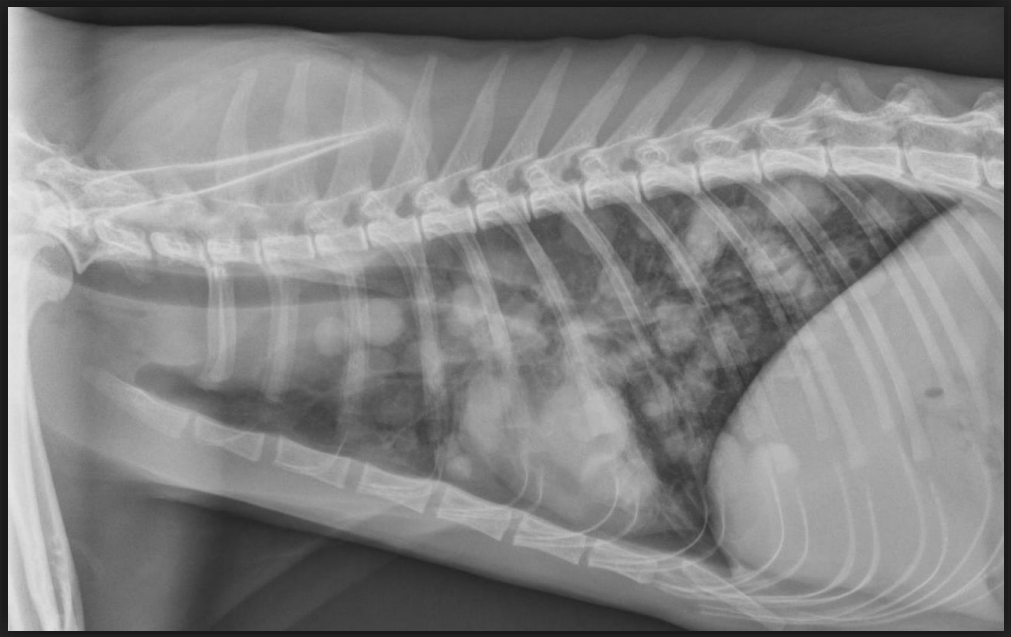
Blastomycosis



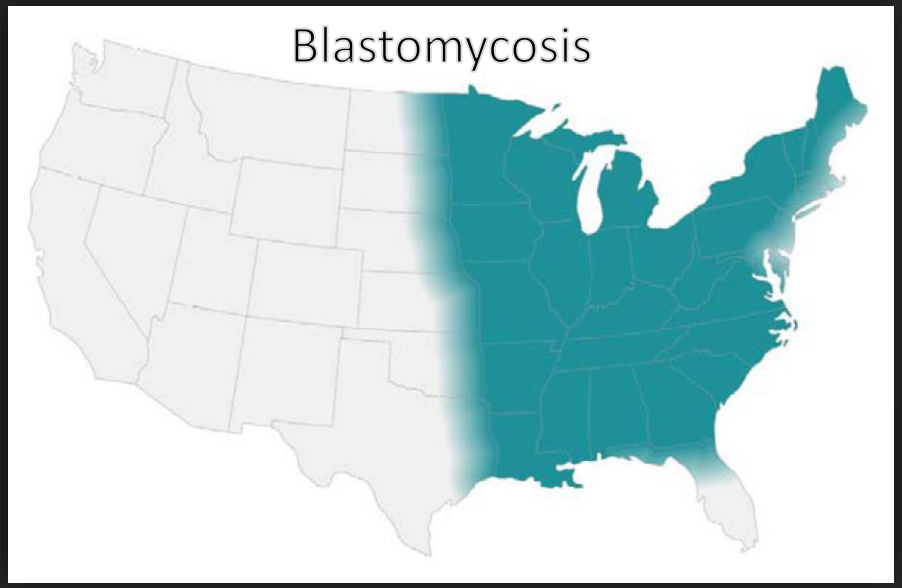
MiraVista
VETERINARY DIAGNOSTICS

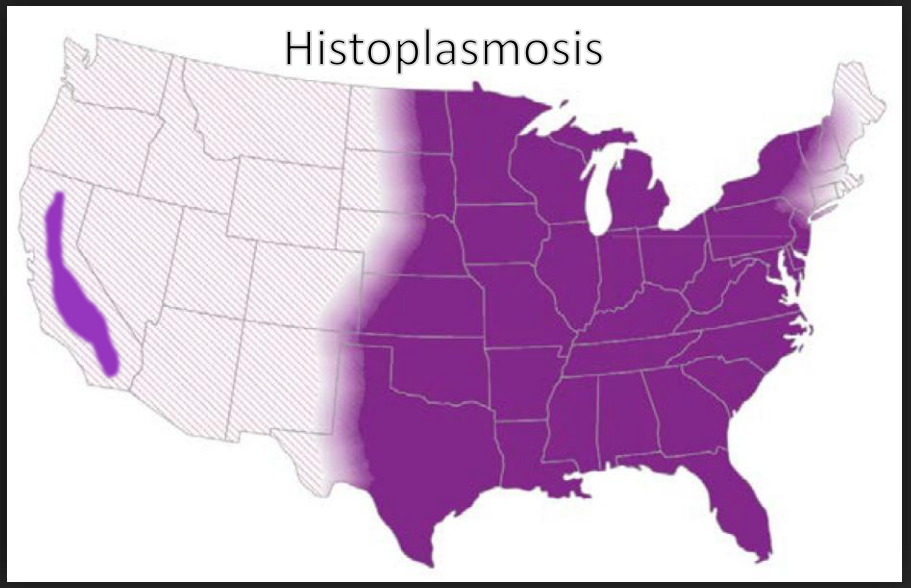
Andrew Hanzlicek DVM, MS, DACVIM
Director, Veterinary Medicine
ahanzlicek@miravistalabs.com
p: 317-455-2166

