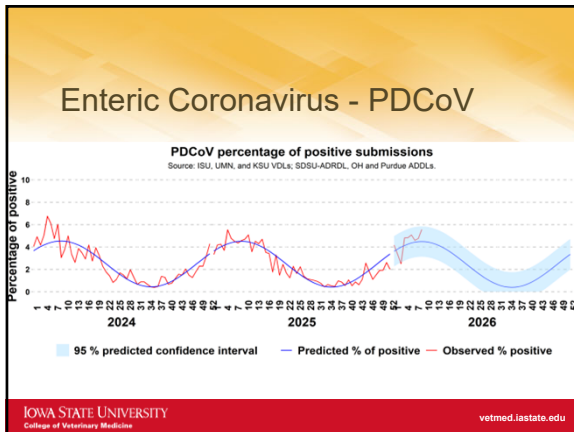
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### Enteric Coronavirus – TGEV

- Historically common cause of scours
  - Pre-weaning and nursery
- Similar clinical signs
- PRCV - mutant

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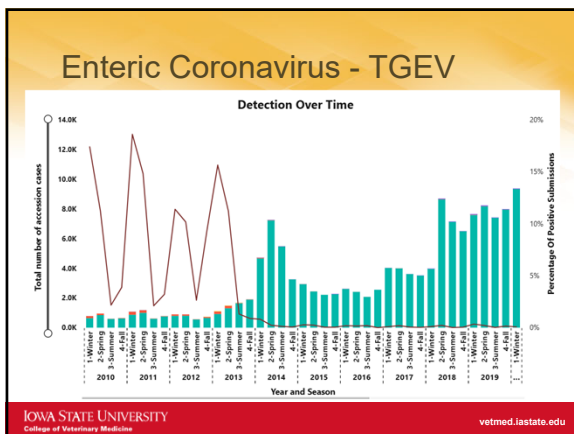
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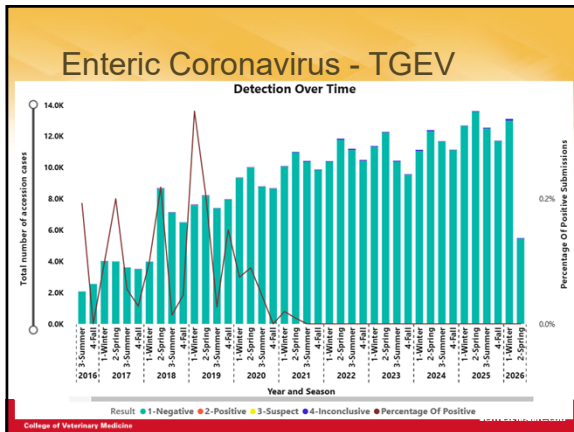
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### Enteric coronavirus

- Next steps?
- PEDV elimination task force
- Biosecurity
  - Wean to market
  - Transportation

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### Influenza A virus - Swine

- Primary respiratory disease
- “Mixing vessel” – zoonosis
  - H5N1

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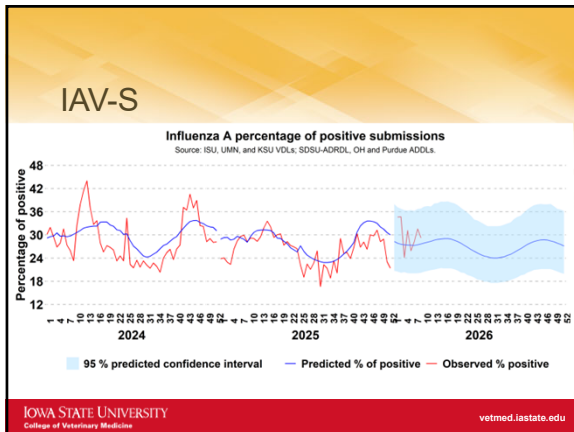
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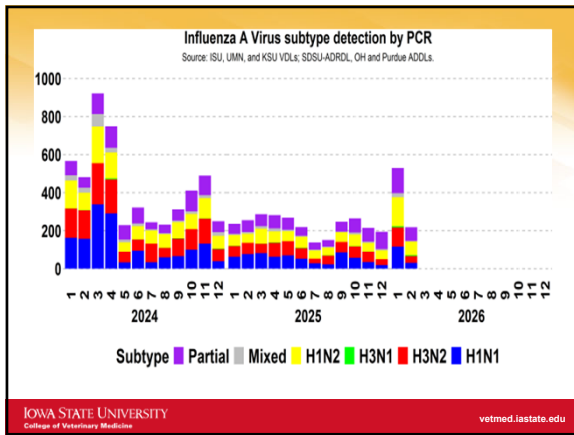
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**IAV-S**

- H5N1 – HPAI
  - Dairy – March 2024
  - NPPC response plan draft
  - Testing impacts?
  - Zoonotic

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### What *variant* classifications *can* and *can not* tell you...

- ✓ More reliable than RFLPs at determining relatedness, and whether virus A is the same or different than virus B
- ✓ Discriminate between new and previous wild-type viruses in a farm (based on ORF5 gene)
- ✓ More useful for epidemiological investigations, such as determining possible sources of introduction and tracking between-farm spread.

- ✗ No classification system reliably provides information on virulence or clinical picture (apparent virulence likely influenced by co-infections and other external factors)
- ✗ Classifications do not directly translate to immunological cross-protection, although viruses labeled as the same variant are more genetically homologous

PRRSV

DR. KIM VANDERWAAL

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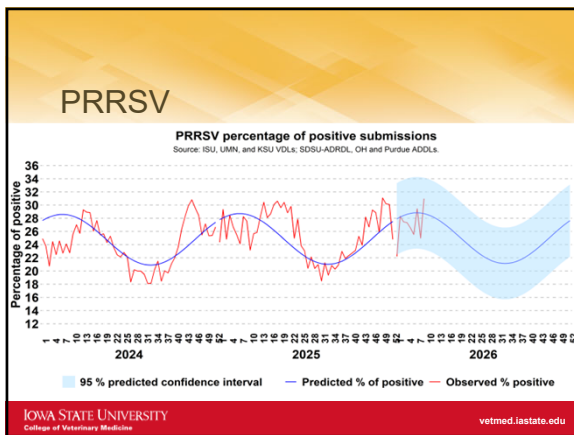
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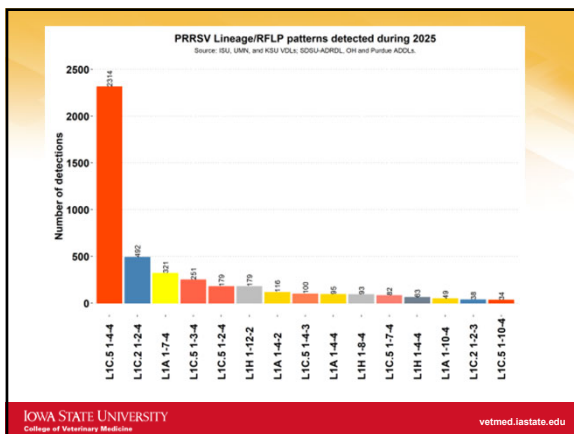
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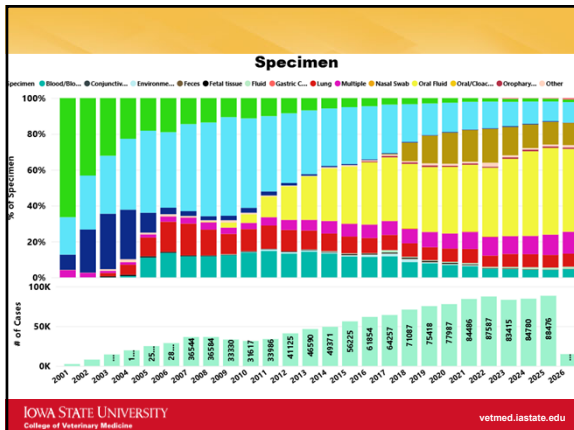
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**Gene Edited Pig**

- CRISPR CAS9 Editing
  - Exon 7 of CD163 and preceding intron deletions
  - Form CD163<sup>-/-</sup>

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**Gene Edited Pig**

- FDA approval achieved
- Next steps?
  - Consumer acceptance
  - Trade partner acceptance
- Timeline?
  - 10 + years

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**PRRSV**

- Next steps?
  - Biosecurity
    - Outbreak investigations
  - Spronk and Dee 2025
    - 6 nonnegotiables

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**6 nonnegotiables (Dee and Spronk)**

- US swine industry must
  - Eliminate PRRSV
  - Improve biosecurity
  - Restrict use of LVI
  - Change behavior regarding the movement of PRRSV infected pigs
  - Improved genetic response
  - Participate in US SHIP

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**US Swine Health Improvement Plan**

**ASF-CSF Monitored Certification**  
"A proven platform for safeguarding, certifying, and bettering animal health"

**Program Participants**  
Producers & Packers  
Implement program in accordance with certifications held

**Official State Agencies**  
Adapt and administer program to meet the needs of their state

**USDA Veterinary Services**  
Facilitate program and maintain program documents

**Congress of Industry Stakeholders & Select State Experts**  
Producers, Packers, VMD's, Veterinarians, Diagnosticians, Microbiologists  
Define & continually update program

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**U.S. SHIP Participant Checklist**  
HOW TO BECOME U.S. SHIP CERTIFIED

**Step 1. Enrollment**

- Contact U.S. SHIP Official State Agency (OSA) in which the participating premises is located
- Enroll live swine production and slaughter facility premises with the U.S. SHIP OSA in which the participating premises is located
- Acknowledge understanding of and compliance with requirements for certification

**Step 2. Certification**

- U.S. SHIP OSA to contact US SHIP participant (Swine Owner) to initiate certification
- U.S. SHIP participants need to demonstrate competency in providing at least 30 days of movement information electronically in a common format (e.g., a pre-checked CSV file) to the U.S. SHIP OSA in a timely manner
- Commercial-scale pork producer participants need to be able to provide the U.S. SHIP OSA access to a completed Secure Pork Supply Biosecurity Plan
- U.S. SHIP OSA confers certification

**Step 3. Maintenance of Certification**

- Meet or exceed the requirements for the U.S. SHIP certification(s) held

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[www.aphis.usda.gov/livestock-poultry-disease/swine/us-ship](http://www.aphis.usda.gov/livestock-poultry-disease/swine/us-ship)

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**Questions**

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**2P OR NOT 2P? MICTURITION DISORDERS**  
**Joe Bartges, DVM, PhD, DACVIM (internal medicine, nutrition), ACVNU (founding member)**  
**Bulldog Veterinary Medicine Professor**  
**The University of Georgia**  
[jbartges@uga.edu](mailto:jbartges@uga.edu)

**MICTURITION**

Micturition involves a coordinated effort between the bladder being compliant and the urethral tone being increased (storage) and urinary bladder detrusor contraction with relaxation of the urethra (voiding). The urinary bladder is composed of smooth muscle (detrusor muscle) and is innervated by sympathetic nervous system (hypogastric nerve, beta-receptors) and parasympathetic nervous system (pelvic nerve) while the urethra is composed of smooth muscle proximally with innervation by the sympathetic nervous system (hypogastric nerve, alpha-receptors) and skeletal muscle distally with innervation by the pudendal nerve. The sympathetic nervous system are adrenergic nerves using norepinephrine as the neurotransmitter and alpha- or beta-adrenergic receptors, the parasympathetic nervous system are cholinergic nerves using acetylcholine as the neurotransmitter with muscarinic cholinergic receptors, and the somatic nervous system are cholinergic nerves using acetylcholine as the neurotransmitter with nicotinic cholinergic receptors. A good method to understand what types of pharmacological therapy are used to treat disorders of micturition is (1) parasympathetic promotes peeing and (2) sympathetic stimulates storage.

Disorders of micturition occur when there is disruption in the normal micturition process. There are several ways of classifying these disorders: storage versus voiding disorders, disorders occurring when the urinary bladder is full versus empty, and neurogenic versus myogenic versus anatomic. It is important to establish status of urinary bladder contractile force and patency of urethral outlet, determine whether disorder is neurogenic or myogenic, and determine underlying etiology or contributing factors. Signalment may help as certain conditions occur more commonly in dogs than in cats (e.g. urinary incontinence occurs more commonly in dogs while idiopathic cystitis occurs more commonly in cats) and vice versa and certain conditions occur more commonly with aging (e.g. ectopic ureter occurs more commonly in young dogs while lumbosacral disease and urinary incontinence occurs more commonly in older dogs). Reproductive status is also important (e.g. estrogen responsive urinary incontinence occurs in spayed female dogs). Historical information to gather include whether a prior neurologic disease has been diagnosed, a description of urination and water intake, and any additional abnormal behaviors or changes. In addition to a physical examination, a thorough neurologic examination should be performed. Part of the physical examination should include examination of the external genitalia as well as a rectal examination evaluating the prostate (in male dogs) and intra-pelvic urethra; these can be performed in most unsedated dogs; however, cats require sedation to perform. Dogs may be walked outside to observe voiding and to assess post-voiding urinary bladder volume. Additional diagnostic testing is tailored to the patient, such as CBC, biochemical analysis, imaging studies, etc.; however, a urinalysis and possible urine culture should be performed in all patients with micturition disorders. It is also possible, but not commonly available, to perform functional testing of the lower urinary tract using urodynamics (cystometry and urethral pressure profilometry).

