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CBS 817

10/5/23

Andrews, Blake J., et al. "Blood concentration of symmetric dimethylarginine correlates with kidney damage as assessed with a proposed histologic grading system for chronic kidney disease in tigers (Panthera tigris)." *Journal of the American Veterinary Medical Association* 260.13 (2022): 1-8.

**Abstract:**

**OBJECTIVE**

To determine the utility of blood symmetric dimethylarginine (SDMA) concentration measurement as a diagnostic tool for chronic kidney disease (CKD) in tigers (Panthera tigris) by comparing results for SDMA with those for traditional renal biomarkers and investigating correlations between these biomarkers and histopathologic kidney changes in tigers with CKD.

**SAMPLE**

Blood, urine, and kidney samples from 35 tigers with CKD from 2 sanctuaries.

**PROCEDURES**

Blood (serum or plasma) and urine samples were collected antemortem. Necropsy, including gross and histologic assessment, was performed for tigers that died or were euthanized for quality-of-life reasons. Results for CKD biomarkers in blood (BUN, creatinine, phosphorus, and SDMA concentrations) and urine (protein concentration, urine protein-to-creatinine ratio, and urine specific gravity) were evaluated for correlation with histologic kidney damage scored with an objective grading scale defined by percentage of inflammation, fibrosis, and tubular atrophy.

**RESULTS**

Symmetric dimethylarginine had the strongest significant correlation (ρ = 0.667) with histologic kidney damage score, followed by urine specific gravity (ρ = –0.639), blood creatinine concentration (ρ = 0.624), and BUN (ρ = 0.588). No significant correlation with kidney score was identified for blood phosphorus concentration, urine protein concentration, or the urine protein-to-creatinine ratio.

**CLINICAL RELEVANCE**

We recommend SDMA be prioritized as a renal biomarker in tigers, with SDMA results considered in addition to those of other traditional renal biomarkers when assessing kidney function in tigers. Additionally, the grading scale we developed could be replicated across patients and pathologists for more consistent postmortem assessment of CKD in tigers.

**Background:**

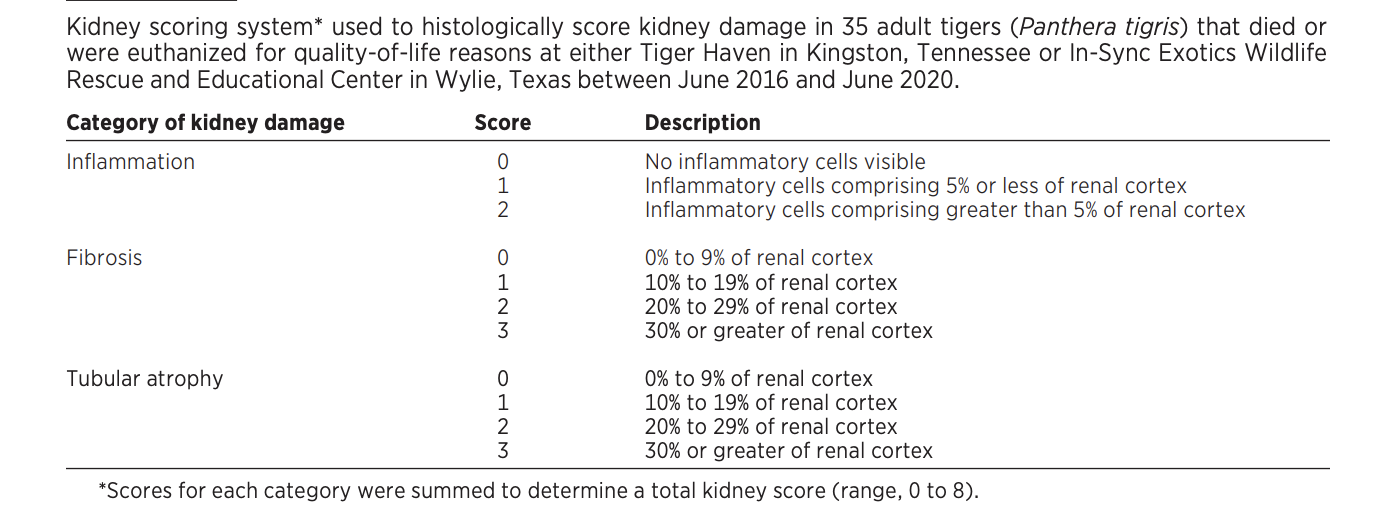
* CKD is one of the most prevalent diseases in felid species, including non-domestic felids
* Antemortem diagnosis of renal disease historically confirmed by elevated BUN, creatinine, or phosphorus, high UPC, and low USG
* SDMA is a product of protein metabolism, >90% excreted through kidneys, marker for kidney function and GFR
* Diagnostic value in other species (cats, dogs, ferrets) for earlier detection of renal disease
* In tigers, blood concentration SDMA has been shown to increase 3.6 months before concentration creatinine
* Creatinine and BUN influenced by extrarenal factors such as muscle mass for creatinine and hepatic function/nutritional status for BUN
* In tigers, ultrasonographic renal dimensions not sensitive or specific for renal disease
* Phlebotomy can be performed via behavioral training in awake or lightly sedated tigers
* Lymphocytic interstitial nephritis is the most prevalent renal lesion in tigers, presumptively result in decreased renal function