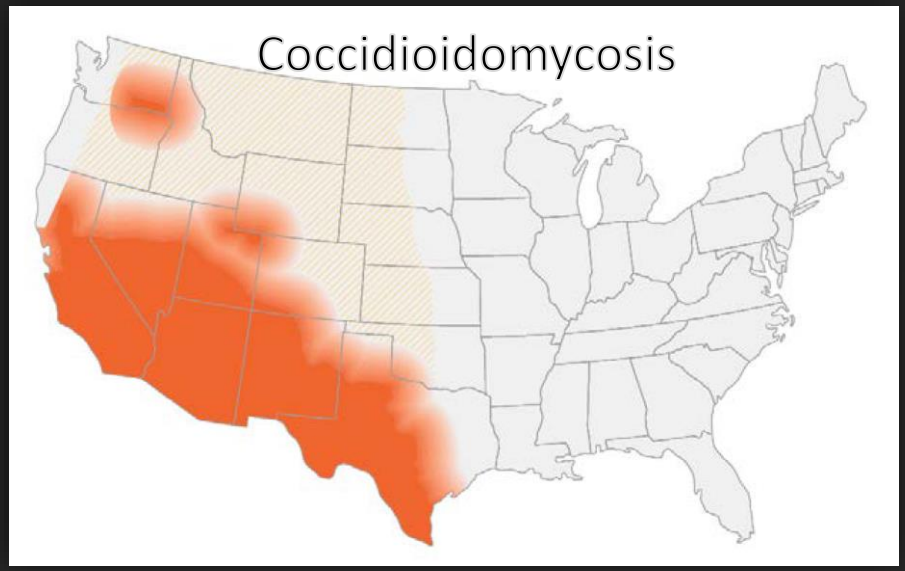
Discussion

1. Epidemiology
2. Clinical Findings
3. Pathology & Culture
4. Biomarkers
   - Antigen
   - Antibody
   - DNA

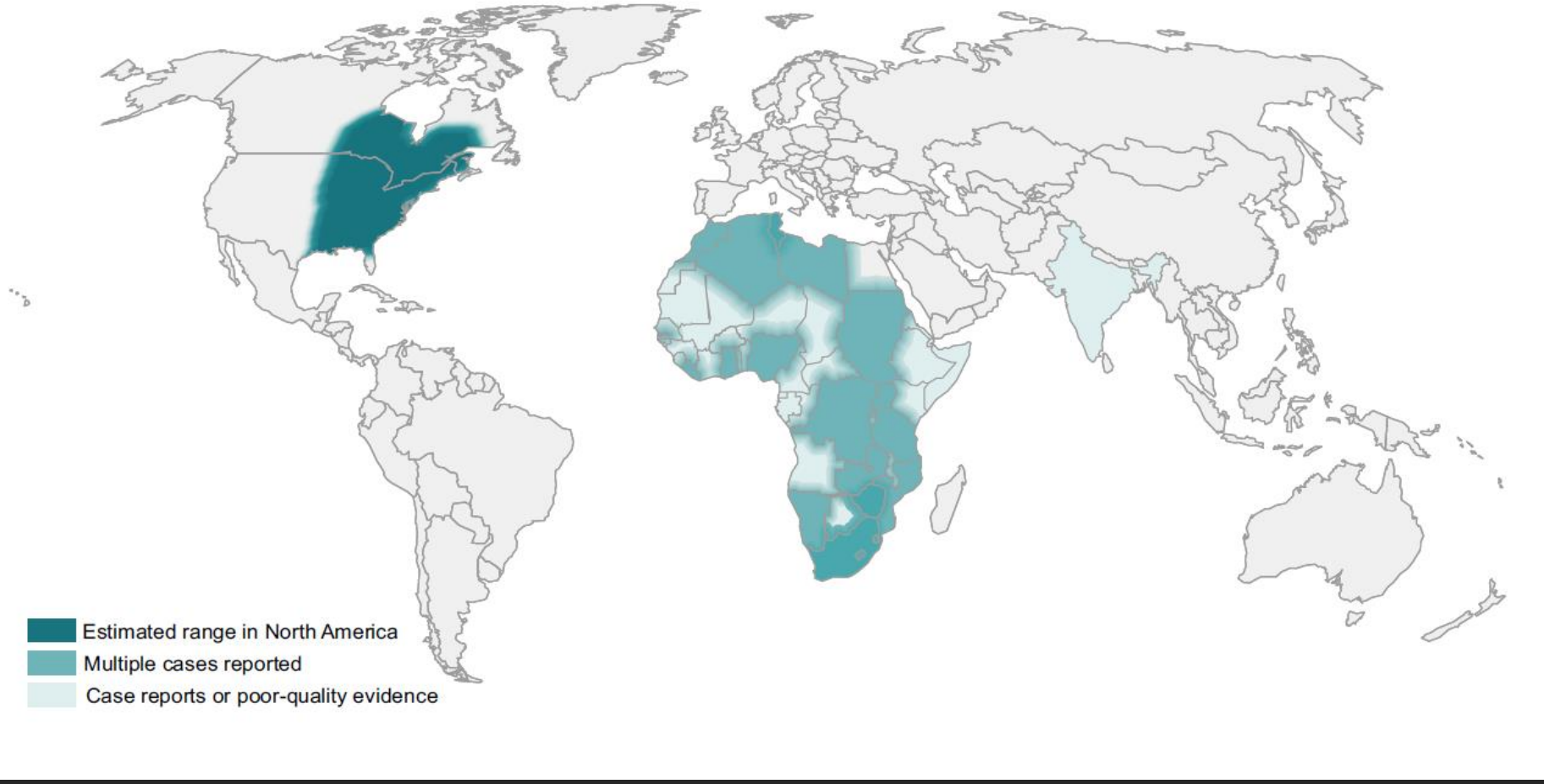
MiraVista
VETERINARY DIAGNOSTICS


Blastomycosis


Histoplasmosis


Coccidioidomycosis

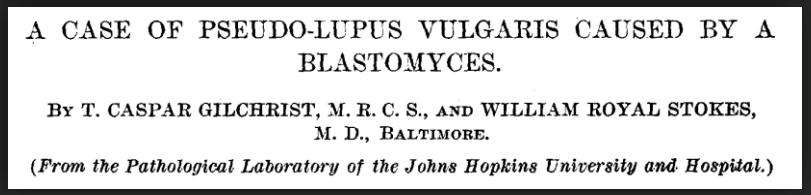
Blastomycosis



Ashraf N, et al. Re-drawing the maps for endemic mycoses. MYCOPATH 2020;185:843-65.

Blastomyces

- Cryptic species
  - *Blastomyces dermatitis*
  - *Blastomyces gilchristii*
- Other species
  - *B. helicus*
- Infection = Inhalation of spores
  - Not contagious



A CASE OF PSEUDO-LUPUS VULGARIS CAUSED BY A BLASTOMYCES.

By T. CASPAR GILCHRIST, M. R. C. S., and WILLIAM ROYAL STOKES, M. D., Baltimore.

(*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*)

Image courtesy Dr. Jeff Powers

Prevalence, distribution, and risk factors for canine blastomycosis in Michigan, USA

Leslie and D

Epidemiologic study of canine blastomycosis in Wisconsin

hD

The epidemiology of blastomycosis in dogs: north central Wisconsin, USA

D. J
*Uni
545

A case-control study of sporadic canine blastomycosis in Tennessee, USA

THOMAS CHEN*, ALFRED M. L

Temporal and spatial distribution of blastomycosis cases among humans and dogs in Illinois (2001–2007)

Geographic information system analysis of blastomycosis in northern Wisconsin, USA: waterways and soil

PH;

DENNIS J. BAUMGARDN
ANNE M. BAUMGARDN

PREVALENCE AND INCIDENCE STUDIES OF HUMAN AND CANINE BLASTOMYCOSIS

II. YEARLY INCIDENCE STUDIES IN THREE SELECTED STATES, 1960–1967

Effects of season and weather on blastomycosis in dogs: Northern Wisconsin, USA

Prevalence and geographic distribution of canine and feline blastomycosis in the Canadian prairies

IBER§

Jennifer L. Davies, Tasha Epp, Hilary J. Burgess

Environmental Risks

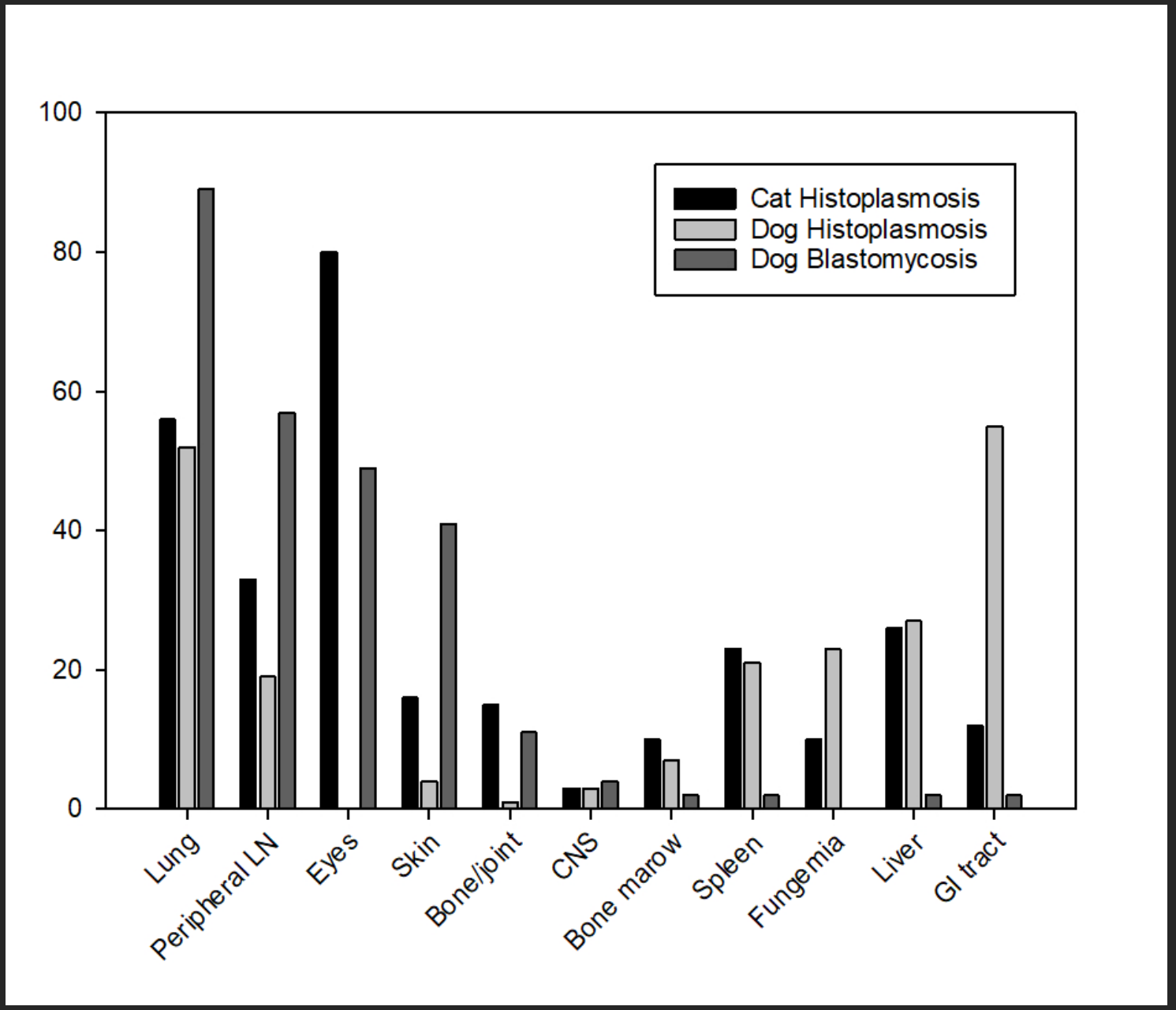
- Niche
  - Organic matter, moisture, acidic/sandy soil
- Wet / dry cycle
  - Living within ½ mile of water
- Disruption of soil
  - Excavation, tilling, etc.

Signalment

- Dogs w highest environmental risk

- Dog>>Cat
  - 1/3 reported cats indoor only
  - Slight Male predisposition
  - Often <7 years

- Sporting & Hunting breeds
  - Predisposed breeds:
    - Cocker spaniel, Doberman, Weimaraner, English spaniel, coonhounds, pointer, Lab, Golden, Brittany


100
80
60
40
20
0
Cat Histoplasmosis
Dog Histoplasmosis
Dog Blastomycosis
Lung
Peripheral LN
Eyes
Skin
Bone/joint
CNS
Bone marow
Spleen
Fungemia
Liver
GI tract

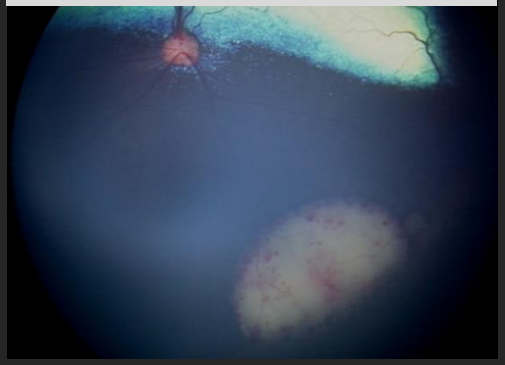
Pathogen	Host	Common Organs	Common Clinical Signs
Blastomyces	Dog>>>Cat	Lung Lymph nodes Eyes/periocular tissues Skin Bones/joints Testicles/prostate (dog)	Anorexia Weight loss Fever Tachypnea Cough Lameness Vision disturbance Cutaneous Lesions
Histoplasma	Cat>Dog	Lung Lymph node Spleen & Liver Eyes/periocular tissues Bone marrow Skin (cat) Bone/joints (cat) GI tract (dog)	Anorexia Weight loss Fever Tachypnea Lameness (cat) Vision disturbance Cutaneous lesions Diarrhea (dog)
Coccidioides (valley fever)	Dog>>Cat	Lung Lymph nodes Skin Eyes CNS Bones/joints Pericardium	Anorexia Weight loss Tachypnea Cough Lameness Cutaneous lesions CNS signs

Pathogen	Host	Common Organs	Common Clinical Signs
Cryptococcus	Cat>>>Dog	Nasal cavity & sinuses Eyes & periocular tissues Lymph nodes Skin CNS Abdominal viscera (dog)	Nasal discharge Facial deformity Cutaneous lesions Blindness CNS signs Vomiting, diarrhea (dog)
Aspergillus (systemic)	Dog>>>Cat	Bone/joints Vertebral end plates CNS Kidney Lymph nodes Skin Eyes Abdominal viscera	Anorexia Weight loss Fever Lameness Vision disturbance CNS signs Cutaneous lesions PU/PD
Aspergillus (sinonasal)	Dog>>Cat	Nasal cavity & sinuses Orbit CNS	Nasal discharge Nasal depigmentation Facial deformity CNS signs