**Disorders Associated with Urine Retention**

Bladder atony may occur due to neurogenic or myogenic causes such as an "upper motor neuron bladder associated with intervertebral disc disease or due to bladder overdistention due to urethral obstruction resulting in over-stretching of the detrusor muscle and disruption of the tight junctions between myocytes. The dog or cat may not posture to urinate with a distended bladder if sensory pathways are disrupted. The treatment is to stimulate bladder contraction and to manage the over-distended bladder. Placement of a urinary catheter or intermittent urinary catheterization to prevent urinary bladder distention will help to re-establish tight junctions. Because the urinary bladder is primarily controlled by the parasympathetic nervous system, a parasympathomimetic drug, such as bethanechol, may be used to stimulate detrusor contraction. In humans with diabetic autonomic neuropathy that is characterized by gastric paresis and urinary bladder paresis, administration of metoclopramide stimulates gastric and urinary bladder emptying; therefore, this may be tried in patients who do not tolerate bethanechol or if it is not available. In situations of non-reversible urinary bladder distention and detrusor atony, a cystostomy tube may be placed.

Increased urinary outflow resistance or obstruction results in increased urine retention. This increase in outflow resistance may be due to mechanical reasons, such as uroliths or cancer, or due to functional reasons, such

reflex dyssynergia or urethral spasm. Often the dog or cat will posture to urinate but cannot void or will void only small amounts of urine. Pharmacologic management involves relaxation of the urethra using a sympatholytic agent, such as phenoxybenzamine, prazosin, acepromazine, or tamsulosin; to relax skeletal muscle of the distal urethra, diazepam, clonazepam, or dantrolene may be tried. If the outflow obstruction does respond to pharmacological therapy, then other therapy may be tried. A permanent urinary catheter may be placed such as Foley inserted transurethral or a cystostomy catheter or a urethral stent may be placed. If the urinary bladder is over-distended, then it should be managed as well.

A permanent urethral catheter or a cystostomy catheter is associated with a high risk of bacterial UTI. Keeping the urinary bladder as much as possible during the day is important. A 1:100 diluted solution of chlorhexidine (chlorhexidine is a 2% solution; therefore, diluting it 1:100 results in a 0.02% solution) may be infused into the urinary bladder after emptying it of urine. Infuse 15 to 30 ml and remove after 10-15 minutes leaving 5 to 10 ml. This is done every time the urinary bladder is emptied. A urethral stent composed of self-expanding Nitinol may be placed using fluoroscopic, ultrasonographic, or Cystoscopic guidance; usually fluoroscopic guidance is used. A contrast cystourethrogram is performed first for measurement to select an appropriately sized stent. A stent that is sized approximately 10-20% greater than the widest area of the urea is chosen with a centimeter at the cranial and caudal aspects extending beyond the diseased area of the urethra.

Reflex dyssynergia is a type of urinary outflow problem where urination begins normally; however, the urethra contracts before the urinary bladder is empty resulting in urine retention and continued passing of small amounts or drips of urine. It occurs more commonly in male than in female dogs and may be due to prostatic disease, central neurologic disease above the 2nd lumbar area of the spinal cord, or idiopathic. The dog postures normally, initiates a good stream, but the stream stops while the dog continues to posture attempting to void. Often contracture of the abdominal musculature occurs to void more urine. Treatment involves urethral relaxation using a sympatholytic agent with or without a skeletal muscle relaxant; a parasymphomimetic drug may administered to stimulate detrusor contraction.

### **Diseases Associated with Urine Leakage**

Urine leakage may occur with bladder overactivity due to hyperexcitability of the storage phase resulting in inability for adequate bladder filling. Bladder overactivity is due to hyperexcitability of the detrusor muscle during the storage phase of micturition. This results in an inability for adequate urinary bladder filling due to a sense of urgency. Clinical signs include increased frequency of urination, pollakiuria, and periuria. Often urethral irritation or urethral spasm is present. Some causes of bladder overactivity include bacterial cystitis, Urocystolithiasis, chemical irritation (e.g. cyclophosphamide-induced sterile cystitis), and feline idiopathic cystitis. Treatment involves decreasing hyperactivity of the detrusor muscle using a parasympatholytic agent such as propantheline bromide, oxybutynin, or tolterodine. Other options include antispasmodic agents such as flavoxate and tricyclic antidepressants (e.g. imipramine and amitriptyline), which may help with refractory urge incontinence by increasing urine storage.

A more common cause of urine leakage occurs with decreased urethral outlet resistance, which may be neurogenic or myogenic in nature. The most common cause of urinary incontinence in dogs is urethral sphincter mechanism incompetency especially in females. In cats and male dogs, search for other causes. In cats, the most common cause of urinary incontinence is spinal disease and in male dogs the most common causes are prostatic disease and lumbosacral disease. Patients are typically continent when awake but leak urine particularly small puddles when relaxed or asleep. Treatment is directed as increasing the smooth muscle of the proximal urethra (internal urethral sphincter) using a sympathomimetic drug (e.g. phenylpropanolamine or pseudoephedrine) or an estrogen in female or testosterone in male dogs. Estrogens increase tone of the internal urethral sphincter by inducing increased sympathetic receptors (alpha adrenergic receptors) and increasing sensitivity of the alpha receptors to the adrenergic neurotransmitter, norepinephrine. The mechanism of response to testosterone in castrated male dogs is unknown. In female dogs, response to sympathomimetic or estrogenic drugs is reported to be 85-90% while in male dogs, response to androgenic drugs is reported to be 50%. Gonadotrophic releasing hormone analogs (GnRH; e.g. leuporelin) has been used in female dogs with urinary incontinence. The proposed mechanism of action is that in ovariectomized dogs there is chronically unsuppressed follicle stimulating hormone (FSH) and luteinizing hormone (LH) release due to lack of negative feedback. GnRH administration reduce FSH and LH over time and it was found to result in urinary continence or improved incontinence in 12 of 13 dogs and 19 of 23 dogs in 2 studies. In dogs that have medically unresponsive urinary incontinence, always culture the urine as a

bacterial urinary tract infection may result in urinary incontinence even when other signs are absent and urinalysis reveals an inactive sediment. In dogs who have medically unresponsive urinary incontinence and negative bacterial urine culture, options include surgical procedures (e.g. culposuspension), urethral bulking, and placement of a hydraulic urethral occluder. Surgical procedures result in continence in 5-75% of dogs but have a high incidence of complications including urethral obstruction. Urethral bulking involves injecting a bulking agent submucosally in the area of the urinary bladder neck or internal urethral sphincter. Currently, there is only one veterinary urethral bulking agent available in the United States, an insoluble crosslinked collagen product; in Europe a crosslinked gelatin is available. Over 80% of dogs achieve continence; however, in many dogs continence persists for approximately 1 year. Other bulking agents used in humans include calcium hydroxyapatite and polydimethylsiloxane. A hydraulic urethral occluder is a small cuff that is placed surgically around but not sutured to the proximal urethra that is attached to a metallic port located submucosally in the inguinal area by a tube. A special needle, Huber needle, is used to adjust the pressure in the cuff by injecting or removing sterile fluid. Approximately 90% of dogs achieve continence with placement of the occluder. Of the remaining 10%, many achieve continence with occluder adjustment; however, some dogs either never achieve continence or become obstructed due to the volume of fluid in the cuff or to fibrous tissue that forms around the cuff necessitating removal of the occluder.

Another cause of urinary incontinence is paradoxical incontinence, which occurs when there is an increase in outlet resistance either due to mechanical reasons (e.g. urethrolithiasis) or functional reasons (e.g. urethral spasm) resulting in urine retention and urinary bladder overdistention. Urine leaks when pressure in the urinary bladder exceeds the pressure causing the outflow obstruction as long as complete urethral obstruction is not present.

Micturition involves a coordinated effort between the bladder being compliant and the urethral tone being increased (storage) and urinary bladder detrusor contraction with relaxation of the urethra (voiding). The urinary bladder is composed of smooth muscle (detrusor muscle) and is innervated by sympathetic nervous system (hypogastric nerve, beta-receptors) and parasympathetic nervous system (pelvic nerve) while the urethra is composed of smooth muscle proximally with innervation by the sympathetic nervous system (hypogastric nerve, alpha-receptors) and skeletal muscle distally with innervation by the pudendal nerve. The sympathetic nervous system are adrenergic nerves using norepinephrine as the neurotransmitter and alpha- or beta-adrenergic receptors, the parasympathetic nervous system are cholinergic nerves using acetylcholine as the neurotransmitter with muscarinic cholinergic receptors, and the somatic nervous system are cholinergic nerves using acetylcholine as the neurotransmitter with nicotinic cholinergic receptors. A good method to understand what types of pharmacological therapy are used to treat disorders of micturition is (1) parasympathetic promotes peeing and (2) sympathetic stimulates storage.

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Urine leakage may occur with bladder overactivity due to hyperexcitability of the storage phase resulting in inability for adequate bladder filling. Bladder overactivity is due to hyperexcitability of the detrusor muscle during the storage phase of micturition. This results in an inability for adequate urinary bladder filling due to a sense of urgency. Clinical signs include increased frequency of urination, pollakiuria, and periuria. Often urethral irritation or urethral spasm is present. Some causes of bladder overactivity include bacterial cystitis, Urocystolithiasis, chemical irritation (e.g. cyclophosphamide-induced sterile cystitis), and feline idiopathic cystitis. Treatment involves decreasing hyperactivity of the detrusor muscle using a parasympatholytic agent such as propantheline bromide, oxybutynin, or tolterodine. Other options include antispasmodic agents such as flavoxate and tricyclic antidepressants (e.g. imipramine and amitriptyline), which may help with refractory urge incontinence by increasing urine storage.

A more common cause of urine leakage occurs with decreased urethral outlet resistance, which may be neurogenic or myogenic in nature. The most common cause of urinary incontinence in dogs is urethral sphincter

mechanism incompetency especially in females. In cats and male dogs, search for other causes. In cats, the most common cause of urinary incontinence is spinal disease and in male dogs the most common causes are prostatic disease and lumbosacral disease. Patients are typically continent when awake but leak urine particularly small puddles when relaxed or asleep. Treatment is directed as increasing the smooth muscle of the proximal urethra (internal urethral sphincter) using a sympathomimetic drug (e.g. phenylpropanolamine or pseudoephedrine) or an estrogen in female or testosterone in male dogs. Estrogens increase tone of the internal urethral sphincter by inducing increased sympathetic receptors (alpha adrenergic receptors) and increasing sensitivity of the alpha receptors to the adrenergic neurotransmitter, norepinephrine. The mechanism of response to testosterone in castrated male dogs is unknown. In female dogs, response to sympathomimetic or estrogenic drugs is reported to be 85-90% while in male dogs, response to androgenic drugs is reported to be 50%. Gonadotrophic releasing hormone analogs (GnRH; e.g. leuporelin) has been used in female dogs with urinary incontinence. The proposed mechanism of action is that in ovariectomized dogs there is chronically unsuppressed follicle stimulating hormone (FSH) and luteinizing hormone (LH) release due to lack of negative feedback. GnRH administration reduce FSH and LH over time and it was found to result in urinary continence or improved incontinence in 12 of 13 dogs and 19 of 23 dogs in 2 studies. In dogs that have medically unresponsive urinary incontinence, always culture the urine as a bacterial urinary tract infection may result in urinary incontinence even when other signs are absent and urinalysis reveals an inactive sediment. In dogs who have medically unresponsive urinary incontinence and negative bacterial urine culture, options include surgical procedures (e.g. culposuspension), urethral bulking, and placement of a hydraulic urethral occluder. Surgical procedures result in continence in 5-75% of dogs but have a high incidence of complications including urethral obstruction. Urethral bulking involves injecting a bulking agent submucosally in the area of the urinary bladder neck or internal urethral sphincter. Currently, there is only one veterinary urethral bulking agent available in the United States, an insoluble crosslinked collagen product; in Europe a crosslinked gelatin is available. Over 80% of dogs achieve continence; however, in many dogs continence persists for approximately 1 year. Other bulking agents used in humans include calcium hydroxyapatite and polydimethylsiloxane. A hydraulic urethral occluder is a small cuff that is placed surgically around but not sutured to the proximal urethral that is attached to a metallic port located submucosally in the inguinal area by a tube. A special needle, Huber needle, is used to adjust the pressure in the cuff by injecting or removing sterile fluid. Approximately 90% of dogs achieve continence with placement of the occluder. Of the remaining 10%, many achieve continence with occluder adjustment; however, some dogs either never achieve continence or become obstructed due to the volume of fluid in the cuff or to fibrous tissue that forms around the cuff necessitating removal of the occluder.