**Key Points:**

* Plasma and serum samples collected from 86 adult tigers for measurement of BUN, creatinine, phosphorus, and SDMA
* Urine collected via cystocentesis/catheterization in certain cases for urinalysis and/or UPC, and histopathology performed on any tigers that died (n=35)
* Novel grading scale created for histologic assessment of kidneys
  + Tubulointerstitial nephritis (interstitial inflammation, fibrosis, and tubular atrophy) is the most dominant renal condition in tigers
  + Inflammation was graded at 20X magnification on a scale of 0 to 2, whereas fibrosis and tubular atrophy were each graded at 100X magnification on a scale of 0 to 3, for a total renal histologic score of 0 to 8.
* SDMA was the biomarker with the greatest correlation to histologic kidney score; significantly correlated with all 3 categories of histologic changes
* Creatinine, BUN, and USG also had significant correlations with kidney score
* Phosphorus, urine protein concentration, and UPC were not significantly correlated with kidney score

**Takeaway:**

SDMA was the most effective among renal biomarkers evaluated for antemortem, indirect assessment of histologic kidney damage. This finding was supported by a grading scale that can be replicated across patients and pathologists for more consistent postmortem assessment of CKD in tigers.

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Mota, Stéphanie M., João Brandão, and Amanda Guthrie. "Comparison of blood symmetric dimethylarginine and creatinine as endogenous markers of kidney function in captive tigers (*Panthera tigris*)." *Journal of Zoo and Wildlife Medicine* 52.2 (2021): 628-637.

**Abstract:**

Chronic kidney disease (CKD) is a common cause of morbidity and mortality in captive tigers (*Panthera tigris*). Blood creatinine (Cr) and blood urea nitrogen measurements are inexpensive and common biomarkers used to evaluate renal function. However, several limitations have been reported regarding their sensitivity and interindividual variability. Symmetric dimethylarginine (SDMA) has been suggested to be a more sensitive biomarker that is less affected by extrarenal factors and has a strong correlation with glomerular filtration rate and blood Cr in several species. This project aimed to identify the usefulness of SDMA as an endogenous marker of kidney function in captive tigers. The hypothesis of this study is that increased circulating SDMA is positively associated with increased blood Cr. SDMA and Cr were measured in 65 banked samples (serum and plasma) from 30 individual captive tigers. The samples were collected over a 38-y period and stored at -21C. SDMA and Cr concentrations were determined using the commercially available SDMA test and enzymatic colorimetric methods, respectively. SDMA had a significant positive association with Cr (for every 1 unit increase of log SDMA, Cr increased by 82%, P = 0.0002). Age and subspecies influenced Cr but not SDMA concentrations. In one animal, blood SDMA increased above the ZIMS reported range approximately 3.6 mo before Cr increased. SDMA is currently indicated for the diagnosis of CKD in domestic felids and seems also promising in nondomestic felids. Further prospective studies might improve the understanding of the performance of this biomarker.