When to be Suspicious

1. Fever unresponsive to antibiotics
2. Multisystemic disease
3. Nodular/ulcerative skin disease
4. Lung disease
5. Lymphadenopathy (incl. TB nodes)
6. Inflammatory [peri]Ocular disease
7. Osteomyelitis
8. Prostatitis/orchitis

Retinal granuloma in dog



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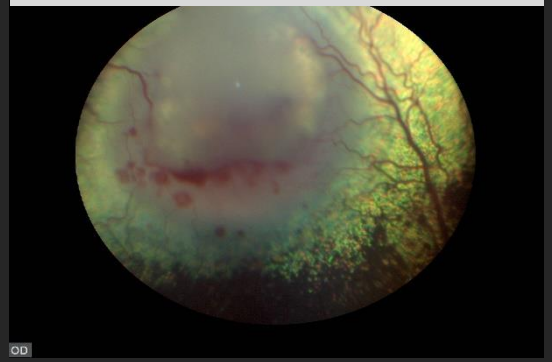
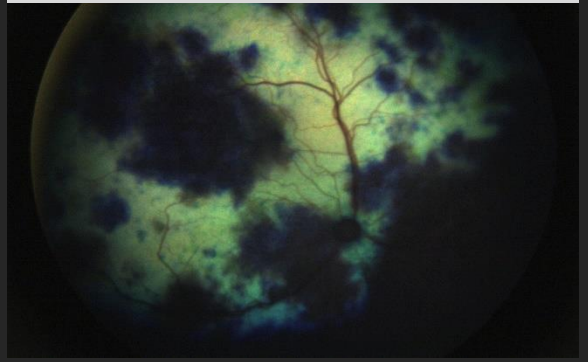
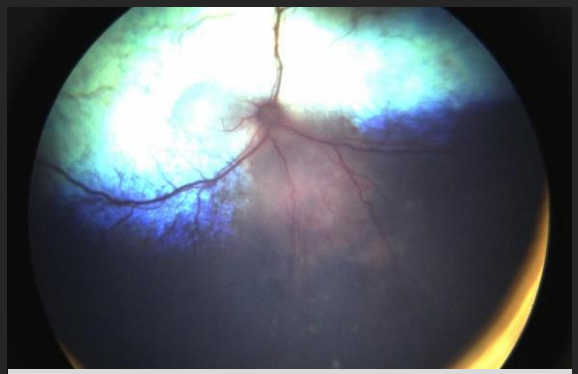


Chorioretinitis in cat





Chorioretinitis in cat

Retinal detachment in cat

Anterior uveitis in dog

Periocular involvement in cat

Photos courtesy of Dr. Rachel Allbaugh and Dr. Emily McCool.

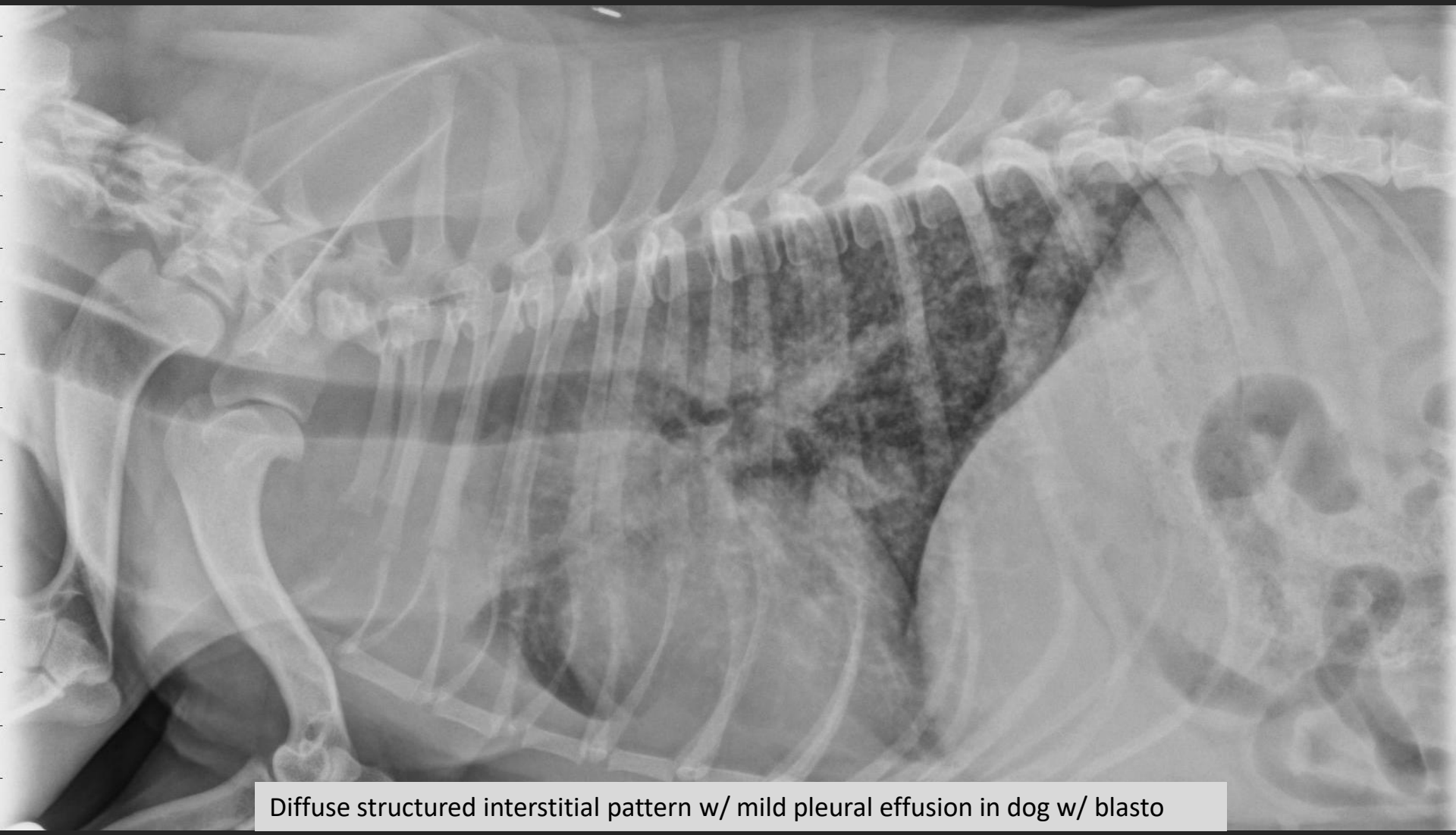
Ulcerative lesion in dog

Nodular ulcerative lesions in cat

Chronic draining skin lesion in dog

Tongue lesion in cat

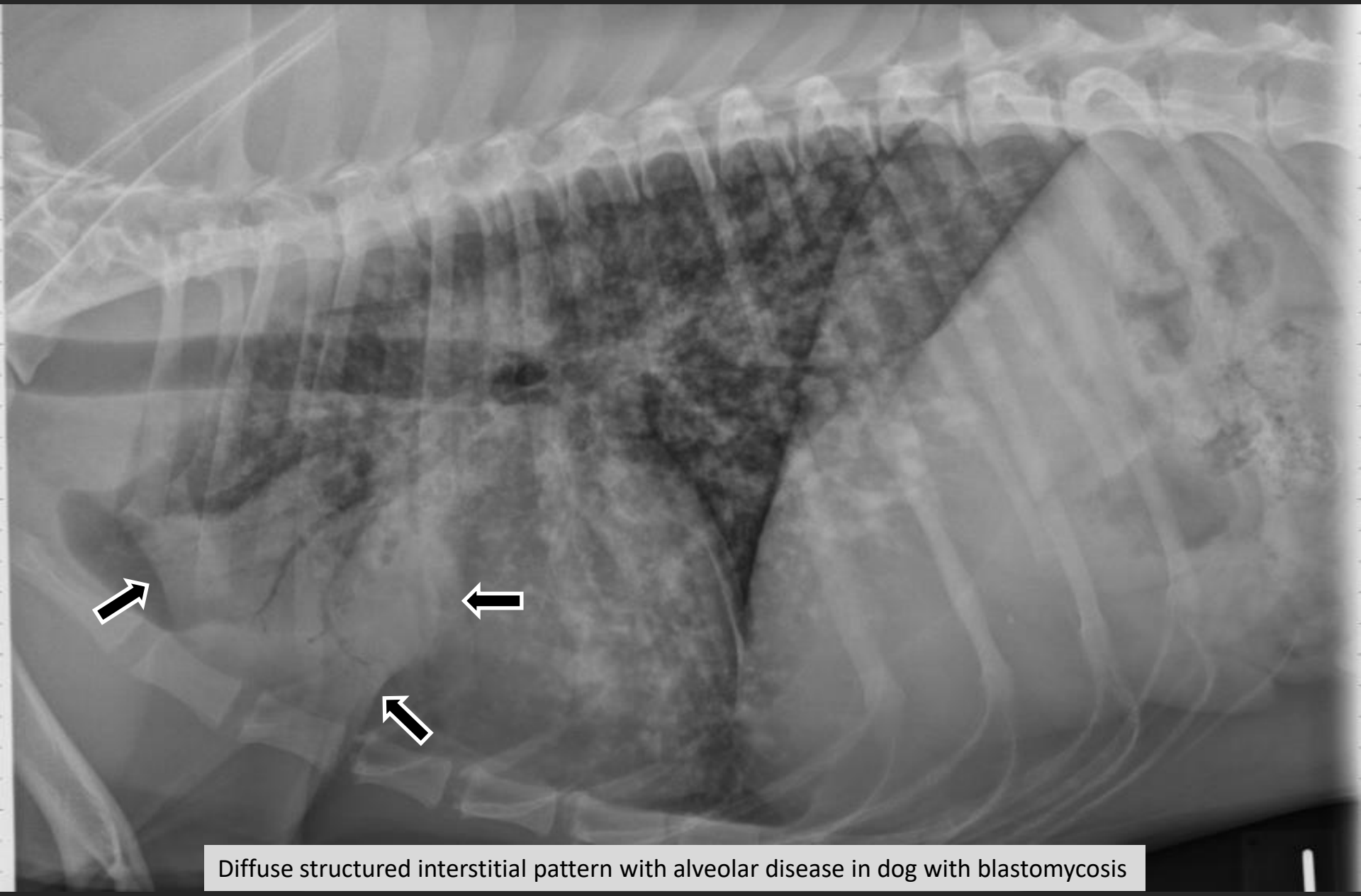
Bone involvement with histoplasmosis, blastomycosis, and coccidioidomycosis.