Another cause of urinary incontinence is paradoxical incontinence, which occurs when there is an increase in outlet resistance either due to mechanical reasons (e.g. urethrolithiasis) or functional reasons (e.g. urethral spasm) resulting in urine retention and urinary bladder overdistention. Urine leaks when pressure in the urinary bladder exceeds the pressure causing the outflow obstruction as long as complete urethral obstruction is not present.

TABLE. Drugs used to manage dogs and cats with micturition disorders.

Agent	Mechanism of action	Recommended dosage	Adverse effects
Agents used to increase urinary bladder contractility			
Bethanechol	Parasympathomimetic; direct cholinergic activity	D: 5-25 mg PO q8h C: 1.25-7.5 mg PO q8h	Nausea, vomiting, salivation
Metoclopramide	Prokinetic; sensitizes to acetylcholine	D, C: 0.2-0.5 mg/kg PO q8h	Behavior changes
Agents used to decrease urinary bladder contractility			
Propantheline	Parasympatholytic; acetylcholine blockade	D: 7.5-30 mg PO q8h C: 5-7.5 mg PO q8h or 7.5 mg PO q72h	Nausea, vomiting, constipation, sedation, increased ocular pressure
Oxybutynin	Parasympatholytic; antispasmodic; detrusor relaxation	D: 1.25-5 mg PO q8-12h C: 0.5-1.25 mg PO q8-12h	Nausea, vomiting, urine retention, diarrhea, sedation
Flavoxate	Direct smooth-muscle relaxant	D: 100-200 mg PO q6-8h	Weakness
Dicyclomine	Anti-muscarinic	D: 10 mg PO q6-8h	Nausea, vomiting, constipation, sedation, increased ocular pressure
Imipramine	Tricyclic antidepressant with anticholinergic, alpha-and beta-agonist effects, detrusor smooth muscle relaxation and urethral muscle contraction	D: 5-15 mg PO q12h C: 2.5-5 mg PO q12h	Seizures, tremors, tachycardia, hyperexcitability
Amitriptyline	Tricyclic anti-depressant	D: 2.2-4.4 mg/kg PO q12h C: 0.5-1 mg/kg PO q24h	Sedation, anticholinergic effects
Agents used to increase urethral resistance			
Estriol (Incurin)	Reproductive hormone	D: 1 mg PO q24h initially; followed by adjustment up or down	
DES	Reproductive hormone	D (females): 0.1-1 mg PO q24h for 5 days (approximately 0.02 mg/kg not to exceed 1 mg total) followed by 0.1-1 mg PO q7d	Signs of estrus, bone marrow suppression
Premarin	Reproductive hormone	D: 20 mcg/kg q24hr x 7-10d; then q1-3d	
Testosterone propionate	Reproductive hormone	D (males): 2.2 mg/kg SQ or IM q2-3d C (males): 5-10 mg IM as needed	Aggression, prostatic disease, perineal hernia
Testosterone cypionate		D (males): 2.2 mg/kg IM q30d or 200 mg IM q30 d	
Phenylpropanolamine	Alpha agonist; urethral smooth muscle contraction	D: 12.5-50 mg PO q8h; 1-2 mg/kg PO q8h C: 1.0-1.5 mg/kg PO q8h	Anxiety, cardiac arrhythmias, anorexia, hypertension
Ephedrine	Alpha agonist; urethral smooth muscle contraction	D: 1.2 mg/kg PO q8h or 5-15 mg PO q8h C: 2-4 mg/kg PO q6-12h or 2-4 mg PO q8h	Anxiety, cardiac arrhythmias, hypertension
Agents used to decrease urethral resistance			
Phenoxybenzamine	Alpha antagonist; urethral smooth muscle relaxation	D: 5-15 mg PO q12h C: 2.5-10 mg PO q24h D, C: 0.25 mg/kg PO q12h	Hypotension, tachycardia, vomiting, diarrhea, increased intraocular pressure
Prazosin	Alpha antagonist; urethral smooth muscle relaxation	D: 1 mg/15kg PO q12-24hr C: 0.25-0.5 mg PO q12-24h	Hypotension
Tamsulosin	Alpha antagonist, urethral smooth muscle relaxation	D: 0.001-0.1 mg/kg 0.02-0.3 mg/10kg C: 0.002 – 0.03 mg/kg	Hypotension
Doxazosin	Alpha antagonist, urethral smooth muscle relaxation	D: 0.1-1.0 mg/kg PO q24h	Hypotension
Terazosin	Alpha antagonist; urethral smooth muscle relaxation	D, C: 0.5-5 mg PO q12-24hr D: 0.1-1.0 mg/kg PO q24h	Hypotension
Fiduxosin	Alpha antagonist, urethral smooth muscle relaxation	D: 0.1-3.0 mg/kg PO q24h	Hypotension
Diazepam	Striated muscle relaxation; central nervous system depressive effect	D: 0.2 mg/kg PO q8h or 2-10 mg PO q8h C: 2.5-5 mg PO q8h or prn or 0.5 mg/kg IV	Sedation, paradoxical excitement
Dantrolene	Striated muscle relaxation; direct action	D: 3-15 mg/kg PO q24h divided or 0.5-1 mg/kg PO q8h C: 0.5-1 mg/kg PO q12h	Weakness, hepatotoxicity
Acepromazine	Urethral muscle relaxation by neuroleptic effect; alpha antagonism	D: 0.1-2 mg/kg PO q8-12h C: 0.1 mg/kg IV or 1.1-2.2 mg/kg PO q12h	Sedation, hypotension, seizures
Aminopromazine	Smooth muscle relaxation	D, C: 2.2 mg/kg PO q12h	

**WHAT FOODS THESE MORSELS BE? NUTRITIONAL FACTS AND FANTASIES**  
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Veterinarians, veterinary technicians, and the public are inundated with information, some accurate and some not, on pet nutrition. Put in “dog nutrition” or “cat nutrition” in Google, and you get over 10 million hits. Add to this, articles and books in print, advice from neighbors and store employees, and commercials on TV and in print, and the information is overwhelming. Discussing pet nutrition is sometimes akin to discussing religion or politics; people are passionate about their beliefs. There are many “fallacies and facts” that could be discussed; however, I will focus only on a few.

Despite advances in pet nutrition, one of the more popular ‘conspiracy theories’ is that pet food companies are poisoning pets. It makes no sense from a business perspective for a business to produce a product that would be detrimental to its consumers. Unfortunately, pet food toxicities and imbalances have and continue to make the news. Recalls for bacterial and aflatoxin contamination as well as vitamin-mineral imbalances such as thiamine deficiency and vitamin D excess exist, which heightens unease amongst pet owners. Distrust in veterinarians and veterinary health professionals results in owners acquiring information from other and often less knowledgeable sources. The perception is that veterinarians are loyal to larger companies because they make money on selling their food, are provided perks by these companies, and that nutritional education was provided by representatives of large companies. Unfortunately, some of this is not incorrect.

An adverse reaction to food is defined as a clinically abnormal response attributed to an ingested food substance and may be further categorized as immunologic or non-immunologic in nature. Food allergy is an immunologically mediated reaction to ingested food. This is different than food intolerance, which is a non-immunologically mediated adverse reaction including toxic reactions, pharmacological reactions, metabolic reactions, and idiosyncratic reactions.

### **Pet food regulations**

The number and variety of dog and cat foods in the market have expanded phenomenally in recent years. With an increased interest in labels on food for human consumption, pet owners are reading pet food labels more closely. An understanding of the information contained and not contained on a label is important to aid in selection of appropriate and nutritionally adequate diets for consumption by dogs and cats.

**Standards** – Pet food labeling is regulated at two levels. The federal regulations, enforced by the Food and Drug Administration’s (FDA) Center for Veterinary Medicine (CVM), establish standards applicable for all animal feeds: proper identification of product, net quantity statement, manufacturer’s address, and proper listing of ingredients. Some states also enforce their own labeling regulations. Many of these follow the model pet food regulations established by the Association of American Feed Control Officials (AAFCO). These regulations are more specific in nature, covering aspects of labeling such as the product name, the guaranteed analysis, the nutritional adequacy statement, feeding directions, and calorie statements. The Pet Food Institute (PFI) is a pet food industry association formed to provide a uniform industry voice. The PFI deals with regulations and issues affecting the industry at large. PFI is not a regulatory agency. The World Small Animal Veterinary Association (WSAVA) is NOT a regulatory agency. It provides guidelines related to dog and cat nutrition; however, diets are not required to be compliant with these guidelines.

**Label** – Pet food labels are divided into 2 parts: the principal display panel on the front and the information panel usually on the back and/or side of the bag or box.

*Principal display panel:* The principal display panel includes the product’s name (statement of identity), the species for which it is intended to be fed to, and the net weight of the product. It may also include a vignette.

*The information panel:* The information panel contains the pertinent nutritional information and the manufacturer or distributor’s information.

In the *ingredient list*, all of the ingredients must be listed in descending order according to preprocessing weight. Ingredients of equal amounts may be listed interchangeably. Most ingredient names are set by AAFCO. The ingredient list does not give information concerning the quality of the ingredients. Further down the ingredient list, the “common or usual” names become less common or usual to most consumers. The majority of ingredients with chemical-sounding names are, in fact, vitamins, minerals, or other nutrients. Other possible ingredients may include artificial colors, stabilizers, and preservatives. All should be either “generally recognized as safe (GRAS)” or approved food additives for their intended uses. One ingredient that has received a lot of negative press is the antioxidant ethoxyquin. Ethoxyquin has been reported to cause allergic reactions, skin problems, major organ system failures, cancer, and reproductive problems. In recent

studies, adverse effects were found to occur at very high doses, but not with doses commonly used in pet foods. Pet food companies have voluntarily lowered the amount of ethoxyquin in food or switched to other antioxidants.

*Guaranteed analysis* provides information regarding major components of the product expressed as percentages. A pet food label guarantees a minimum amount of crude protein, a minimum amount of crude fat, a maximum amount of crude fiber, and a maximum amount of water. Other information may be included such as maximum amount of sodium or minimum amount of taurine. The term “crude” refers to the specific method of testing the product, not the quality of the nutrient itself. Guarantees are declared on an “as fed” basis, that is, the amounts present in the product as it found in the can or bag. Coming soon, the guaranteed analysis will look more like a Nutrition Facts panel in human food due to the Pet Food Model Regulations.

The *nutritional adequacy statement* is included if the food is nutritionally complete and balanced and contains all of the required nutrients. The statement will include the words “complete and balanced”, the lifestage or lifestages for which the food is intended, and how the product was found to be adequate. Lifestages include “growth” (in dogs “growth for large and giant breeds” and “growth for non-large or giant breeds”, “pregnancy”, “lactation”, and “maintenance”. Some general-purpose foods may be used in all lifestages, while other foods may be used in only one lifestage (for example, adult dogs). The nutritional adequacy statement is one of the most important pieces of information on a pet food label. A “complete and balanced” pet food must be substantiated for nutritional adequacy by one of two means. The first method is for the pet food to contain ingredients formulated to provide levels of nutrients that meet an established profile. Presently, the AAFCO Dog or Cat Food Nutrient Profiles are used. Products substantiated by this method should include the words “(name of product) is formulated to meet the nutritional levels established by the AAFCO Dog/Cat Food Nutrient Profiles”. This means the product contains the proper amount of protein, calcium, and other recognized essential nutrients needed to meet the needs of the healthy animal. The recommendations of the National Research Council (NRC) were once used, but they are no longer considered valid for this purpose. The alternative means of substantiating nutritional adequacy is for the product to be tested following the AAFCO Feeding Trial Protocols. This means that the product, or “lead” member of a “family” of products, has been fed to dogs or cats under strict guidelines and found to provide proper nutrition. These products should bear the nutritional adequacy statement “animal feeding tests using AAFCO procedures substantiate that (name of product) provides complete and balanced nutrition”. Feeding trials are the best way to confirm the adequacy of a product because the food would actually have been fed to an animal prior to distribution and sale. A product that does not meet either of these methods must state that “the product is intended for intermittent or supplemental feeding only”. The only exception to this is for products conspicuously identified as a “snack” or “treat” which by common understanding aren’t usually fed exclusively.