**Background:**

* Several retrospective studies have identified chronic kidney disease (CKD) as one of the most common causes of morbidity and death of geriatric felids in captivity
* The most common pathological findings reported in tigers with renal disease include interstitial nephritis, pyelitis, intratubular concrements, and tubular degeneration
* Creatinine (Cr) and blood urea nitrogen (BUN) are inexpensive and common biomarkers used to evaluate kidney function. However, several limitations have been reported regarding their sensitivity and interindividual variability.
* SDMA is a product of intracellular protein methylation and appears to be eliminated primarily by the kidney, less affected by external factors compared to Cr and BUN
* SDMA is more sensitive to decline in GFR, allowing for earlier diagnosis of CKD
* Early recognition of decreased kidney function in tigers will allow earlier diagnosis, better monitoring, and earlier initiation of treatment

**Key Points:**

* The objectives of the project were to (1) evaluate the agreement between the historical Cr value measured at the time of the original collection and the recent Cr result of the same sample; (2) evaluate the relationship between blood SDMA and Cr levels; (3) analyze the influence of age, sex, and subspecies on the levels of blood SDMA and Cr; (4) determine whether blood SDMA could be used as an earlier biomarker rather than blood Cr for diagnosing kidney disease
* Paired blood SDMA and Cr concentrations were determined using a commercially available high-throughput immunoassay (IDEXX SDMA Test) and enzymatic colorimetric methods, respectively (65 samples from 30 tigers)
* All kidneys from dead tigers at ZSL London Zoo or ZSL Whipsnade Zoo were stored in 10% neutral buffered formalin and examined histologically
* Historical Cr results obtained at the time of blood collection (available for 50/65 samples) did not change substantially over time when compared with recent Cr results
* SDMA had a significant positive association with Cr (for every 1 unit increase in log SDMA, Cr increased 82%)
* Cr increased by 4% each year as age increased (P = 0.0002) and Sumatran tigers demonstrated 41% higher blood Cr concentration than Amur tiger Cr (P = 0.047). Neither age nor subspecies was associated with SDMA concentration
* In one of seven tigers, blood SDMA increased above the ZIMS range approximately 3.6 months before an increase in Cr.

**Takeaway:**

The hypothesis of a positive association between blood SDMA and Cr was confirmed. Age and subspecies influenced Cr but not SDMA concentrations. In one animal, blood SDMA increased above the ZIMS reported range approximately 3.6 mo before Cr increased. SDMA is currently indicated for the diagnosis of CKD in domestic felids and seems also promising in nondomestic felids.

Cushing, Andrew C., et al. "Method comparison for measurement of symmetric dimethylarginine in tigers (*Panthera tigris*)." *Journal of Zoo and Wildlife Medicine* 53.1 (2022): 200-203.

**Abstract:**

Renal disease is well documented in nondomestic felids and is monitored and diagnosed by serum concentration of blood urea nitrogen, creatinine, and phosphorous. Symmetric dimethylarginine (SDMA) has proven to be an earlier and more sensitive biomarker for the assessment of glomerular filtration rate. Although SDMA is commonly measured in nondomestic felids, information concerning the validity of the assay is lacking. The purpose of the study was to perform a method comparison between high-throughput immunoassay and the reference method, liquid chromatography–tandem mass spectrometry (LC-MS/MS), to quantify SDMA concentrations in tiger blood samples. Concentrations of SDMA were measured for 81 individual tiger samples. The SDMA immunoassay demonstrated excellent correlation to the LC-MS/MS reference method. A Passing and Bablok linear regression analysis had a slope of 1.03 (95% CI, 0.99–1.11), an intercept of 1.64 (95% CI, 0.46–2.34), and a Pearson *R*= 0.99. The mean bias was 1.53 µg/dl (95% CI, 0.63–2.42 µg/dl), and the limit of agreement was ±7.96 µg/dl. The degree of bias is within established acceptance criteria of 1–3 µg/dl for the immunoassay. Although this study provides good evidence of the utility of the immunoassay to measure SDMA in tiger serum and plasma, further assay validation is recommended.