Diffuse structured interstitial pattern w/ mild pleural effusion in dog w/ blasto

Image courtesy of Dr. Jennifer Reinhart.

Diffuse unstructured interstitial pattern with mass-like lesion (arrow) in dog with blasto



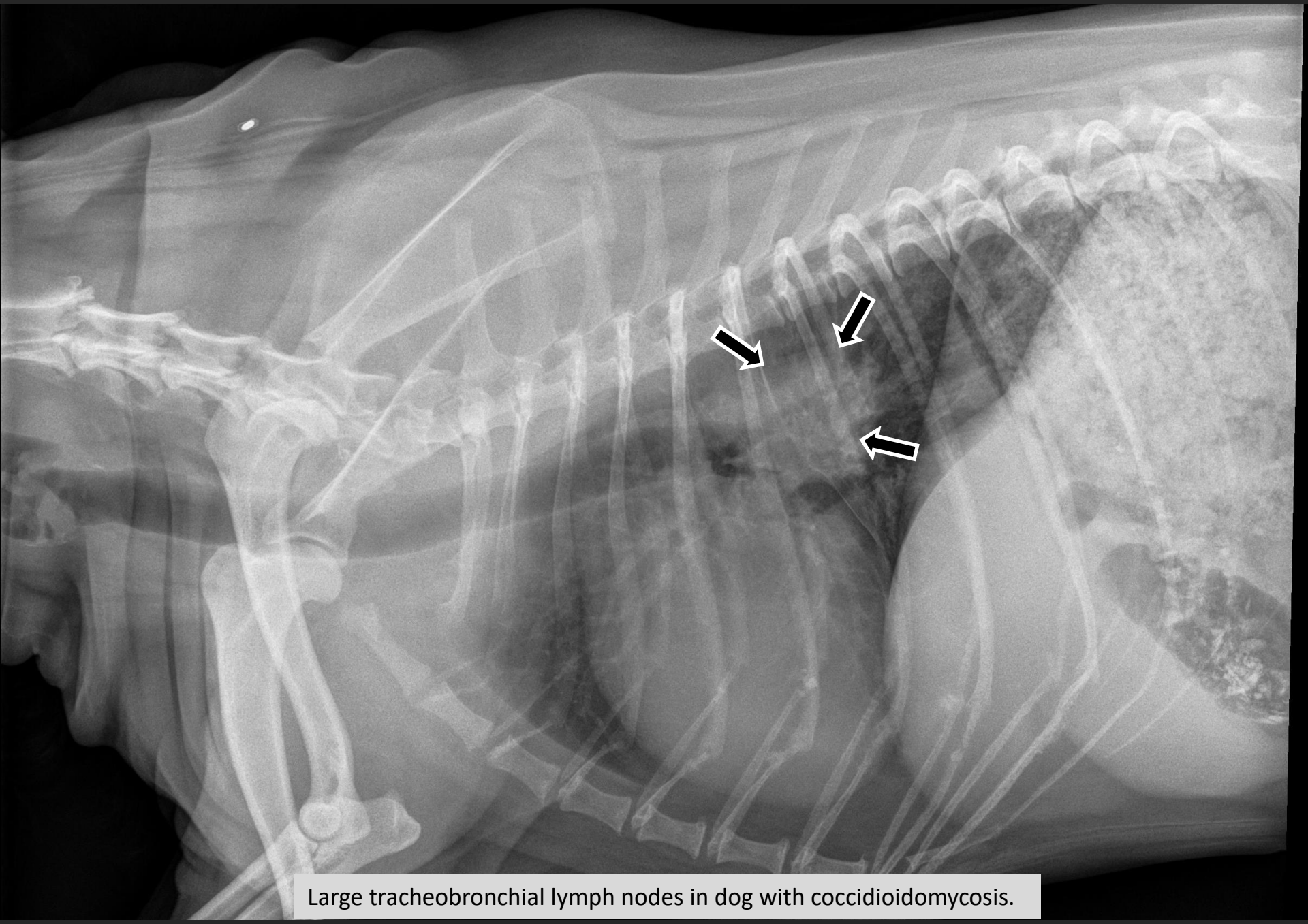
Diffuse structured interstitial pattern with alveolar disease in dog with blastomycosis

Image courtesy of Dr. Jennifer Reinhart.

Mass-like lesion in dog with pulmonary blastomycosis

Image courtesy of Dr. Heidi Bortnowski.

Diffuse structured interstitial pattern with pulmonary effusion in dog with blastomycosis

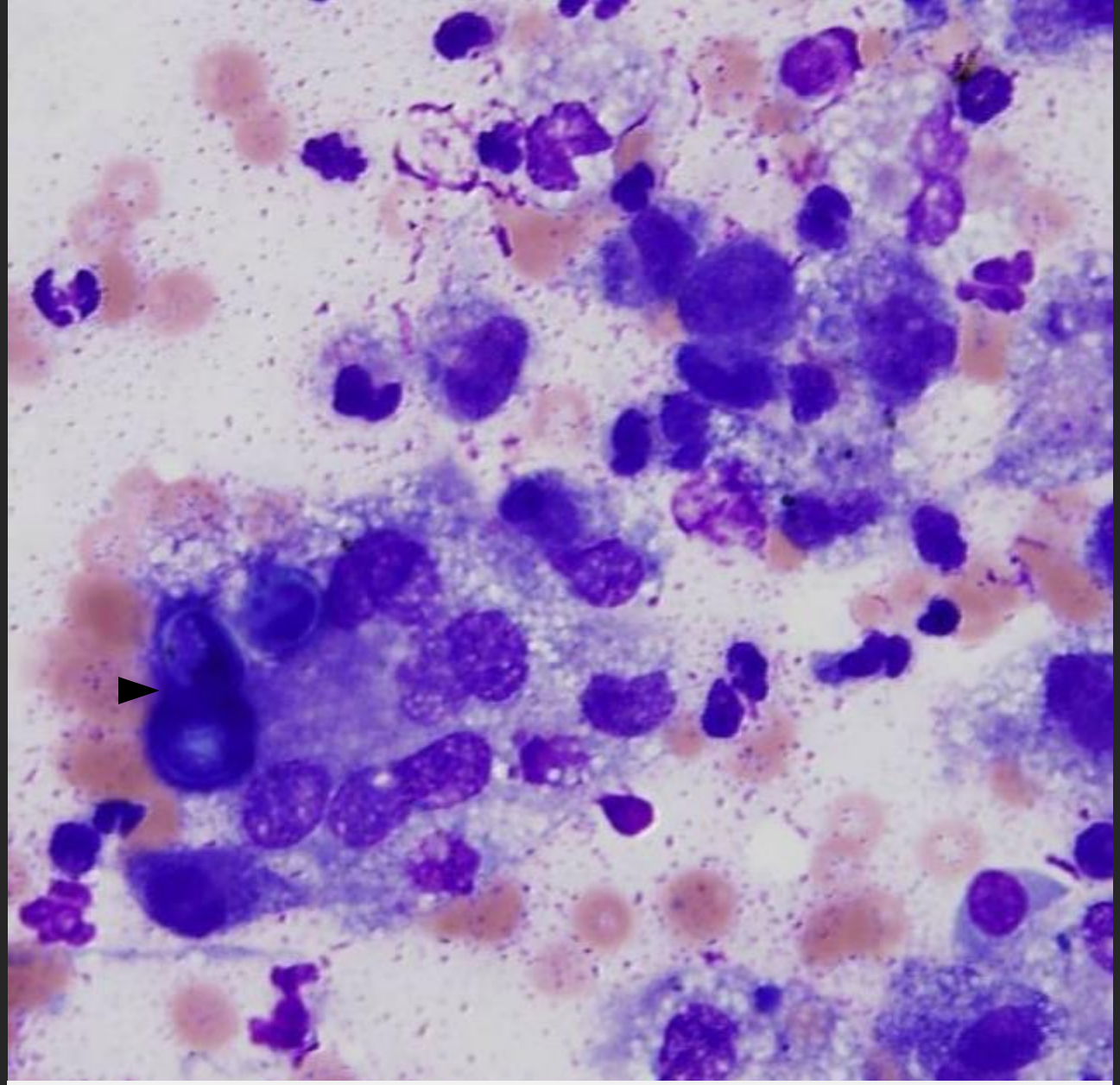


Large tracheobronchial lymph nodes in dog with coccidioidomycosis.

Large tracheobronchial lymph nodes in dog with coccidioidomycosis.