### **Potential adverse food events**

Hazardous food components encompass dietary components that are present in the food. These may be components that should be present, but are present in an unbalanced manner, or components that should not be present. Nutrient imbalances may occur when there is a problem in the formulation or manufacture of a diet, or if the owner supplements a complete and balanced diet with an incomplete and unbalanced food or supplements. Examples of excesses include hypervitaminosis A (raw liver or cod liver oil) and hypervitaminosis D (recent food recall). Examples of toxicity associated with ingestion of foodstuffs include onion poisoning, which causes a Heinz body hemolytic anemia in cats, and chocolate toxicity, which causes vomiting, diarrhea, and central nervous system disease due to theobromine. Raisins and grapes have been associated with acute renal failure in dogs. Examples of deficiencies include generic foods that may be unbalanced, fat deficiency, and vitamin and trace element deficiencies. Pet foods contain many food additives from antioxidants to humectants in semi-moist food, to coloring agents. These are approved by the FDA for inclusion in pet foods and are similar to additives used in human foods. Occasionally, food may become contaminated. This may occur if the manufacturer uses contaminated foodstuffs or the food may become contaminated after production. Mycotoxins are a rare problem in pets; however, there have been sporadic reports of mycotoxin-containing foodstuffs being used in the manufacture of dog food resulting in disease and death. Pet foods may become contaminated if mold is allowed to grow. This should not occur in pet foods, but if the food becomes moist or if the fat becomes rancid, it may occur. Occasionally, food may become “spoiled” and bacterial contamination may occur. Such organisms as Salmonella, Campylobacter, and Botulism have been reported. Lastly, ingestion of animal tissues containing residues of toxic substances may result in disease. For example, if a cat eats a mouse that has been killed using a warfarin-like rodenticide, the cat may develop a hemorrhagic disease due to the vitamin-K-dependent coagulation factor inhibition.

Mechanical injuries. Food may sometimes contain something that causes mechanical injury to the animal or the animal may ingest such an item. An example is a dog that ingests a bone, which becomes lodged in the esophagus or a cat that ingests a needle with a string attached.

Poisonous plants and animals. It occurs occasionally \ in small animals. For example, ingestion of Easter Lilies results in renal failure in cats.

Metals and minerals. Lead and zinc toxicity may occur with ingestion.

Food associated illness and toxicity. Recognizing food-associated illness can be difficult as often cases present sporadically with no apparent connection. Recognizing clusters of cases geographically (e.g. regionally) or during the same time period (e.g. animals in same household) is important. Take a good diet history from the owners. Introduction of a new food or a new bag of food, poor palatability or acceptance of the food by the pet(s), and pets eating the same food whether in the same household or different households may provide clues to problems with diet. Keep in mind that animals may present with similar clinical signs and histories but consuming different diets and/or snacks/treats. Discuss cases with your colleagues as they may be having similar experiences that can support your concerns.

#### ***Reporting potential adverse reactions:***

Contact the manufacturer – they should be willing to listen and take information as well as answer questions as to whether other complaints have occurred

FDA: <http://www.fda.gov>

FDA – report a problem: <http://www.fda.gov/Safety/ReportaProblem/default.htm>

AVMA: <http://www.avma.org> – specifically, this link for reporting adverse events with drugs, vaccines, and pet food:

[http://www.avma.org/animal\\_health/reporting\\_adverse\\_events.asp](http://www.avma.org/animal_health/reporting_adverse_events.asp)

To report an adverse event associated with pet food (or other animal feed), please contact your state FDA's Consumer Complaint Coordinator(s). Contact information can be found on the FDA's Web site at

<http://www.fda.gov/opacom/backgrounders/complain.html>. When reporting, please include as much information as possible, including the specific product name, lot numbers, veterinarian's report and diagnosis, and any other pertinent information. It is important to gather as much information as possible and to save as much as possible. Document the product name, type of food, manufacturer/distributor information, and date code/best buy code. Keep a copy of the packaging if you can. If the owner has a copy of the purchase receipt, it helps. Retain samples of the food; keep at least 4 cans or pouches of canned or semi-moist food and 1 kg of dry food. Do not send all of the samples for analysis – keep or have the owner keep some. Have the owner document consumption of the food by pet(s) with as much detail as they can recall. Keep good records including signalment, clinical signs, and test results. If a pet dies, perform a necropsy or have a necropsy performed. Make sure to tell the diagnostic lab performing the necropsy of your suspicion of toxicity. Save tissue and fluid samples, if possible. Document communication with the manufacturer and with FDA/AVMA. If other pets may have been exposed, test them. Keep good records and samples of suspect food.

#### **DIET-ASSOCIATED AVIAN INFLUENZA**

Recently, concern has been raised about consumption of raw food diets that contained raw poultry and H5N1/highly pathogenic avian influenza virus. Domestic cats consuming raw diets appeared to be at risk. While H5N1 has been diagnosed in cats, most cases were associated with consuming wild birds or raw dairy products or owners bringing the virus home. Diets that contained H5N1 were not found consistently in the lots, only in individual bags suggesting contamination of the food rather than a manufacturing issue. All pet foods must meet the Food Safety Modernization Act, which has resulted in a substantial number of cases and recalls due to infectious food contamination.

#### **PET FOOD CLAIMS**

The belief that there is a large amount of research related to pet foods including therapeutic pet foods by pet foods companies is, sadly, erroneous. Life stage foods that have been through feeding trials have data as they are required to meet AAFCO feeding trial claims; however, remember that only the lead product of a family of diets must pass the feeding trial. Thus, the rest of the diets in the family of products may not have been subjected to a feeding trial even though the label nutritional adequacy statement states otherwise. The requirements for research proof is minimal. A pet food may claim a benefit for structure or function based on literature support but not actual research. A diet with a claim of clinically tested must have 1 test with a positive outcome. A diet with a clinically proven claim must have at least 2 tests with positive outcomes. A diet may carry an FDA regulated food claim if the FDA has approved prior to market. If a drug claim is made, then it must acquire FDA approval following drug testing protocols.

#### **NOTED PET FOOD RECALLS**

Melamine-cyanuric acid consumption was associated with thousands of renal failure and death in dogs. The source was wheat gluten which contained melamine and cyanuric acid as a means to increase the nitrogen content although not biologically available. This affected many pet food companies and products and resulted, in part, in growth of the grain-free pet food industry. In 2019 and several following years, hundreds to thousands of dogs became ill with several deaths occurring due to elevated vitamin D in diets made by Hill's Pet Nutrition. There were several recalls that occurred and the FDA concluded that Hill's response did not address the root cause of the issue as they failed to follow their own procedures.

#### **DIET-ASSOCIATED DCM**

In July 2018, the FDA issued a statement relating dilated cardiomyopathy (DCM) in dogs to consumption of certain diets that have pulse ingredients and potatoes as main ingredients. Pulse ingredients are a subset of legumes harvested as a dry crop with low concentrations of lipid. They are fine powders created from fractions of peas, lentils dry beans, and chickpeas, and made without the use of processing aids or chemical compounds. They are used in food and feed-grade products and are marketed as offering natural solutions to increase the nutritional value of foods without altering flavor, aroma and color properties, and they have been used as ingredients in dog food for their protein and fiber for over 20 years.

The FDA release stated:

“We are concerned about reports of canine heart disease, known as dilated cardiomyopathy (DCM), in dogs that ate certain pet foods containing peas, lentils, other legumes or potatoes as their main ingredients. These reports are highly unusual as they are occurring in breeds not typically genetically prone to the disease,” said Martine Hartogensis, D.V.M., deputy director of the FDA’s Center for Veterinary Medicine’s Office of Surveillance and Compliance. **“The FDA is investigating the potential link between DCM and these foods.** We encourage pet owners and veterinarians to report DCM cases in dogs who are not predisposed to the disease.” – FDA, July 2018

The media attention this received resulted in what could be described as widespread panic (with respect to Athens’ own rock band) and denouncing of all grain-free diets. The original concern was presumed to be DCM occurring secondary to low circulating taurine concentrations as had been found previously. This was, in part, based on the relationship of low circulating taurine with dilated cardiomyopathy in cats, and in part from the fact that pulses are generally high in lysine and low in methionine. The result of this speculation was an increased need for dietary taurine or its precursor methionine due to higher gastrointestinal fermentation of taurine and thus greater fecal excretion with higher dietary fiber intake. Whether this has any link to dietary pulses or inclusion of pulses in grain-free dog food has not been proven. In one 24-week study evaluating graded concentrations of soybean meal up to 17% (as-fed basis) in dog foods, nutrient status of dogs was unaffected; however, in another study, inclusion of more than 15% soybean meal (dry-matter basis) decreased crude protein digestibility. It is possible that some dog foods exceed this at levels (more than 40%) resulting in taurine and/or methionine deficiency; however, these high levels have not been investigated. As dogs often are fed a single diet for extended periods of time, consumption of a diet that is marginally replete or deficient in one or more nutrients due to formulation may result in clinical disease over time.

Keep in mind that nutrient profiles established by the Association of American Feed Control Officials (AAFCO) are above known minimal requirements often using purified diets as found in publications by the National Research Council (NRC), but still represent minimal nutritional requirements that pet food companies must meet in order a diet to be considered “complete and balanced” and “providing adequate nutrition when fed as the sole source of nutrition” to dogs or cats in one or more life stages. Some of the essential amino acid recommendations are, in fact, identical between AAFCO and NRC, which may be an issue as AAFCO nutrient profiles are designed to take into account nutrient loss with high heat processing. Also, feeding trials are relatively short when compared to the length of time a dog may consume a diet. For example, an adult dog feeding trial lasts 6 months and requires minimal evaluations. Furthermore, the lead product in a family line of products may undergo feed trial testing; however, the other products in the family as long as they are not substantially different from the lead product may carry a feeding trial nutritional adequacy claim but would not have actually been through an AAFCO feeding trial. Thus, an AAFCO feeding trial nutritional adequacy claim would not likely detect marginal deficiencies (or toxicities).

Dilated cardiomyopathy is a disease characterized by increased chamber diameter and possible arrhythmias as well as sudden death. Development appears to be slow and clinical signs may be non-existent during development, progressing to lethargy, anorexia, respiratory effort, cyanosis, and syncope, and possibly congestive failure (ascites, pleural effusion, or pulmonary edema) and death, which may be the only clinical sign. There is a predisposition in certain breeds, primarily larger breeds of dogs, and there are known genetic mutations in some dog breeds. Doberman pinschers, Boxers, Great Danes, Newfoundlands, Irish Wolfhounds, English and American Cocker Spaniels, Golden Retrievers, and Portuguese Water Dogs have a high prevalence; however, many other breeds are found to have genetic risk for DCM. When dogs who are not known to be genetically predisposed are diagnosed then diet and physiology or other factors are thought to be associated with the disease.

The first link between taurine deficiency and DCM was demonstrated in cats, which was shown to be reversible with supplementation. In dogs, DCM diagnoses related to low whole blood taurine concentrations have been reported in Cocker Spaniels, Dalmatians, Boxers, Newfoundlands, Portuguese Water Dogs, English Setters, Alaskan Malamutes, and Scottish Terriers. Supplementation with taurine improved cardiac function. Interestingly, when compared with cats, dogs can endogenously synthesis taurine from methionine and cysteine.

These studies do not establish that decreased taurine intake is the mechanism for development of DCM. Dietary supply of precursor AAs necessary for taurine synthesis (i.e., methionine and cysteine), metabolic intermediates, and cofactors (such as methyl donors) cannot be ruled out as factors that contribute to the susceptibility of dogs to developing genetic and diet-related DCM. When DCM is diet-related, the formulation and the provision of all nutrients, including indispensable AAs, to facilitate optimum health and wellbeing of dogs should be considered.

The FDA report suggests canine DCM in dogs that are not genetically predisposed is related to consumption of legumes; however, this is at present unproven. Dogs have no minimum or maximum requirement for ingredients and ingredients provide nutrients, which do have such requirements. Thus, animals have nutrient requirements and not ingredient requirements. In diets that have nutrient deficits, imbalances, or exceed maximums, the final nutrient composition of the diet, not the ingredients, should be critiqued. In addition, animal nutritionists should consider that the nutrient concentration of ingredients can vary, nutrient availability is not 100%, and diets formulated to marginally meet requirements could actually be deficient.

Carnitine is required for sufficient energy production in cardiac muscle; thus, it is not surprising that carnitine deficiency is associated with DCM. In 1991, a family of Boxers diagnosed with DCM were also diagnosed with carnitine deficiency. However, carnitine deficiency as a causative factor in the development of DCM or a consequence of cardiac malfunction remains as a subject of debate. Despite the interest in this metabolite, little progress has been made on determining the effect of carnitine supplementation on alleviating risk of DCM. However, both taurine and carnitine are often supplemented in suprphysiological concentrations once DCM is diagnosed. This practice is supported by positive clinical outcomes, albeit without comparison groups. Concentrations of carnitine in the plasma are relatively insensitive to dietary carnitine, and more invasive techniques (biopsies) are required to determine the concentration of carnitine in muscle tissue. The invasive nature of testing carnitine status is likely the reason why carnitine is rarely explored when investigating possible causes of canine DCM.