**Background:**

* CKD is well-documented in tigers, and is traditionally diagnosed/monitored by serum BUN, creatinine, phosphorus, urinalysis, and USG.
* Creatinine elevation does not occur until GFR has decreased by more than 70%, and BUN is affected by nutritional and hepatic factors
* SMDA is an earlier and more sensitive marker of CKD in domestic cats and dogs
* SDMA is produced intracellularly by catabolism of arginine-methylated proteins, >90% excreted through kidneys, freely filtered through glomerus with little to no renal metabolism
* Tigers often suffer from CKD, and early detection could lead to implementation of-renal protective treatments
* A commercial SDMA immunoassay is available for application in veterinary species and has been validated in a number of species
  + Information concerning the validity of the commercially available assay lacking in tigers

**Key Points:**

* Purpose was to perform a method comparison of a highthroughput immunoassay (IDEXX SDMA Test) to the reference method, liquid chromatography–tandem mass spectrometry (LC-MS/MS), to quantify SDMA concentrations in tiger serum and plasma samples.
* Serum or plasma samples from 81 tigers obtained from sample bank at large non-domestic felid rescue
* The SDMA immunoassay demonstrated excellent correlation to the LC-MS/MS reference method, which has been determined to be a sensitive, accurate, and robust method for SDMA determination in serum or plasma
* The degree of bias determined in the comparison of methods is within established acceptance criteria of 1–3 lg/dl for the immunoassay
* Full analytical validation of the immunoassay for tigers would require additional studies
* Although the SDMA immunoassay has been validated for the domestic cat (*Felis catus*) and the cheetah (*Acinonyx jubatus*), further studies are required to determine whether the assay has similar accuracy and precision for tiger samples.

**Takeaway:**

The SDMA immunoassay (IDEXX SDMA Test) demonstrated excellent correlation to the reference method, liquid chromatography–tandem mass spectrometry (LC-MS/MS) in tigers. Although this study provides good evidence of the utility of the immunoassay to measure SDMA in tiger serum and plasma, further assay validation is recommended.

*JZWM* 2021 52(3):886-892

[**Biomarkers Of Gastrointestinal Disease In Cheetahs (*Acinonyx jubatus*)**](https://doi.org/10.1638/2021-0012)

Fox L, Haefele H, Uelmen J, et al

**ABSTRACT:** Gastrointestinal disease is a common clinical problem in captive cheetahs (*Acinonyx jubatus*). It is reported that gastritis affects the vast majority of the captive population of cheetahs. Pancreatitis and acute and chronic enteritis have also been reported. These issues pose significant long-term health and welfare implications for cheetahs. Cobalamin, folate, methylmalonic acid (MMA), gastrin, feline pancreatic-specific lipase immunoreactivity (fPLI), and feline trypsin-like immunoreactivity (fTLI) immunoassays are important biomarkers of gastrointestinal disease in domestic cats. The goal of this study was to determine if these immunoassays validated in domestic cats could be used clinically in cheetahs, by establishing reference intervals (RI) for these biomarkers in cheetahs. A cohort of 40 clinically healthy cheetahs was selected from three zoological institutions on the basis of being free of clinical gastrointestinal disease and extra-gastrointestinal disease that could affect biomarkers, as well as having banked frozen serum. Cheetah biomarker RI, with domestic cat RI for comparison in parentheses, are as follows: cobalamin 470-618 pg/ml (290-1500 pg/ml), folate 2.2-15.7 ng/ml (9.7-21.6 ng/ml), MMA 365-450 nM/L (139-897 nM/L), fPLI 0.5-1.2 µg/L (0-4 µg/L), and gastrin 30-50 pg/ml (<10-39.5 pg/ml). This study shows that RI for gastrointestinal biomarkers can be notably different, even between species that are as closely related as the domestic cat and the cheetah. Additionally, it was found that the fTLI assay does not cross-immunoreact with cheetahs. In conclusion, this study emphasizes the importance of developing species-specific RI for biomarker assays and using caution when extrapolating RI from other species.