Diagnosis

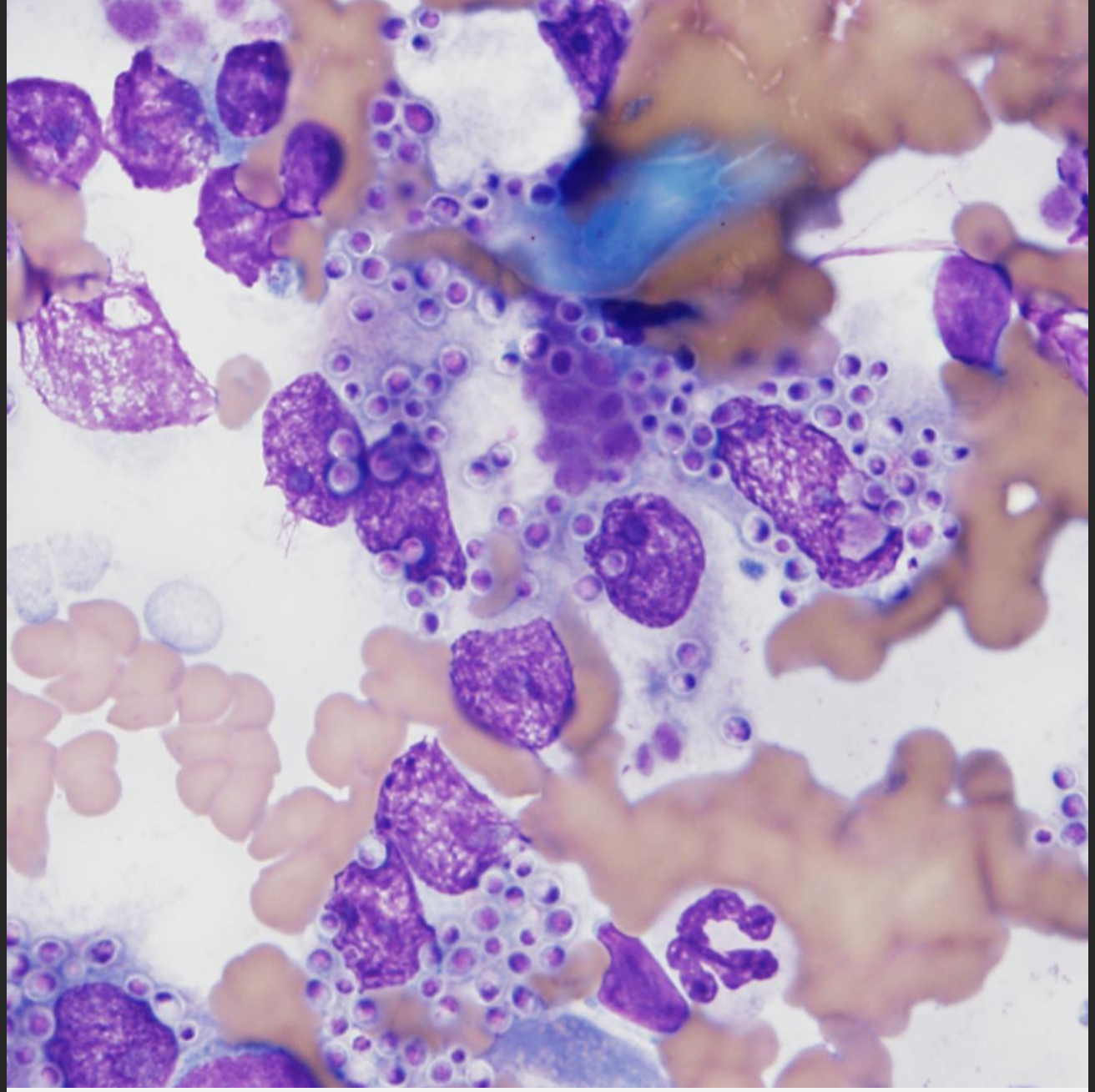
- Pathology
  - Cytopathology – LN, skin, bone, airway wash
  - Moderate sensitivity (≈70%)
  - False (-) w/ low number of organisms
  - Not feasible all anatomic locations
- Culture
  - Long turnaround time (>4 weeks)
  - Questionable sensitivity (≈35%)
  - Risk to lab personnel



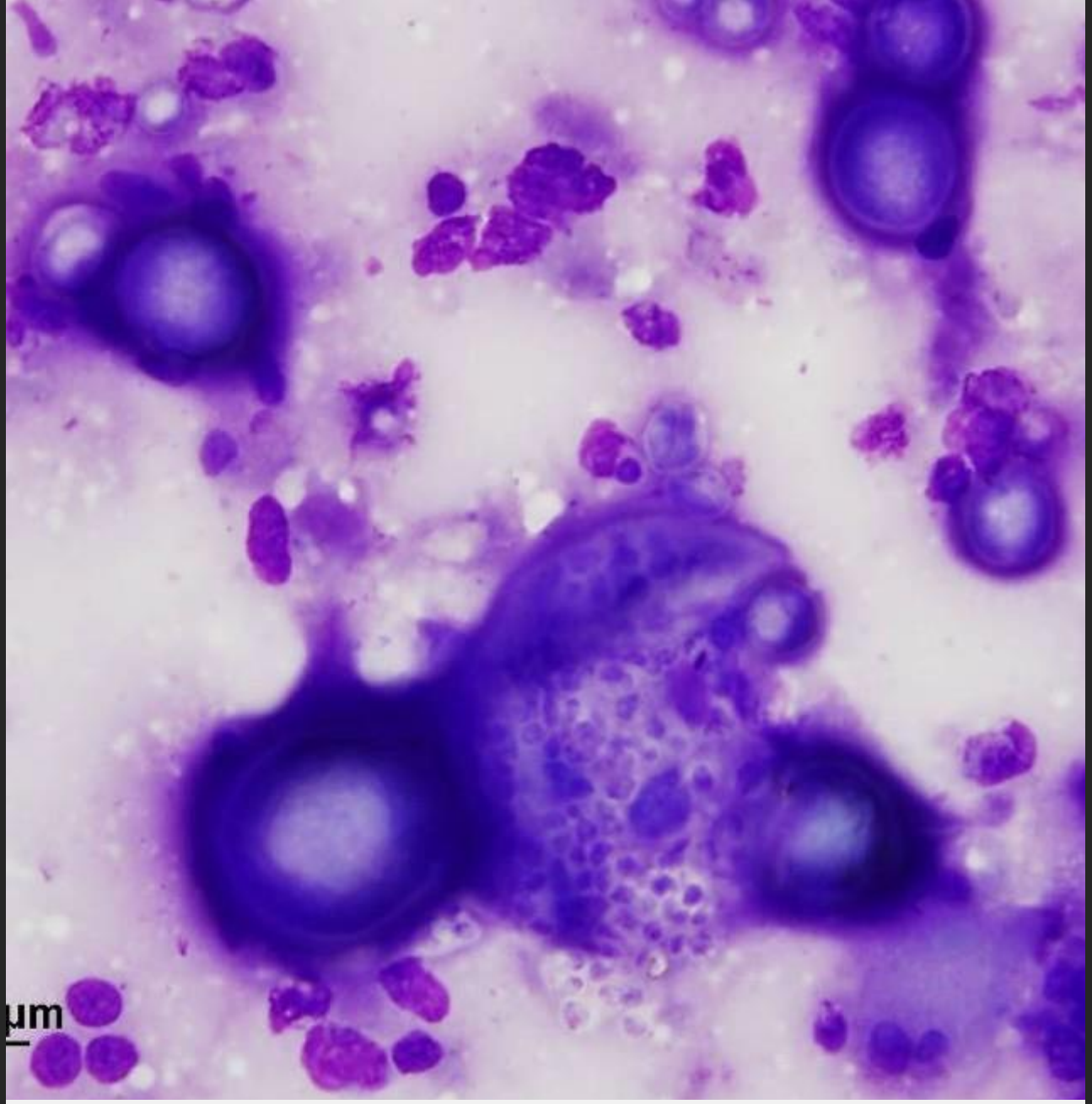
Blastomyces: Extracellular yeast with double refractile wall and broad-based budding

Cytology images courtesy of Dr. Jim Meinkoth.

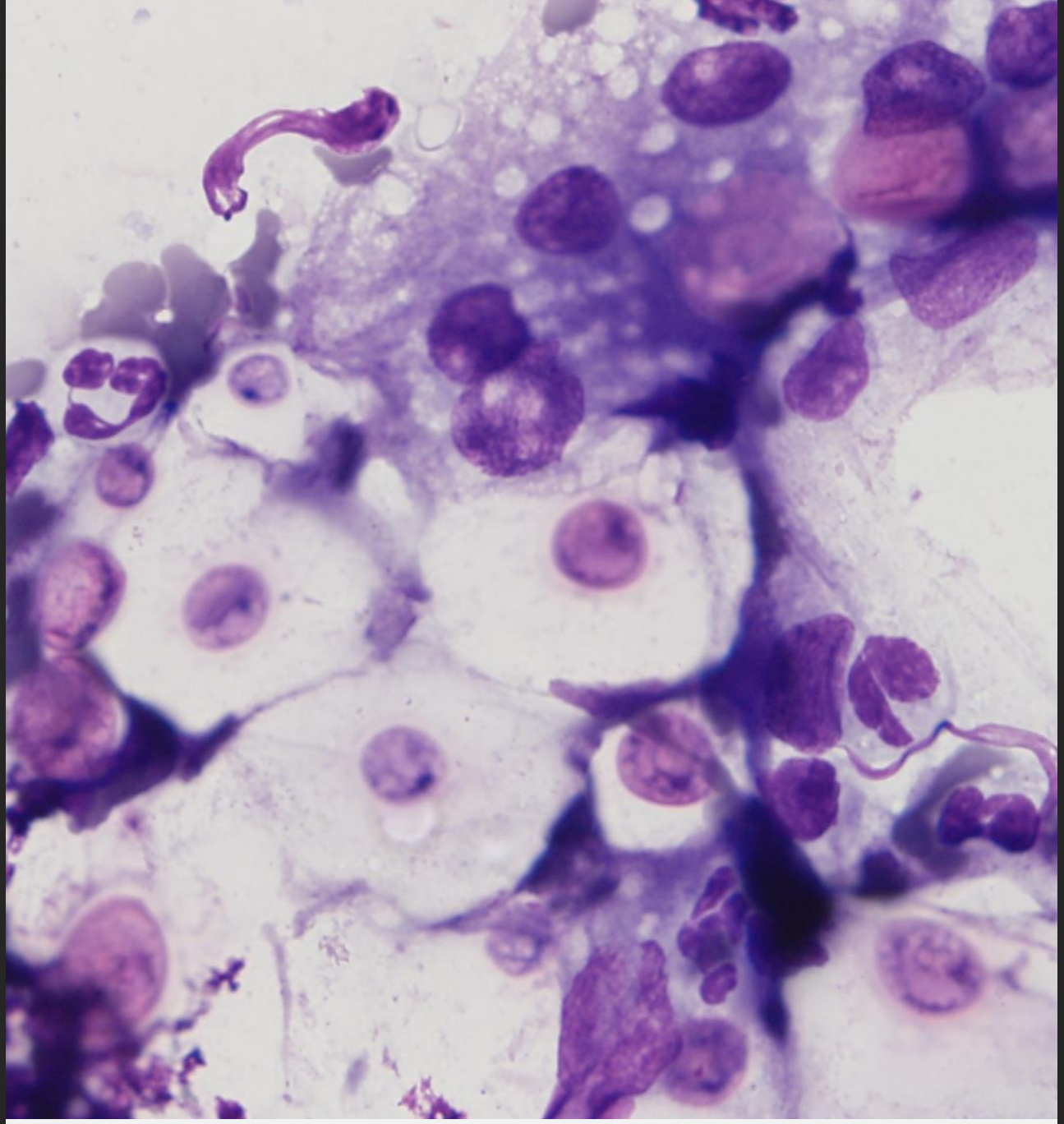
Cytology images courtesy of Dr. Jeff Powers.