### **What evidence is there for diet-associated dilated cardiomyopathy?**

Several recent papers, both original research and reviews, likewise highlight the unknowns surrounding grain-free diets (typically legume or pulse-based, but sometimes also with “exotic” ingredients such as kangaroo, bison, or wild boar) and DCM.

In one retrospective study of 91 dogs, 48 dogs were included while 43 were excluded. These dogs were diagnosed with DCM and had a known history. Twelve of the included dogs were eating grain based diets (2 were of ‘unusual breeds’) at the time of DCM diagnosis, and 36 were eating grain free diets (5 were of ‘unusual breeds’). Of the grain free dogs, 14 were eating one specific grain free diet, and 22 were eating other grain free diets. Foods from large pet food companies were included. The number of dogs eating each grain based diet brand ranged from 1 to 3. The number of dogs eating each grain free diet brand ranged from 1 to 5 for other grain free diets with 14 dogs eating one specific grain free diet. A diet change from grain free to grain based diets manufactured by a major brand pet food company with veterinary nutritionists on staff was consistently recommended for all dogs in the grain free group after June 2017 but was not recommended for the grain based group and inconsistently recommended for the grain free group before this time. Two dogs in the GF group were switched to a major brand food that was grain free. All but one dog in the grain free group received supplementation with taurine (30 mg/kg twice daily) after diagnosis and diet change, even if whole blood taurine concentrations were within or above the reference range. Interestingly, only 2 dogs had low blood taurine concentrations and they were consuming grain based diets. Two dogs switched from that diet to other grain free diets showed improvement in their DCM. This suggests that grain-free composition per se may not be the root cause of DCM.

Another published case series of 24 Golden Retrievers with DCM and known diet histories were evaluated, and an association between grain-free diets and DCM was suggested. Client-owned golden retrievers with documented blood taurine deficiency and DCM met inclusion criteria and were enrolled in a multicenter, prospective, observational study to evaluate dietary factors that may contribute to this condition as well as describe their clinical response to treatment. Echocardiography was performed by a board-certified cardiologist. A total of 24 client-owned golden retrievers diagnosed with taurine deficiency and DCM were enrolled in the clinical portion of this study. Diets consumed by these dogs included 9 grain-free brands. Of interest, 23 of 24 dogs with known diet amount consumption were consuming less than estimated maintenance energy requirements. At baseline, 11/24 dogs were diagnosed with congestive heart failure and prescribed diuretic therapy (furosemide). Nine out of these 11 dogs had resolution of congestion at time of follow-up. Of these nine dogs, five had successful discontinuation of furosemide therapy, and four had a reduction of their maintenance furosemide dose by 50–56%. In the two remaining dogs, one dog remained in congestive heart failure and the other was lost to follow-up. The remaining 13 dogs were considered to have occult DCM and no diuresis was prescribed. At baseline, 24 dogs were prescribed taurine supplementation at a median dose of 1500mg orally twice per day (daily dose range of 2000-4500mg) and thirteen dogs were additionally prescribed L-carnitine supplementation at a median dose of 2000mg per day (range 500- 6000mg). Additional medications included pimobendan (Boehringer Ingelheim Vetmedica, Inc., Duluth, GA, USA) (n = 13), enalapril (n = 7), benazepril (n = 4), spironolactone (n = 6), and diltiazem (n = 2). Follow-up data was available in 16 dogs. One dog was successfully removed from all cardiac medications and remained on only taurine and L-carnitine supplementation. In addition, taurine and L-carnitine supplements were successfully discontinued in four dogs based upon echocardiographic resolution of DCM. A control group of healthy Golden Retrievers were also evaluated; however, none underwent echocardiography. Mean whole blood taurine concentration in samples obtained from 52 apparently healthy golden retrievers (mean age 5.1 +/- 2.8; mean weight 27.7 +/- 4.6 kg) was 279.1 +/- 51.5 (min 164 nmol/ml, max 382

nmol/ml). Forty-three of 52 had complete diet histories available. Twelve of 52 dogs had whole blood taurine concentrations of 200–250 nmol/mL, and 4/52 dogs (7.7%) had whole blood taurine concentrations < 200 nmol/mL. Interestingly, all 4 dogs with whole blood taurine concentrations < 200 nmol/mL, and 10 dogs with whole blood taurine concentrations between 200–250 nmol/ml in which complete diet histories were available, were on diets that were legume-rich, and/or were grain-free. None had DCM.

### **So what information is provided by the FDA report of June 2019.**

In July 2018, the FDA announced that it had begun investigating reports of canine dilated cardiomyopathy (DCM) in dogs eating certain pet foods, many labeled as "grain-free," which contained a high proportion of peas, lentils, other legume seeds (pulses), and/or potatoes in various forms (whole, flour, protein, etc.) as main ingredients (listed within the first 10 ingredients in the ingredient list, before vitamins and minerals). Many of these case reports included breeds of dogs not previously known to have a genetic predisposition to the disease. The FDA's Center for Veterinary Medicine (CVM) and the Veterinary Laboratory Investigation and Response Network (Vet-LIRN), a collaboration of government and veterinary diagnostic laboratories, continue to investigate this potential association. Based on the data collected and analyzed thus far, the agency believes that the potential association between diet and DCM in dogs is a complex scientific issue that may involve multiple factors.

Between January 1, 2014 and April 30, 2019, the FDA received 524 reports of DCM (515 canine reports, 9 feline reports). Approximately 222 of these were reported between December 1, 2018 and April 30, 2019 (219 canine reports, 3 feline reports). Some of these reports involved more than one affected animal from the same household. The breakdown of reported illnesses below reflects the number of individual animals affected. The American Veterinary Medical Association estimates that there are 77 million pet dogs in the United States. Most dogs in the U.S. have been eating pet food without apparently developing DCM. It's not known how commonly dogs develop DCM, but the increase in reports to FDA signal a potential increase in cases of DCM in dogs that are not genetically predisposed.

Reviews of the canine reports shows that most reports were for dry dog food formulations, but raw food, semi-moist food, and wet foods were also represented albeit uncommonly despite many being grain free. The FDA reported on the 16 most frequently fed brands of food to dogs; however, their data is a mix of brands and companies. Six of the largest pet food companies in the world had diets reported in this report.

In November 2020, a retrospective study was published in the Journal of Veterinary Internal Medicine. In this study, records were evaluated between January 1, 2014, and September 30, 2018, at an academic referral hospital. Dogs had to be newly diagnosed with DCM based on a fractional shortening of < 25%, normalized left ventricular internal diameter in diastole > 1.8, and normalized left ventricular internal diameter in systole > 1.2. The dog's main diet (ie, the diet providing the majority of the dog's calories) at the time of diagnosis was recorded, as was whether or not the diet was changed and each dog's final main diet. For the purposes of the study, diets were classified as traditional when they were grain-inclusive extruded diets that did not contain peas, lentils, or potatoes as main ingredients (ie, top 10 ingredients on the ingredient list), and the manufacturer of which met the World Small Animal Veterinary Association (WSAVA) Global Nutrition Committee recommendations. Nontraditional extruded diets were defined as those that were grain-free, containing nontraditional ingredients (eg, peas, lentils) as main ingredients, or whose manufacturer did not meet the WSAVA Global Nutrition Committee recommendations. Seventy-one dogs were included in the final analysis. Fifteen of the dogs were eating a traditional diet and 56 were eating a non-traditional diet. There were no differences in echocardiographic parameters between dogs eating traditional diets and dogs eating non-traditional diets. Fifty of 71 dogs had congestive heart failure; 7 of 15 eating traditional food and 43 of 56 eating non-traditional food. Dogs were treated with various medications and 30 dogs received taurine supplementation while 3 dogs received carnitine supplementation. For the 56 dogs in the non-traditional diet group, 31 had their diets changed whereas 25 did not. For the 15 dogs in the traditional diet group, 6 had their diets changed whereas 9 did not. Forty-five of 71 dogs (63%) had follow-up echocardiographic information at least 90 days after diagnosis. Diet group and presence of congestive heart failure were associated with a significant change in normalized left ventricular internal diameter in systole; other echocardiographic parameters were not different between diet groups whether diet was changed or not. At time of data analysis, 11 dogs were alive; 10/31 dogs in the nontraditional diet group who had diets changed, 0/25 in the nontraditional diet group that did not have their diets changed, and 1/15 dogs in the traditional diet group. Of the 60 dogs that were no longer alive, 21 dogs died suddenly, 38 dogs were euthanized due to worsening congestive heart failure or other causes, and 1 dog died of unknown cause(s). In all dogs and in dogs with congestive heart failure there was a longer survival time in the non-traditional diet group that had a diet change when compared with those in the non-traditional diet group that did not have a diet change; survival curves were identical. There was no difference, though, between dogs eating traditional diets and the other 2 groups. This study does not provide much supportive evidence concerning "non-traditional diets" and DCM. Survival and response to treatment including diet change were not found except in those dogs who were eating a non-traditional diet and had a diet change. Unfortunately, diet information is not provided and so it is difficult to draw other conclusions.

A retrospective study had also been published on February 1, 2021. In this study, medical records from January 1, 2015 to July 10, 2019 at the North Carolina State University College of Veterinary Medicine were retrospectively evaluated for a diagnosis of canine DCM and concurrent CHF. A diagnosis of DCM was made echocardiographically based on three criteria: fractional shortening (FS)  $\leq$  25%, normalized left ventricular internal diastolic diameter (LVIDdN)  $>$  1.63, and normalized left ventricular internal systolic diameter (LVIDsN)  $>$  0.92 obtained via M-mode from the right parasternal short-axis view. A diagnosis of CHF was made based on clinical signs, thoracic radiography, and response to diuretic therapy. Dogs were included in the study if their diet history was known or could be obtained retroactively via communication with the owner. A total of 107 dogs were diagnosed with DCM and concurrent CHF during the study period. Of these, 67 dogs met the inclusion criteria with 43 dogs within the pGF group and 24 dogs within the GI group. Of the 67 dogs in the study, 33 of 43 in the pGF diet group and 23 of 24 dogs in the GI diet group are of breeds predisposed to DCM. Of the dogs in the pGF group, the specific variety of GF diet and corresponding ingredients could be obtained for 41/43 dogs. Nine of the dogs were reported to have eaten multiple varieties of GF diets concurrently. In these cases, each of the reported diets was evaluated for a total of 54 specific diet varieties. One dog was fed a homecooked diet that consisted entirely of lentils and cooked eggs. Of the 40 dogs with a history of commercial GF diets for which variety was known, all of the diets (54/54) were of a kibble form and had at least one legume or legume product listed within the first five ingredients. Using the Cox proportional-hazards model, it was found that the effect of prior diet on survival was not statistically significant ( $P = 0.074$ ).

In 2020, a symposium was held at Kansas State University sponsored by the FDA. There were several presentations by the FDA, representatives of food companies, cardiologists, and other academicians. Pulse ingredients have been around for decades and the FDA stated “no clear evidence indicating that grain-free foods with pulse ingredients are inherently dangerous”. Further, the FDA acknowledged reports of non-hereditary DCM associated with dogs eating grain-containing diets. One study showed no increase in incidence from 2000 to 2019 with only a slight but not significant increase in small and mixed-breed dogs from 14 cardiology practices across the US. A study was also presented that showed that feeding grain-free diets was not associated with changes in taurine, carnitine, or amino acids in Labrador Retrievers. One presentation suggested a possible link to infectious agents such as viruses in some dogs. Another study suggested a possible link to subclinical anemia. The FDA concluded that DCM is a scientifically complex, multi-faceted disease, and it has a clear genetic component and other potential factors may contribute. The FDA feels that this is not a regulatory issue and so no recalls have occurred and further specific brand names will no longer be released.

### **So, what's the bottom line about diet-associated dilated cardiomyopathy?**

- There are no scientifically published data to show cause and effect of diet with dilated cardiomyopathy
- Taurine and carnitine deficiency have not been shown to be important
- The issue is that the FDA asked for cases of DCM in dogs eating a certain type of diet and so the data they generated is what they asked for – that is, “if you only look for what you want to see, you will only see what you wanted to look for.” They did not ask for ALL cases of DCM and diet histories and so their data are skewed and biased
- The same is true about publications to date which have
  - Not show a cause and effect
  - Dogs with DCM progress regardless of diet
  - Dogs who ate grain free diets that were switched still died; however, they lived longer than dogs with DCM who ate grain-based diets
- Subsequently, the FDA in 2022 stated they will no longer provide updates as there is not enough scientific evidence to substantiate the claim that this is a diet-induced or diet-associated disease

The association and strength of association of diet with DCM is weak. One possibility is that the essential amino acid requirements for dogs in AAFCO adult nutrient profiles are not much different than the NRC recommended requirements despite the fact that AAFCO recommendations are typically higher to account for losses in processing. Thus, foods meet or exceed AAFCO nutrient profiles and are complete and balanced; however, it may be the regulated profiles that are incorrect.