**Background**

* Cheetahs - IUCN ‘vulnerable,’ M&M predominantly chronic degenerative disease (not infectious)
  + Glomerulosclerosis, veno-occlusive disease, chronic lymphoplasmacytic gastritis, systemic amyloidosis
  + Higher cortisol concentrations and larger adrenal cortices compared to wild cheetahs suggest chronic stress is a factor
* Reported GI diseases: pancreatitis, enteritis, astrovirus, coronavirus, *Clostridium* spp.
  + 80% of captive cheetahs have histologic changes of gastritis
  + *Helicobacter* spp. suspected to contribute
    - Wild cheetahs have similar infections, but only 3% develop gastritis
* Folate (vitamin B9): water-soluble; co-factor for amino acid and vitamin synthesis; role in DNA replication, repair, and methylation; deficiency in cats causes poor appetite, growth, and bone marrow changes
  + Reduced with proximal small intestinal disease
  + Reduced storage with hepatic disease and reduced excretion with renal disease
  + Increased with small intestinal dysbiosis (bacteria synthesize folate)
* Cobalamin (vitamin B12): water-soluble, synthesized by microbiota in herbivores, carnivores depend on dietary intake
  + Role in DNA synthesis - deficiency affects rapidly dividing cells (GI, hematopoietic), can cause GI disease, central and peripheral neuropathies, immunodeficiencies, and myelopathies
  + Reduced with ileum disease (distal SI) from destruction of ileal cobalamin receptors
  + Reduced EPI from carrier protein deficiency (intrinsic factor) and pancreatic protease deficiency that would normally digest cobalamin-binding protein (R protein)
  + Reduced with small intestinal dysbiosis
* MMA: increases when cells are deficient in cobalamin; a marker of cellular cobalamin deficiency
  + Cobalamin-dependent reactions occur intracellularly, so MMA is a better indicator
  + Excreted through kidneys, so interpret cautiously with kidney disease
* Gastrin: peptide hormone produced by G cells in stomach and proximal duodenum, stimulates gastric acid production, has trophic effects on gastric mucosa
  + Mildly increased with gastritis or IBD in dogs and CKD in cats
  + Marked increases suggest gastrinomas
  + Increased after PPI administration
* fPLI - measures pancreatic lipase
  + Elevation indicates acinar cell damage, most likely from pancreatitis
  + Chronic pancreatitis can lead to acute pancreatitis, DM, or EPI
  + False negatives are possible in cats with mild or chronic pancreatitis from fibrosis and atrophy that doesn’t cause leakage of pancreatic enzymes
* TLI - trypsin and trypsinogen from pancreatic acinar cells
  + Severely decreased with EPI
  + Clinical signs: impaired nutrient absorption, soft, voluminous stools, weight loss, vitamin deficiencies

**Key Points**

* Retrospective from three zoos, some had gastric biopsies opportunistically
  + Cheetahs with moderately severe or worse gastritis were excluded
* No correlation of any biomarker with sex
* Decreasing fPLI correlated with increasing age, but low fPLI is not clinically relevant
* No statistical correlation between cobalamin and MMA
* Couldn’t establish RI for fTLI because all were lower than the assay range
  + Lack of species cross-immunoreactivity for this assay
* Six cheetahs with moderate-severe gastritis had high serum gastrin concentrations

**TLDR:**

* fTLI assay does not cross-immunoreact with cheetahs
* MMA did not correlate with cobalamin
* Decreasing fPLI with increasing age in cheetahs
* Cheetahs with gastritis may have high serum gastrin
* RI for GI panels established in cheetahs

**Related Articles:**

Munson L, Nesbit JW, Meltzer DGA, Colly LP, Bolton L, Kriek NPJ. Diseases of captive cheetahs (*Acinonyx jubatus jubatus*) in South Africa: a 20-year retrospective study. J Zoo Wildl Med. 1999;30(3):342–347