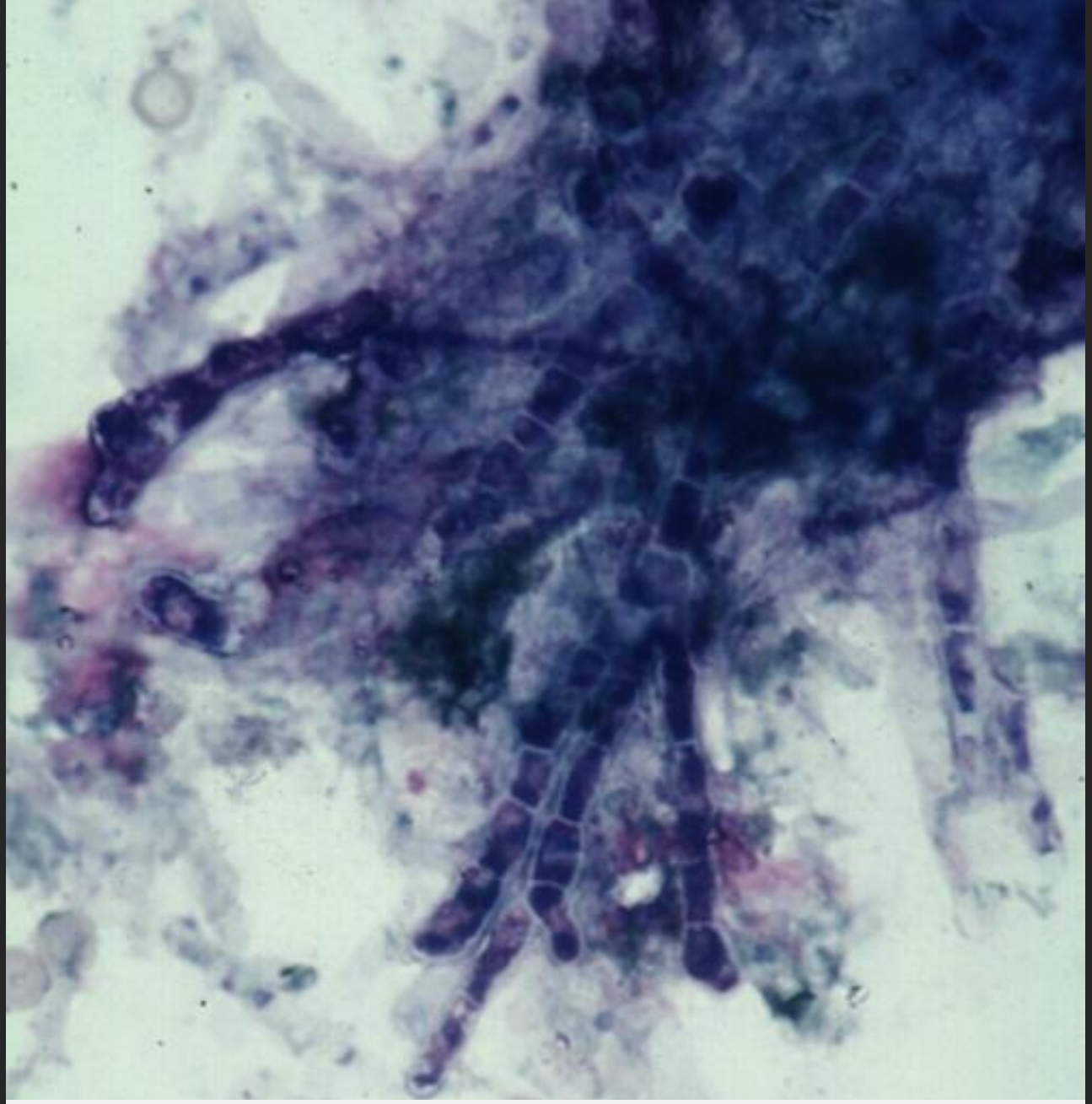
Histoplasma: Multiple intracellular yeast with small clear capsule and eccentrically placed dark staining nuclei



Coccidioides: Multiple variably sized yeast, large spherules with endospores that rupture



Cryptococcus: Extacellular yeast with large clear capsule



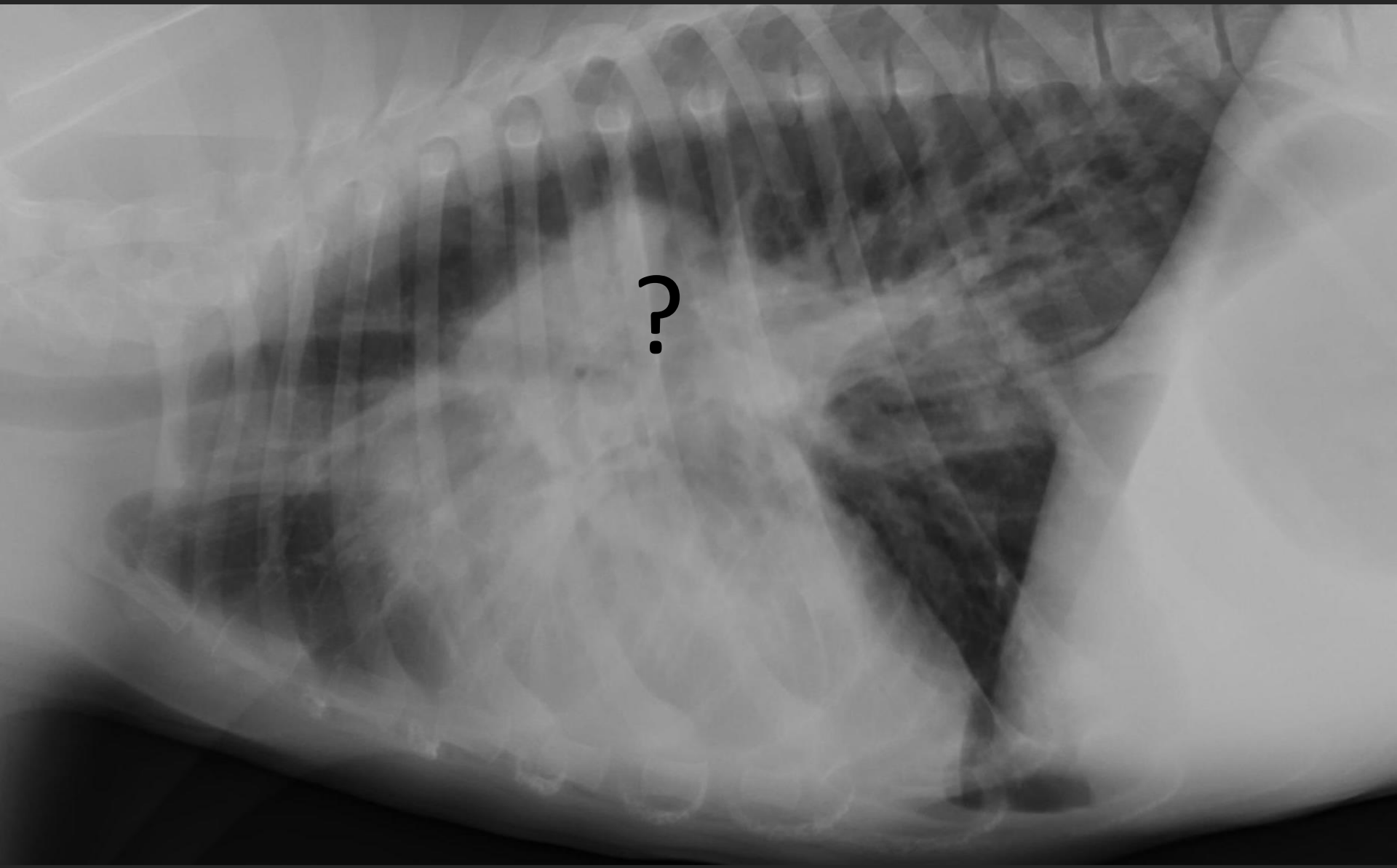
Aspergillus: Narrow, septated, acute angled branching, globuse ends

Utility of diagnostic tests for and medical treatment of pulmonary blastomycosis in dogs: 125 cases (1989–2006)

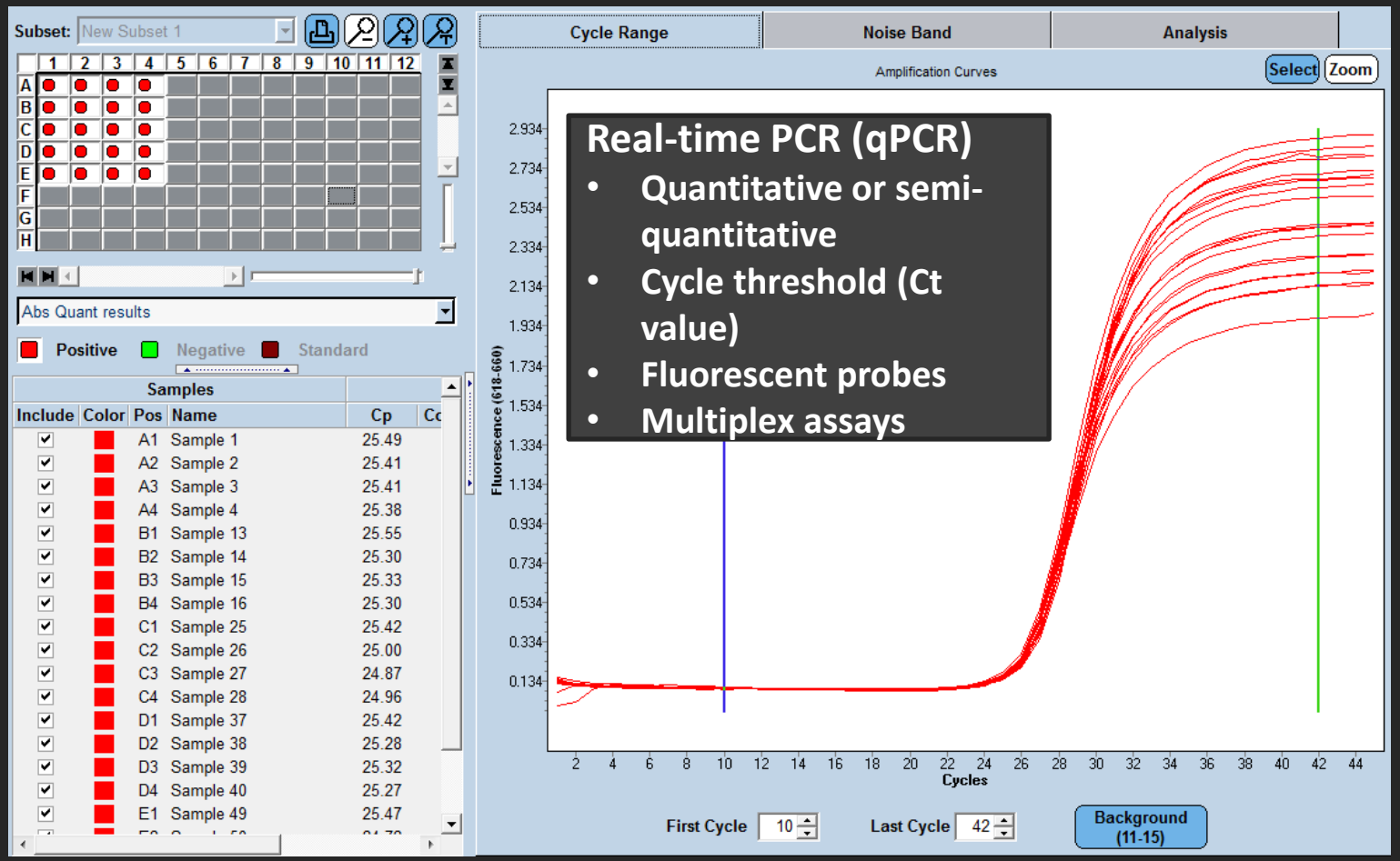
Laura J. Crews, DVM, MS; Daniel A. Feeney, DVM, MS, DACVR; Carl R. Jessen, DVM, PhD, DACVR; Allison B. Newman, DVM; Leslie C. Sharkey, DVM, PhD, DACVP