If an owner wishes to feed a grain-free diet, a serum NT-proBNP may be checked and monitored as this is a measure of cardiac stretch (dilation).

# COURSE SYLLABUS AND LEARNING MATERIAL

VPEG + UGA College of Veterinary Medicine | April 18, 2026

## Regulatory Compliance in an Entangled Age: Controlled Substance Inventory Management, Artificial Intelligence, and Georgia Regulatory Updates (2-hour LEAP CE)

UGA Center for Continuing Education and Hotel; 1197 South Lumpkin Street; Athens, GA 30602

1:40 PM to 3:25 PM LEAP CE Activity

**Instructor: Heather Lindell Tally, PharmD, PhD, DICVP**

### Detailed Program Agenda

## Regulatory Compliance in an Entangled Age: Controlled Substance Inventory Management, Artificial Intelligence, and Georgia Regulatory Updates (2-hour LEAP CE)

Agenda:

In this course, a review of references and resources available from both state and federal agencies is presented. Specific code and regulations are discussed including federal information and state information for Georgia. Controlled substance recordkeeping practices in the veterinary setting are discussed with an emphasis on references and resources; inventory; transfer and disposal of controlled substances; and violations and penalties. An introduction to incorporating artificial intelligence into veterinary practice is detailed with an active learning exercise. Updates regarding Georgia's 2025 legislation related to veterinary telehealth and pet transfers are reviewed to complete the activity.

Objectives:

At the conclusion of this lecture the participant should be able to

- Utilize references and resources pertaining to controlled substances;
- Perform a proper controlled substance inventory;
- Perform a proper controlled substance transfer;
- Detail disposal options for controlled substances;
- Discuss controlled substance violations;
- Engage AI technology within a veterinary setting; and
- Recall 2025 Georgia legislation relating to veterinary telehealth and pet transfers.

Outline:

- |      |                                    |     |                                     |
|------|------------------------------------|-----|-------------------------------------|
| I.   | Review of references and resources | IV. | Violations, outcomes, and penalties |
|      | a. Federal                         | V.  | Georgia Legislation                 |
|      | b. State                           |     | a. 2025 new updates                 |
|      | c. Other                           |     | i. Veterinary telehealth            |
| II.  | Recordkeeping                      |     | ii. Pet transfers                   |
|      | a. Flow                            |     | b. Future legislation               |
|      | b. New updates                     |     |                                     |
| III. | Inventory                          |     |                                     |
|      | a. Controlled substances           |     |                                     |
|      | b. Elements                        |     |                                     |
|      | c. AI incorporation                |     |                                     |

## References and Resources

Having a list of readily available references and resources in your practice is helpful when you have a question. From looking up a drug dose in a particular species to looking up the requirements of a prescription in your state may be questions you need to answer. There are many drug dose formularies and you likely have one in your clinic. You may not have a list of regulatory references; therefore, a list is provided for you here:

Federal Controlled Substance Law

<https://ecfr.io/Title-21/Volume-8/Chapter-I>

Federal Controlled Substance Regulation

<https://ecfr.io/Title-21/Volume-9/Chapter-Ii>

Federal Drug Law

<https://www.fda.gov/RegulatoryInformation/LawsEnforcedbyFDA/FederalFoodDrugandCosmeticActFDCAAct/FDCAActChapterVDrugsandDevices/default.htm>

Federal Drug Regulation

<https://www.ecfr.gov/current/title-21>

## Recordkeeping & Inventory

Proper inventory management and recordkeeping are integral components of a secure drug management system. From ordering to dispensing, keeping track of your products can help you identify areas of concern, medication safety factors, and diversion risks. Keep in mind prescriptions are not for drug ordering purposes. Prescriptions are animal specific. To order a drug product for use in your clinic, you will use a purchase order or special DEA form in the case of CII substances. For controlled substances, the ordering process is to be a closed system. If you are the DEA registrant and your DEA registration number is being used to order controlled substances, you are ultimately responsible. A criminal charge may apply to person ordering and diverting controlled substances using your DEA registration number without your knowledge; however, you are not immune from receiving a civil charge. Keep track of what is going on in your practice.

A DEA Form 222 must be completed when ordering CII drugs. Indicate the number of lines used and cross out other unused lines to prevent anyone from altering the form. Single sheet DEA Form 222s are now used; therefore, it is important to make a copy for your records before it is sent to the seller. When the products come in it is extremely important to record the date and quantity received on the copy. Orders for CIII, IV & V drugs do not require use of a DEA Form 222. Many vendors are happy to help you fill out your form and many have guidance documents you can request. Vendors require that 222 forms be completed using exact terms or numbers that may be unique to their company. It is advisable to give them a call for directions the first time a CII is ordered from them. Invoices for CII items must be kept separate from other invoices. Invoices for CIII, IV or V items must either be filed separately or be marked with a red "C", one inch high in the lower right-hand corner of the invoice. All invoices for controlled substances must be readily retrievable.

DEA has created the Controlled Substance Ordering System (CSOS) allowing for secure electronic transmission of controlled substance orders without the supporting paper DEA Form 222. The adoption of CSOS standards is the only allowance for the electronic transmission of Schedule II controlled substance orders between controlled substance manufacturers, distributors, pharmacies, and other DEA authorized ordering entities. CSOS uses Public Key Infrastructure (PKI) technology, which requires CSOS users to obtain a CSOS digital certificate for electronic ordering. To participate in CSOS you must apply for a CSOS Digital Certificate as must your suppliers. For more information and online CSOS application visit: <https://www.deadiversion.usdoj.gov/drugreg/csos/csos.html> .

Note: Drug enforcement agencies receive copies of your invoices and order forms for controlled substances. Orders for excessive quantities or unusual items may result in a site inspection.

A centralized receiving log, with sections for each drug received, is advisable. Extensive documentation makes finding errors easier. From this centralized log you can sign out a product as it is used. Assigning a number to each bottle, vial, etc. is a good way to keep track of the usage. Keeping a perpetual inventory is advised. Within this inventory log for each product you will keep track of dispensations and administrations. Reconciliation of the inventory each day controlled substances are used is highly recommended. Catching errors sooner rather than later is much easier to justify. You are required to do a biennial inventory of your controlled substances. The biennial inventory includes ALL stocks on hand including those stocks separated for disposal. Some states require the biennial inventory during an odd numbered year. Biennial inventories are not an option. An initial inventory is required to be shown for each drug as well.

Electronic assistance with inventory management is becoming commonplace. When incorporating electronic assistance, consider trackability, reliability, regulatory compliance elements, storage capacity, and backup options. Artificial intelligence (AI) in tandem with electronic controls and human oversight is another tool for inventory management systems.

## **Violations and Penalties**

Federal Controlled Substance Control and Enforcement

<https://uscode.house.gov/view.xhtml?path=/prelim@title21/chapter13/subchapter1&edition=prelim>

Georgia Controlled Substance Crimes and Offenses

[GA CS Crimes and Offenses](#)

## **Georgia Legislation**

2025-2026 Legislative session

Veterinary TeleX

<https://www.legis.ga.gov/legislation/69961>

Pet Sales

<https://www.legis.ga.gov/legislation/70060>

## **Conclusion**

Having access to references and resources within your practice helps you find the answers to the questions you may have. Keeping up with changes may be hard to do in a busy practice. Laws, rules, policies, and practice applications are dynamically changing (e.g., teleX, pet sales). A good way to keep up is attending continuing education or webinars covering current topics and legislative updates. Proper inventory management and recordkeeping are important and mandatory. No one wants to find out they are missing controlled substances when they are being inspected by the DEA or GDNA. Keep on top of your inventory with effective controls addressing maintenance and disposal. Keep a perpetual inventory and tidy recordkeeping. You will be glad you did. Violations and penalties associated with noncompliance can be prevented.



# GOOD DOG VETERINARY CARE

Creating a Culture to Attract Top DVM Talent

# PRESENTATION OVERVIEW

- ABOUT US
- GROWING FROM 1 DVM TO 12 DVMS
- WORKING "IN" VS. "ON" THE BUSINESS
- BECOME "THAT" COMPANY
- ATTRACTING TALENT
- RETAINING TALENT
- Q & A



## DR. PATRICK SINGLETARY

- UGA CAES ('12) + UGA CVM ('16)
- Former President UGA CVM VBMA
- Former President OTS
- Former President AGR



# WHO WE ARE

**DR. PATRICK AND NATALIE SINGLETARY**  
**OWNERS + FOUNDERS GOOD DOG VETERINARY CARE**

## GOOD DOG VETERINARY CARE

- "All-Dog" Practice
  - First and only in GA
  - Breed specific care
- Advanced Veterinary Care
  - Advanced surgical procedures
  - Advanced diagnostics: abdominal ultrasound, echocardiograms, dental rads
- Mission: Be a Light in Veterinary Medicine + Be Exceptional Stewards of our Business

### USE YOUR TALENTS

Blessed by God to be given the knowledge and strength to persevere through vet school and grow and scale Good Dog Veterinary Care.



# SEEK MENTORS

**YOU ARE THE "LID" IN  
YOUR ORGANIZATION**

- Dave Ramsey
- Patrick Lencioni
- Dan Martell
- John Maxwell
- John Delony
- Brandon Dawson
- Natalie Dawson
- Jim Collins
- Ryan Deiss
- Patrick Bet-David

**MENTORS SHOULD BE  
FURTHER AHEAD OF YOU.  
WHAT HAVE THEY BUILT?**

## HOW DID WE DO IT?

- No over night success!
- Spiral growth + momentum
- 6 years = 6 chapters of business
- Strategic steps that have led us from dreaming to reality

# OUR GROWTH

**DR. PATRICK AND NATALIE SINGLETARY**  
**OWNERS + FOUNDERS GOOD DOG VETERINARY CARE**

## GOOD DOG VETERINARY CARE

### HOW IT STARTED: 2019

- 1 DVM
- 1 Location
- 1 Surgical Suite
- 3 Support Team Members
- 4 Exam Rooms
- 0 Student Externs

### HOW IT'S GOING: 2026

- 12 DVMs
- 3 Locations
- 4 Surgical Suites
- 50+ Support Team Members
- 20 Exam Rooms
- 30 Student Externs



**“UNLESS THE  
LORD DOES  
BUILD THE  
HOUSE, IN  
VAIN ITS  
BUILDERS  
STRIVE.”**

Psalm 127:1







# WHAT DO YOU WANT FROM OWNERSHIP?

Option #1: Work IN your business

Option #2: Work ON your business

Both are great choices. BUT. Be Intentional. Make a decision if you want to work in your business or grow your business. Don't be passive. Have a plan.

Communicating is key to building your DVM Team and setting expectations when attracting talent.

**WORKING  
"IN"  
VS.  
WORKING  
"ON"**

## **BE HONEST WITH WHAT YOU WANT**

To work "on" your business, you must be intentional with pursuing

STRATEGIC GROWTH to give you margin in your business. To get to work "on" your business you first must work "in" your business.

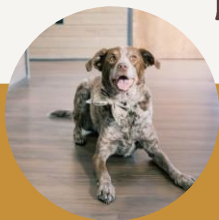


# OUR GROWTH TIMELINE

WORKING "IN" THE BUSINESS (2019-2022)  
WORKING "ON" THE BUSINESS (2023-  
PRESENT)



**2019**  
OPENING YEAR  
(WEST COBB)



**2020**  
GRIND YEAR



**2021**  
FIRST ASSOCIATE  
HIRED



**2022**  
1ST LOCATION  
EXPANDS



**2023**  
2ND LOCATION  
OPENS  
(SMYRNA)



**2024**  
3RD LOCATION  
OPENS (EAST COBB)



**2025**  
OPTIMIZATION  
AND CORE  
LEADERSHIP



**2026**  
PURSUING  
LOCATION #4

# STRATEGIC MOMENTS IN OUR GROWTH OVER THE LAST 6 YEARS

Momentum is a POWERFUL tool!



## 1ST ASSOCIATE

Hardest Hire

Once you hire your first associate, the momentum is there! Here's what this

looked like for us:

2019 to 2020 - 1 DVM

2021 - 2 DVMs

2022 - 4 DVMs

2023 - 7 DVMs

2024 - 10 DVMs

2025 - 12 DVMs



## 2ND + 3RD LOCATIONS

Scalability

Our second location was set up to run without us from day one. It took us 4 years to accomplish that with our first location. But... the second location gave us the momentum for a third location.

Two locations can be "lucky."

Three is strategic.



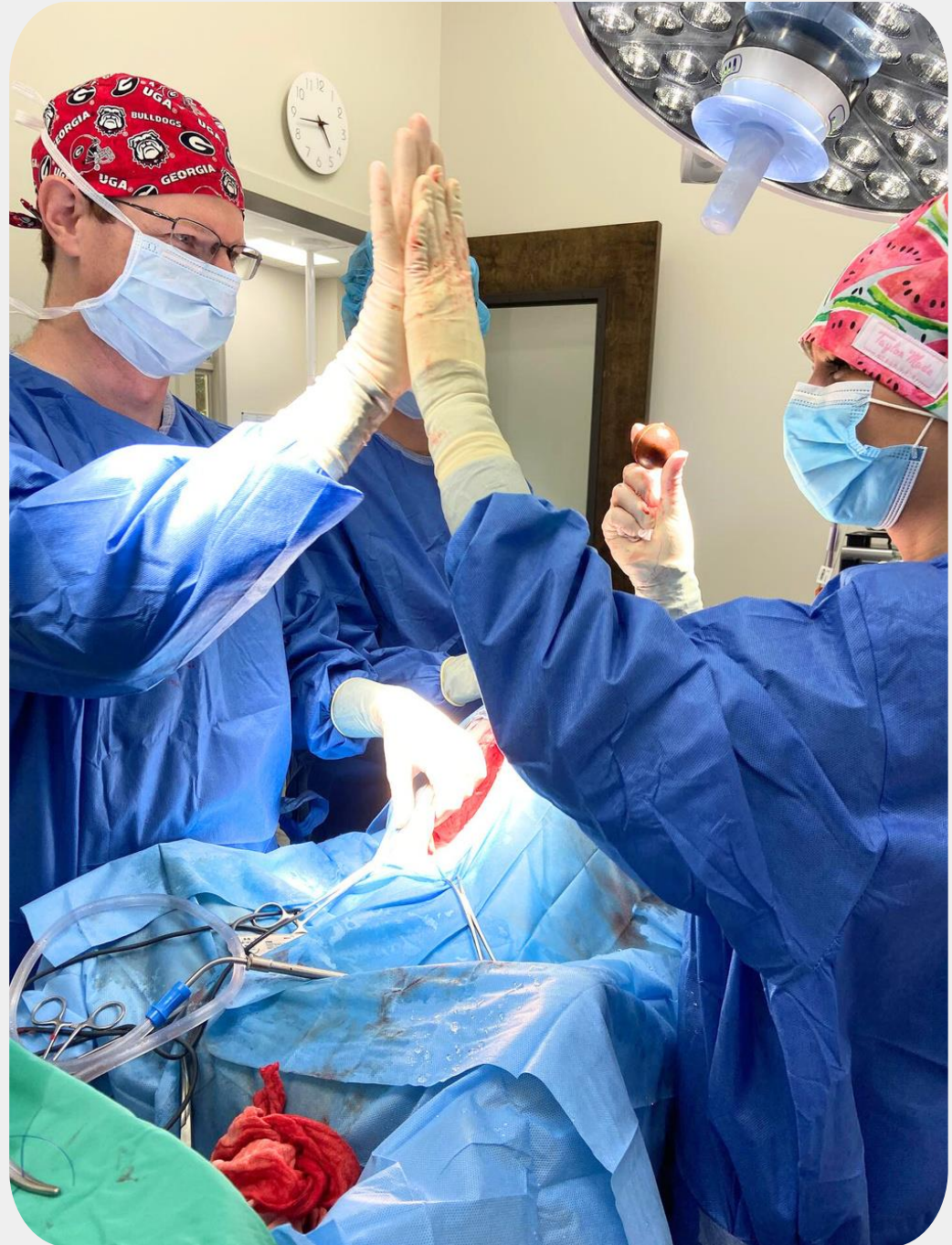
## HAVE A VISION

... and Make It Plain

We have all day strategic planning sessions every December for each of our 3 locations + our Company. We "have a vision and make it plain." The year doesn't happen to us. We make the year (and desired outcome happen). We are intentional with where we want to be and how to get there.

**“BECOME THE ORGANIZATION THAT THE PEOPLE YOU ARE LOOKING FOR ARE LOOKING FOR.”**

**-DAVID SALYERS,  
VP MARKETING  
CHICK-FIL-A**





**STAGE 1:  
BECOME THAT  
COMPANY**



**STAGE 2:  
IDENTIFY AND  
ATTRACT THE  
PEOPLE YOU ARE  
LOOKING FOR**



**STAGE 3:  
RETAIN  
TALENT**

## **3 STAGES**

“Become the organization that the people you are looking for are looking for.” - David Salyers



**MISSION,  
VISION, CORE  
VALUES**

**BRANDING**

**OPERATIONAL  
EXCELLENCE**

**STAGE 1: BECOME "THAT"  
COMPANY CURATE THE CULTURE**



# CURATE THE CULTURE

## MISSION, VISION, VALUES

### CREATE AND DEFINE

- Mission: Why do you exist?
- Vision: Where are you going?
- Values: What guides your work daily?

### MAKE THEM THE SOUL OF THE ORGANIZATION

- Use them! Tactical ways:
- In interviews
- Recited daily in team rounds
- Concrete way to give intentional praise
- Concrete way to coach team members



# CURATE CULTURE

## BRAND BUILDING



**GOOD DOG**

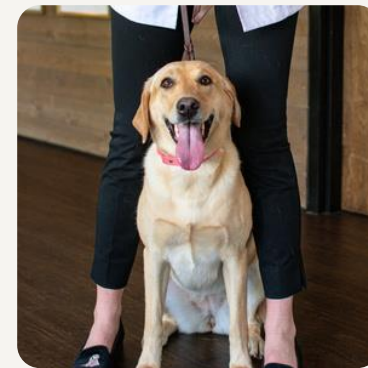
VETERINARY CARE

### NAME + LOGO + COLORS

- Name: does not include a DVM name or a specific location
- Logo: can stand alone - see logo and you know what it represents
- Colors: reflected every where - from this Powerpoint, to social media, to hospital decor
- Do your key brand elements tell a cohesive story that other DVMs want to be a part of?

# BRAND BUILDING

3 Locations. 1 Brand.



Do team members want to join your team based off the brand? Do you think of “Good Dog” without seeing our name or logo in the image?



# CURATE CULTURE

## CREATE OPERATIONAL EXCELLENCE

### DUPLICATE YOURSELF

- Master Process List
  - Ex: Next Slide
- 1:3:1 Strategy
  - Train the team to bring you solutions not problems

### DELEGATION

- Organizational Chart
  - Ex: Next Slide
- Key Result Areas
- Define Direct Report Structure
- Daily Meeting Cadence
  - Rounds
- Weekly Meeting Cadence
  - All Team
- Bi Weekly One on One Cadence

# CURATE CULTURE

## CREATE OPERATIONAL EXCELLENCE

### MASTER PROCESS LIST

- Over 400 Processes written and defined for our team
- How can you set a DVM up for success if they don't know what success looks like? Write it down.

Master Process List				
1	Process Name	Tr Tab	Link	View Access
431	Interpreting Balance Sheets	8.1.2	Interpreting Balance Sheets.pdf	<b>View Only (GDVC Email Required)</b>
432	1099 Collection & Filing Process	2.7.4	1099 Collection & Filing Process	<b>View Only (GDVC Email Required)</b>
433	Overdue Services Process	3.3.16	Overdue Services Process	<b>View Only (GDVC Email Required)</b>
434	W-9 Maintenance Process	2.6.40	W-9 Maintenance Process	<b>View Only (GDVC Email Required)</b>
435	BLANK W9 Form	2.6.41	W-9.pdf	<b>Restricted (Co. + OMs Only)</b>
436	Filings for the Sate of GA - Ga Secretary of State	2.7.5	Filings for the State of GA	<b>Restricted (Company Leadership Te</b>
437	GA Department of Labor (DOL) New Business Req	2.8.2	GA Department of Labor (DOL) New Busi...	<b>Restricted (Company Leadership Te</b>
438	GA Department of Revenue (DOR) New Business I	2.8.3	GA Department of Revenue (DOR) New B...	<b>Restricted (Company Leadership Te</b>
439	Process for Maintenance Calendar all Locations	1.6.4	Process for Maintenance Calendar all Loc...	<b>View Only (GDVC Email Required)</b>
440	Renewing an Occupation Tax Certificates - ALL LC	2.6.42	Renewing an Occupation Tax Certificates ...	<b>Restricted (CEO, VPSO, DOO, OM</b>
441	Property Taxes vs. Personal Property Taxes	2.7.6	Property Taxes vs. Personal Property Tax...	<b>Restricted (Company Leadership Te</b>
442	Legacy at West Cobb Apartment Complex Partner	9.2.6	Legacy at West Cobb Apartment Complex...	<b>View Only (GDVC Email Required)</b>
443	Complimentary Dental Consult Analytics	9.9.2	Complimentary Dental Consult Campaign...	<b>View Only (GDVC Email Required)</b>
444	How to fill out the Georgia DOL-800 Separation Nc	2.6.43	How to fill out the Georgia DOL-800 Separation Notice	<b>View Only (GDVC Email Required)</b>

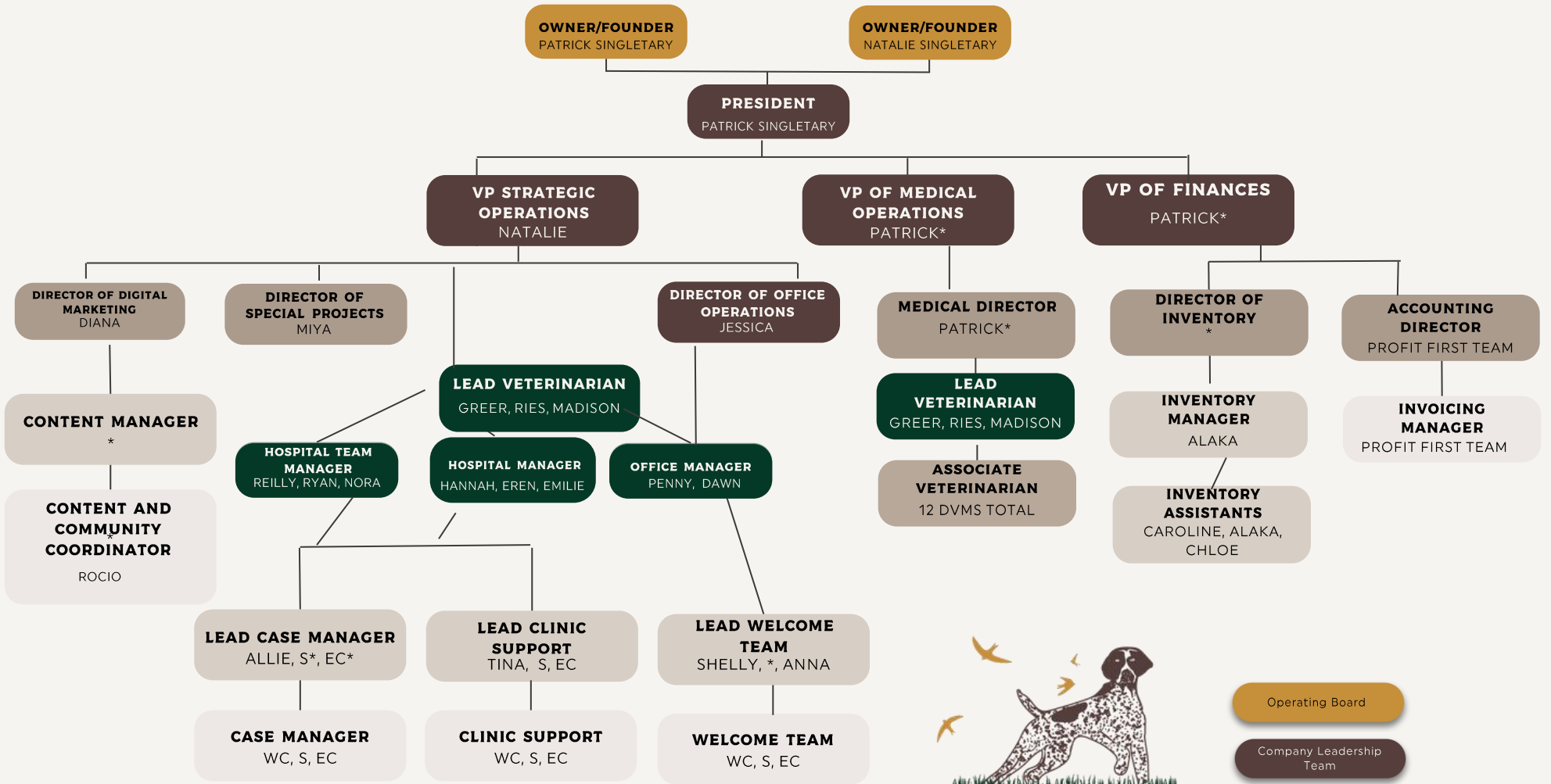
All Processes Glossary 0.0 1.0 2.0 3.0 4.0 5.0 6.0 7.0

# CURATE CULTURE

## CREATE OPERATIONAL EXCELLENCE:

### GOOD DOG VETERINARY CARE

### COMPANY ORGANIZATIONAL CHART

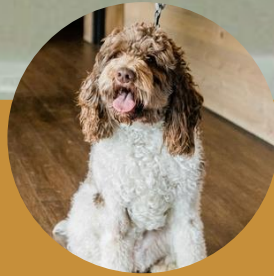


- Operating Board
- Company Leadership Team
- Location Leadership Teams

\*Positions to be filled



**IDENTIFY**



**RECRUIT**



**ATTRACT**

**STAGE 2: IDENTIFY AND ATTRACT  
THE PEOPLE YOU ARE LOOKING FOR**



# IDENTIFY WHO YOU ARE LOOKING FOR

**NEW GRADS OR EXPERIENCED DVMS?**

## OUR DVM TEAM BREAKDOWN

- Class of 2016 (1 - PS)
- Class of 2017 (1 - SW)
- Class of 2019 (1 - GP)
- Class of 2020 (1 - TB)
- Class of 2021 (1 - MA)
- Class of 2022 (1 - RR)
- Class of 2023
- Class of 2024 (1 - AY, JT) \*
- Class of 2025 (4 - SM, PW, CD, CL) \*

\*Joined our team as a New Grad (6/12)



# IDENTIFY WHO YOU ARE LOOKING FOR

Advantages and opportunities to both!