Diagnostic procedure	No. of dogs tested	No. (%) with positive results
Histologic examination		
Lung necropsy specimen	22	22 (100)
Lung biopsy specimen	6	6 (100)
Ocular tissue	6	6 (100)
Bone	3	3 (100)
Thoracic mass	1	1 (100)
Cytologic examination		
Transthoracic FNA	57	46 (81)
Transtracheal lavage fluid	39	27 (69)
Sputum	4	4 (100)
Lymph node	24	19 (79)
Skin	32	31 (97)
Prostate gland	3	3 (100)
Ocular tissue	3	2 (67)
Joint fluid	2	2 (100)
AGID[a]	24	12 (50)
Fungal culture	6	2 (33)

Multiple diagnostic tests were performed in 69 dogs.
FNA = Fine-needle aspirate. AGID = Agar gel immunodiffusion test.



DNA Detection



MiraVista VETERINARY DIAGNOSTICS

PCR Limitations

- Laboratory v Clinical Validation
  - Is DNA expected in sample type?
    - Blood, urine, BALf, CSF, other
  - **Diagnostic performance** for that **sample type** in **naturally occurring disease**?

- Commercially available panels
  - Systemic Mycoses, FUO, Uveitis
  - Diagnostic performance data???

PCR Limitations 2

- Variability
  - Laboratory / Platform
  - Sample type - inhibitors
  - Purification / concentration
  - Single vs. Multi-copy gene
  - Many others

- Colonization v Contamination v Infection
  - More pertinent to molds and *Candida*

Urine polymerase chain reaction is not as sensitive as urine antigen for the diagnosis of disseminated histoplasmosis

Yi-Wei Tang[a,b,*], Haijing Li[a], Michelle M. Durkin[c], Sefers E. Sefers[b], Sufang Meng[a], Patricia A. Connolly[c], Charles W. Stratton[a,b], L. Joseph Wheat[c]

[a]*Department of Medicine, Vanderbilt University School of Medicine, Nashville, TN 37232, USA*
[b]*Department of Pathology, Vanderbilt University School of Medicine, Nashville, TN 37232, USA*
[c]*MiraVista Diagnostics, Indianapolis, IN 46241, USA*

Received 19 July 2005; revised 22 September 2005; accepted 17 October 2005

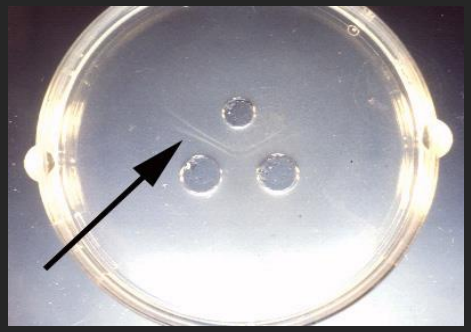
Table 2
Clinical sensitivity correlates PCR with culture and antigen detection in urine from patients with histoplasmosis and healthy volunteers

Specimen classification	Healthy volunteers	*Histoplasma* antigen-positive
All	0/25	4/51 (7.8%)[a]
Culture positive	NA	4/5 (80%)
Culture negative	NA	0/46 (0%)
Antigen 1–19.9 U	NA	0/24 (0%)
Antigen >20 U	NA	4/27 (18.5%)

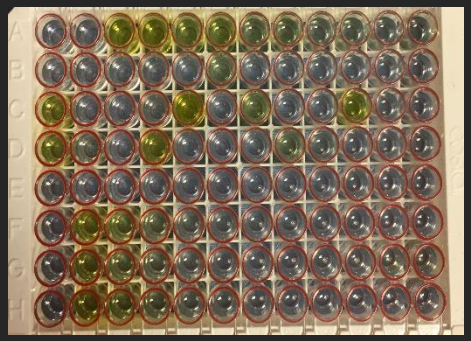
NA = not applicable.
[a] Number positive by PCR/number tested (PCR positive rate).

Antibody Detection

- Immunodiffusion (ID)
  - Clear agarose gel
  - Visual inspection
    - line of immunoprecipitation
  - Low complexity



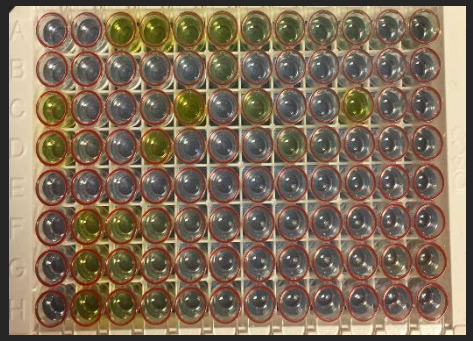
- Enzyme immunoassay (EIA)
  - More sensitive than ID
  - Scalable
    - Shorter TAT
      - 2 hours v 3 days
    - Lower cost



MiraVista
VETERINARY DIAGNOSTICS

Antigen Detection

- Enzyme immunoassay (EIA)



- Latex agglutination (LA)
  - Only used for Crypto GXM
  - High performing test

- Lateral flow device
  - Point-of-care

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VETERINARY DIAGNOSTICS

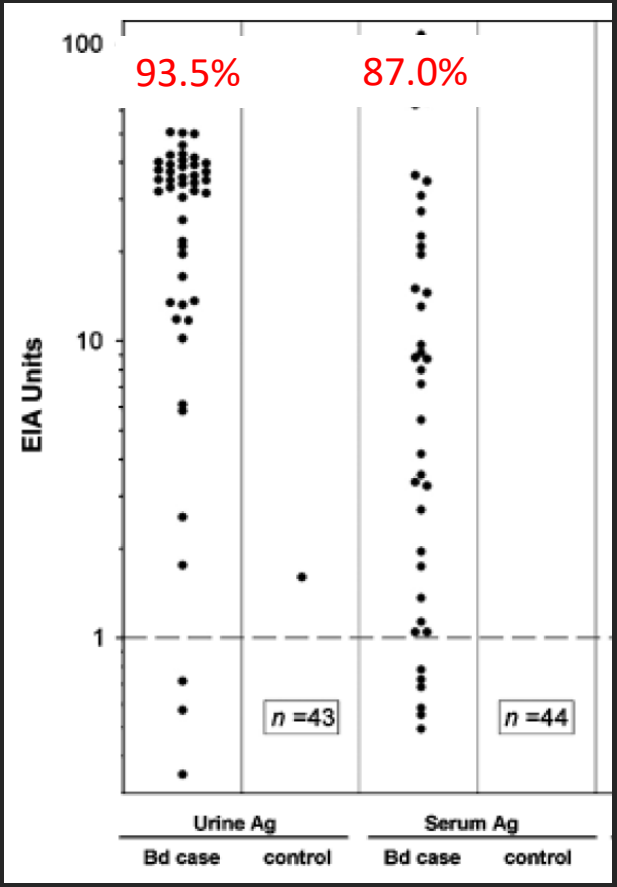
Blasto Antigen

- Antigen eia
  - Galactomannan (GM)
    - Soluble cell wall polysaccharide
      - continuously shed then replenished
  - Urine
    - 92-94 sensitivity
    - >98 specificity
  - Serum
    - 85-90 sensitivity
    - >98 specificity

J Vet Intern Med 2008;22:839–843

Antigen and Antibody Testing for the Diagnosis of Blastomycosis in Dogs

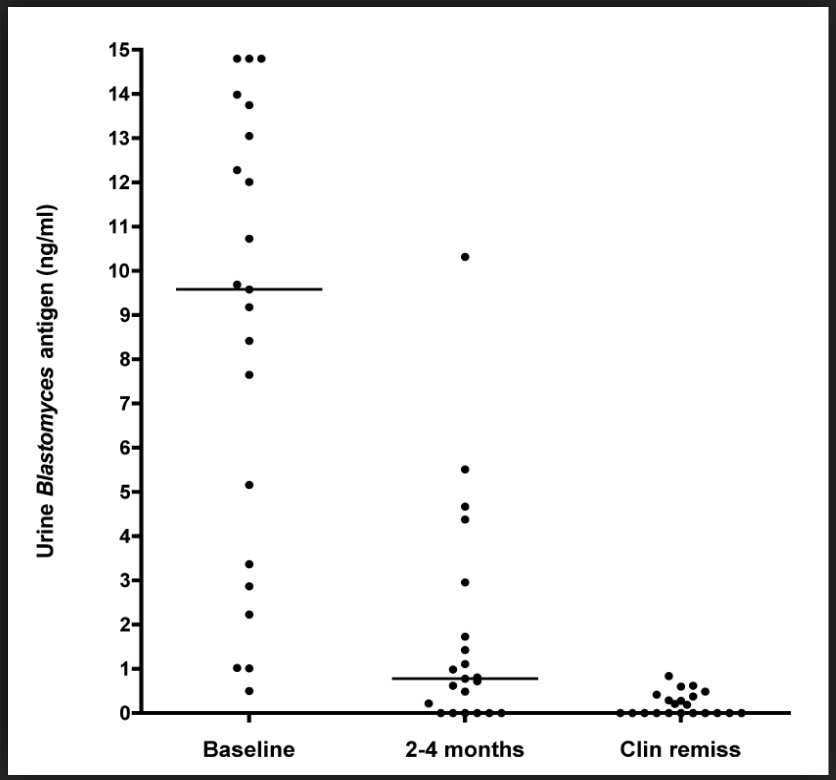
D. Spector, A.M. Legendre, J. Wheat, D. Bemis, B. Rohrbach, J. Taboada, and M. Durkin