## NEW GRADS

Advantages

- Can teach great habits early

Opportunities

- Can take longer to produce and intentional mentorship is needed

## EXPERIENCED DVMS

Advantages

- Feel confident practicing medicine

Opportunities

- Harder to adapt to your unique business model and culture



# RECRUIT WHO YOU ARE LOOKING FOR

## NEW GRAD RECRUITMENT STRATEGIES

We have done this very well! In the last 3 years, we have had 6 new DVMs join our team. Here is how we did it:

- Start developing meaningful relationships during vet school! This is the #1 way to attract new grad talent.
  - Vet school presentations (next slide)
  - Externships (next slide)
  - Career Fair
  - Dean's Tailgate Sponsor
- Understand that it will take years to see the fruits of these relationships develop. Play the long game!

# RECRUIT WHO YOU ARE LOOKING FOR

## NEW GRAD RECRUITMENT STRATEGIES

### GIVE PRESENTATIONS AT VET SCHOOLS

- Top Goal: Encourage students to bring light, joy, and hope to their future practice. Veterinary medicine desperately needs talented, "on mission," veterinarians. Will you be one?
- Go into it with a desire to truly give back. From developing genuine relationships, career opportunity conversations will develop naturally. Understand that many mentorship relationships will not develop into a new grad joining your team... but some will!



**TIPS! SPONSOR LUNCH, LEAVE TIME FOR Q&A, STAY AFTER FOR MORE QUESTIONS**

# RECRUIT WHO YOU ARE LOOKING FOR

## NEW GRAD RECRUITMENT STRATEGIES HOST STUDENT EXTERNS

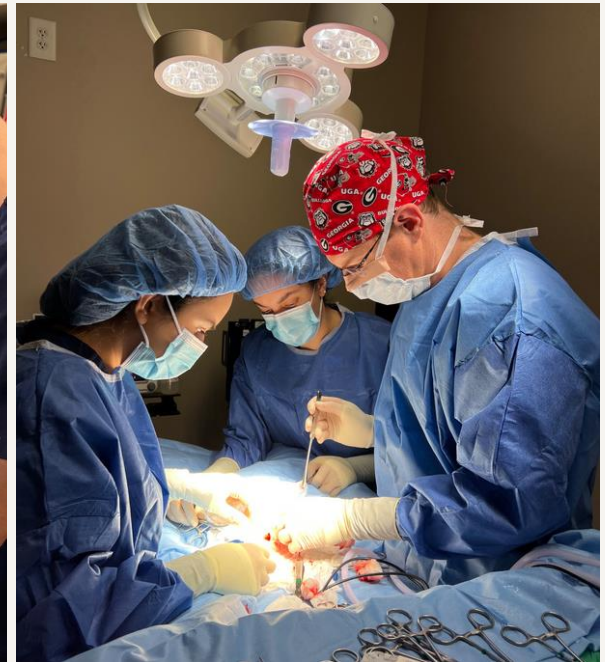
- 1 Extern (2022), 25 Externs (2023-2024) 30 Externs (2025-2026)
- Accept 1 extern at a time
- All 6 new grad DVMs in the last 3 years have externed with us
- Pour into every single extern



Merrianna Parker ('24)



Kat Lager ('26)



Jana Demian ('24)

**TIPS! EXTERNSHIP PACKET, HANDS ON EXPERIENCE,  
1:1 TIME**



# RECRUIT WHO YOU ARE LOOKING FOR

## EXPERIENCED GRAD RECRUITMENT STRATEGIES

- DVMs are looking at your brand - are you making them want to start a conversation?
- Top recruiting strategies
  - Compelling website
  - Compelling social media
  - Compelling reviews
- Make them reach out to you!
  - All 5 experienced DVMs on the team reached out TO US. They came to us - we didn't go to them. We hired before we needed to hire. We have not hired once from Indeed, etc.

# RECRUIT WHO YOU ARE LOOKING FOR

## EXPERIENCED GRAD RECRUITMENT STRATEGIES



Locations ▾

Services ▾

About ▾

More ▾

Refer A Friend

BOOK

## Top 5 Reasons to Join our Team

APPLY ▾



Your Role and Skills Matter



We've Got Your Back



Leadership That Develops Strong Teams



Top-Notch Medical Care & Client Experience



Opportunities to Grow with us



### Good Dog Veterinary Care West Cobb

4.9 ★★★★★ 348 Google reviews

Veterinarian in Cobb County, Georgia

### Roles in our team



Welcome Team



Officer Manager



Clinic Support



Case Manager



Groomer



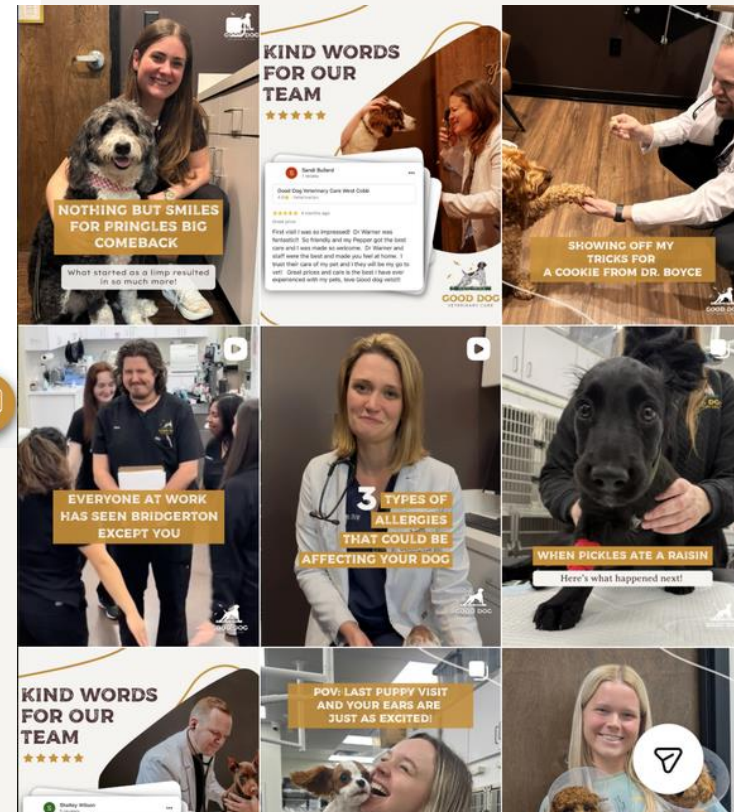
RVT



Veterinarian



Medical Director



# RETAIN WHO YOU ARE LOOKING FOR

## Key Steps



### ONBOARD

#### New Grad Packet

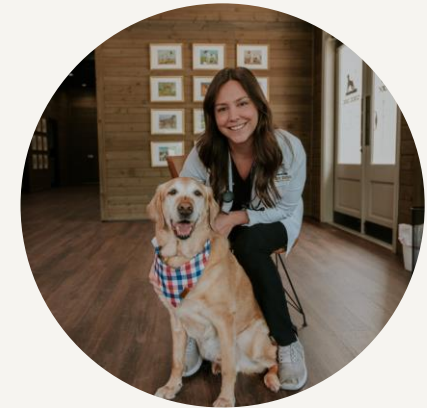
Have a plan and make it clear. We have a dedicated packet that outlines expectations for a New Grad's first year. The timeline is first 2 weeks shadowing, second 2 weeks being shadowed, Surgery Assistance Months 1 - 6, assistance as needed Months 6-12.



### LEAD

#### 1:1s Biweekly

1:1s are the opportunity for the DVM to bring their top goals and opportunities to their leader. A biweekly cadence is a must. PPF goals are discussed at this time.



### DEVELOP

#### TM Maturity Model

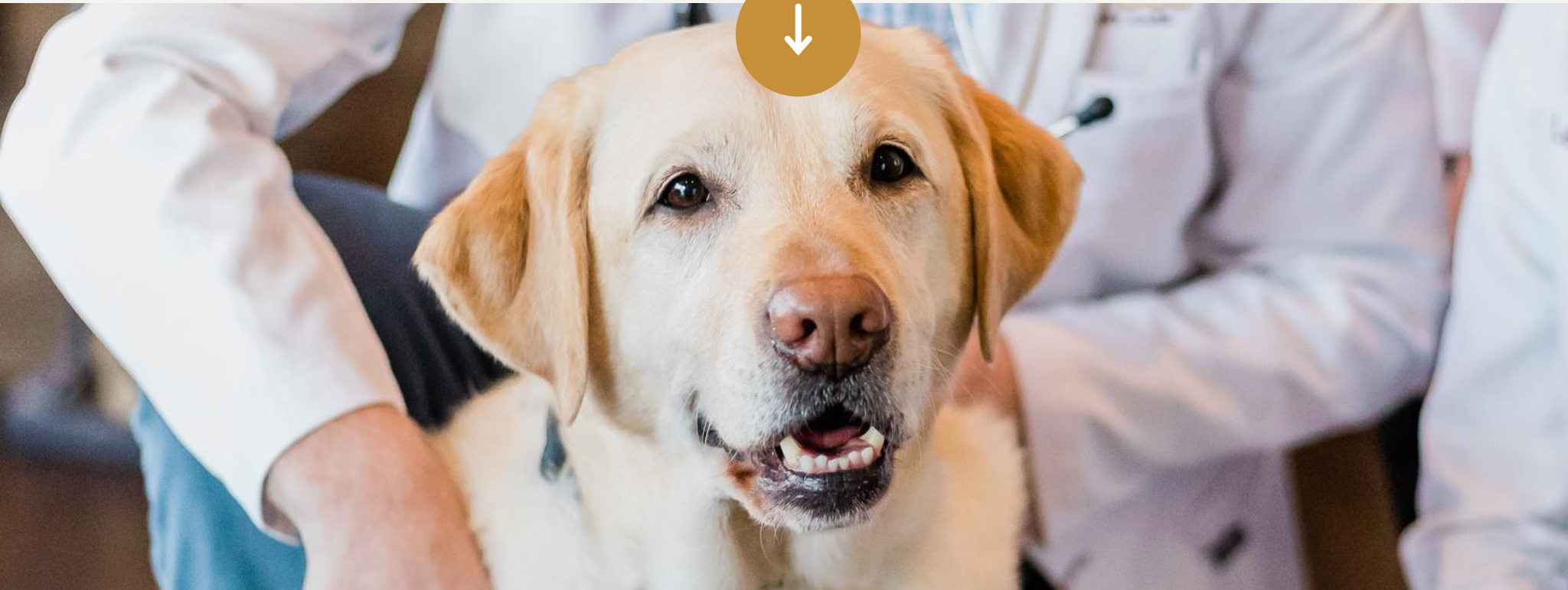
How do you ensure your Associate DVMs do not become stagnate? The Team Member Maturity Model allows a path for growth and development. DVMs are on the path to Lead DVM development and Lead DVMs are on the path to Medical Director or new location Lead.

**“People leave leaders, not companies.” Are you prepared to lead well?**

# FINAL THOUGHTS

## BECOME "THAT" ORGANIZATION

"Become the organization that the people you are looking for are looking for." - David Sayers



**START THE WORK. BECOME THAT  
COMPANY. THEN... DVMS WILL COME!**

# WHAT'S NEXT?

We are committed to stewarding our business well to be a light to our team, clients, and patients.

We are committed to remaining privately owned and operated as we grow and scale.





# Questions? Let's keep in touch!

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@patrick\_singleetary\_dvm (Coming soon!)

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