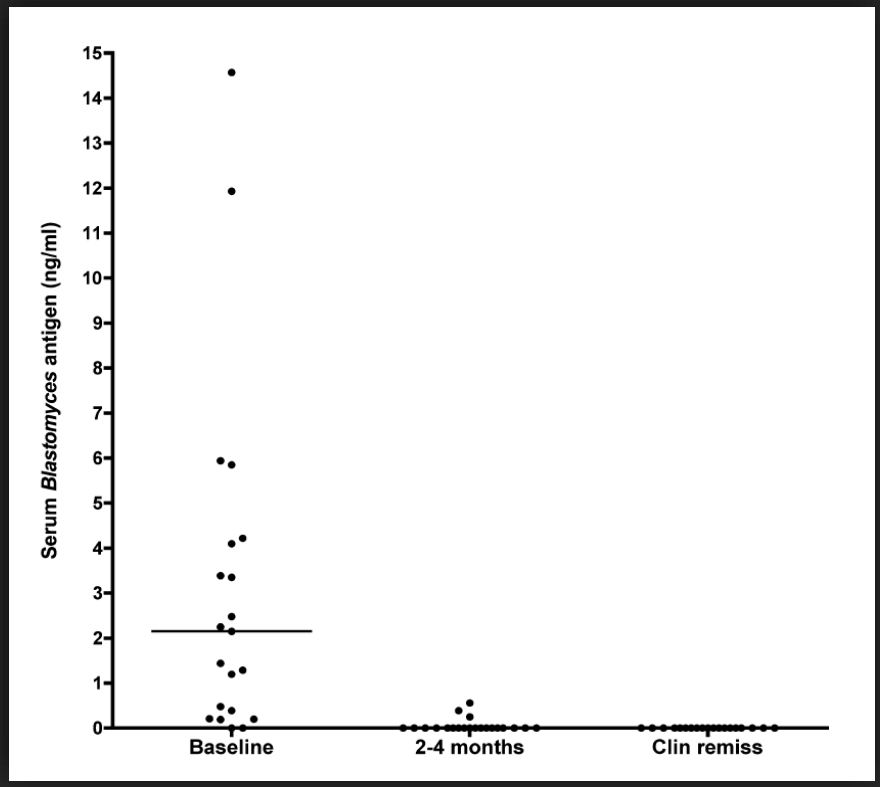


J Vet Intern Med 2014;28:305–310

Serum and Urine *Blastomyces* Antigen Concentrations as Markers of Clinical Remission in Dogs Treated for Systemic Blastomycosis

D.S. Foy, L.A. Trepanier, E.J. Kirsch, and L.J. Wheat

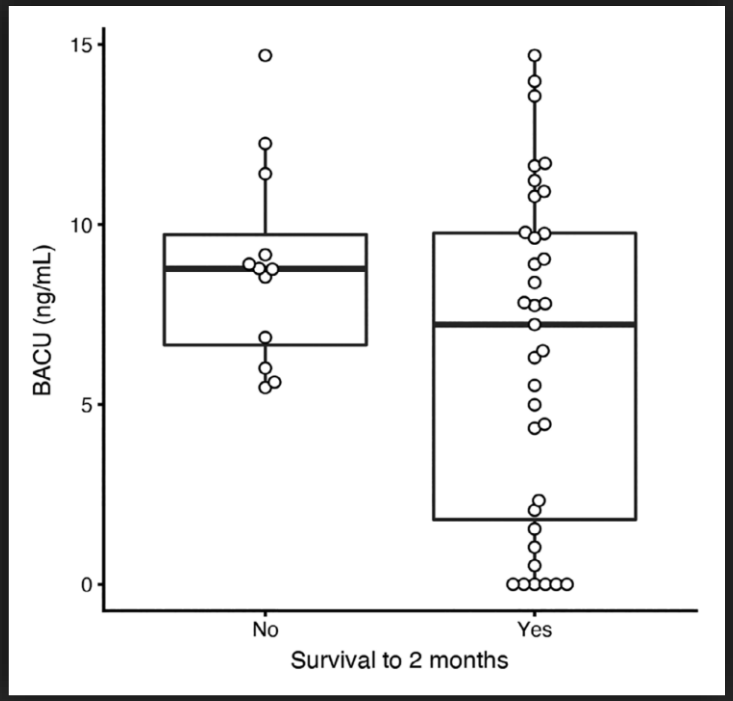




Monitoring Tool	Criteria	Notes
Treatment Duration	Minimum of 6 months	▪ Required duration is often much longer.
History	≥1-month past resolution of clinical signs	▪ Mild exercise intolerance might persist, most notable in working or performance animals. ▪ Persistent tracheobronchial lymphadenopathy can cause cough, requiring concurrent corticosteroid treatment.
Physical Examination	≥1-month past resolution of physical exam abnormalities	▪ Differentiating active ocular disease from permanent inactive change is important.
Imaging Studies	≥1-month past resolution of imaging abnormalities	▪ Pulmonary scarring can be permanent and can cause static focal unstructured interstitial lung disease. ▪ Radiographic bone lesions should improve but might never return to normal.
MVista® Blasto Antigen (urine)	≥1-month past no detectable antigen OR Antigen ≤0.4 ng/ml on 2 consecutive rechecks at least 3 months apart	▪ Most dogs, and essentially all cats, have no detectable antigen at the time of remission. ▪ Submit antigen test at diagnosis, every 3 months during treatment, and at 6 months then every 12 months after treatment.

Retrospective analysis of the effects of *Blastomyces* antigen concentration in urine and radiographic findings on survival in dogs with blastomycosis

Laura O. Motschenbacher | Eva Furrow | Aaron K. Rendahl | Esther G. Nell | Kari L. Anderson | Lindsay K. Merkel | Edward E. Patterson



- Urine antigen <5 ng/ml
  - 6m survival = 100%
- Urine antigen ≥5 ng/ml
  - 6m survival = 69%

MiraVista VETERINARY DIAGNOSTICS

Blasto Antibody

- IgG Antibody EIA
  - 95 sensitivity
  - 95 specificity
  - Uses:
    - Antigen (-) still suspicious (5-10% cases)
    - Confirm low (+) antigen result
    - Differentiate *Blasto* from *Histo*
- Antibody Immunodiffusion
  - Not recommended- Low Sensitivity
    - 3 published studies:
      - 33/86 = 38%

MiraVista VETERINARY DIAGNOSTICS

Evaluation of an enzyme immunoassay for antibodies to a recombinant *Blastomyces* adhesin-1 repeat antigen as an aid in the diagnosis of blastomycosis in dogs

Alyssa C. Mourning, DVM; Edward E. Patterson, DVM, PhD; Emily J. Kirsch, BS; Janelle S. Renschler, DVM, PhD; Linda A. Wolf, DVM; Jasmin K. Paris, BVSc; Michelle M. Durkin, MS; Lawrence J. Wheat, MD

Test and group	Sample: Type	Sample: No. tested	Positive	Negative	Sensitivity (95% confidence interval [%])	Specificity (95% confidence interval [%])
Quantitative *Blastomyces dermatitidis* antigen EIA						
Blastomycosis	Urine	21	21	0	100 (80.8–100)	—
	Serum	20	20	0	100 (80–100)	—
Nonfungal pulmonary disease	Urine	21	1	20	—	95 (74.1–99.8)
	Serum	18	0	18	—	100 (78.1–100)
Histoplasmosis	Urine	8	6	2	—	25 (44.5–64.4)
	Serum	—	—	—	—	—
Healthy controls	Urine	20	0	20	—	100 (80–100)
	Serum	20	0	20	—	100 (79–100)
A-antigen antibody AGID						
Blastomycosis	Serum	20	13	7	65 (40.8–84.6)	—
Nonfungal pulmonary disease	Serum	18	0	18	—	100 (78.1–100)
Histoplasmosis	Serum	8	0	8	—	100 (59.8–100)
Healthy controls	Serum	20	0	20	—	100 (80–100)
rBAD-1 antibody EIA						
Blastomycosis	Serum	20	19	1	95 (75.1–99.9)	—
Nonfungal pulmonary disease	Serum	19	0	19	—	100 (79–100)
Histoplasmosis	Serum	8	1	7	—	88 (47.4–99.7)
Healthy controls	Serum	20	1	19	—	95 (68.3–98.8)

*Samples from all dogs were not available for testing in every assay as a result of sampling error or miscommunication. From the blastomycosis group, this included 1 dog each lacking results for the serum antigen EIA, antibody EIA, and AGID. From the nonfungal pulmonary disease group, this included missing results for the serum antigen EIA (3 dogs), AGID assay (3 dogs), and antibody EIA (2 dogs). Sera from dogs with histoplasmosis were not assessed with the antigen EIA.

— = Not applicable.

Utility of diagnostic tests for and medical treatment of pulmonary blastomycosis in dogs: 125 cases (1989–2006)

Laura J. Crews, DVM, MS; Daniel A. Feeney, DVM, MS, DACVR; Carl R. Jessen, DVM, PhD, DACVR; Allison B. Newman, DVM; Leslie C. Sharkey, DVM, PhD, DACVP

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Transthoracic FNA	57	46 (81)
Transtracheal lavage fluid	39	27 (69)
Sputum	4	4 (100)
Lymph node	24	19 (79)
Skin	32	31 (97)
Prostate gland	3	3 (100)
Ocular tissue	3	2 (67)
Joint fluid	2	2 (100)
AGID[a]	24	12 (50)
Fungal culture	6	2 (33)

Multiple diagnostic tests were performed in 69 dogs.
FNA = Fine-needle aspirate. AGID = Agar gel immunodiffusion test.

Ocular findings in cats with blastomycosis: 19 cases (1978–2019)

Jacob

Clinical aspects of natural infection with *Blastomyces dermatitidis* in cats: 8 cases (1991–2005)

Cutaneous blastomycosis and dermatophytic pseudomycetoma in a Persian cat from Bangkok, Thailand

Lerpen

Ariya Cl

Cutaneous and Systemic Blastomycosis, Hypercalcemia, and Excess Synthesis of Calcitriol in a Domestic Shorthair Cat

Blastomycosis in indoor cats: Suburban Chicago, Illinois, USA

& Lawrence

Cerebral *Blastomyces dermatitidis* infection in a cat

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