Munson L, Terio KA, Worley M, Jago M, Bagot-Smith A, Marker L. Extrinsic factors significantly affect patterns of disease in free-ranging and captive cheetah (*Acinonyx jubatus*) populations. J Wildl Dis. 2005;41(3):542–548

*JZWM* 2023 53(4):744-754

[**Determination Of Specific Enteropathogen Presence In Captive Cheetahs (*Acinonyx jubatus*) Fed Various Diets Using Fluorescence In Situ Hybridization**](https://doi.org/10.1638/2022-0023)

Peel M, Torres RG, Hernández BA, Oakley BB

**ABSTRACT:** Chronic enteropathies pose an important difficulty in the captive management of cheetahs (*Acinonyx jubatus*) because of suspected multifactorial pathogenesis and the complex nature of enteric microbiota dynamics. Enterobacteriaceae, *Campylobacter* spp., *Clostridium perfringens*, *Helicobacter* spp., and *Salmonella* spp. are enteropathogens of interest because of their zoonotic potential and suspected contribution to enteropathies. This study aimed to determine the presence of these enteropathogens of interest in fecal samples from cheetahs (*N* = 48) fed different diets from three different institutions and to investigate the associations between diet, fecal score, and specific enteropathogen presence. Fluorescence in situ hybridization (FISH) with rRNA-targeted oligonucleotide probes were used to visualize and quantify putative enteropathogens in each sample concurrent with selective culturing for *Salmonella* and *Clostridium perfringens*. From FISH counts, carcass-fed animals had greater numbers of Enterobacteriaceae compared with animals fed low-fat dog food, although this trend was not statistically significant (*P* = 0.088). Furthermore, no significant associations were found between fecal score and bacterial load. Abundance of *Campylobacter* spp., *Clostridium perfringens*, or *Helicobacter* spp. as measured by FISH were not correlated with diet or fecal score. On the basis of these data, in agreement with published literature, it is concluded that these microbes may be commensals in the cheetah gastrointestinal tract and do not appear to be a primary cause of abnormal fecal scores.

**Key Points:**

* Chronic gastritis can be associated with *Helicobacter* spp. though disease is multifactorial
* Many presumed enteropathogens may be normal commensal flora
  + More enteropathogens were isolated from managed vs. free ranging cheetah
    - *C. perfringens* most common isolate
* FISH diagnostic determined to be a reliable diagnostic for entropathogens in this study
* Abundance of specific bacteria and Enterobacteriaceae was not significantly different by fecal score or diet
  + Enterobacteriaceae increased in carcass fed cheetahs (not significantly different)
* *Helicobacter* spp., *C. perfringens*, and *Campylobacter* spp. found in the majority of samples and were not correlated with fecal score or diet. *Salmonella* spp. not detected.
  + These bacteria should be considered commensals/opportunistic pathogens
* Carcass fed animals had a significantly higher prevalence of soft feces

**TLDR:** FISH was a reliable method to detect *Helicobacter* spp., *C. perfringens*, and *Campylobacter* spp. in healthy cheetahs, and there was no correlation to diet or fecal score

**Related Articles:**

Terio KA, Munson L, Marker L, Aldridge BM, Solnick JV. Comparison of *Helicobacter* spp. in cheetahs (*Acinonyx jubatus*) with and without gastritis. J Clin Microbiol. 2005;43(1):229–234

Munson L, Nesbit JW, Meltzer DGA, Colly LP, Bolton L, Kriek NPJ. Diseases of captive cheetahs (*Acinonyx jubatus jubatus*) in South Africa: a 20 year retrospective survey. J Zoo Wildl Med. 1999;30(3):342–347

Munson L, Terio KA, Worley M, Jago M, Bagot-Smith A, Marker L. Extrinsic factors significantly affect patterns of disease in free-ranging and captive cheetah (*Acinonyx jubatus*) populations. J Wildl Dis. 2005;41(3):542–548

A RETROSPECTIVE STUDY OF BRAIN LESIONS IN CAPTIVE NONDOMESTIC FELIDS

Alexander R. Viere, BS, Andrew C. Cushing, BVSc, Cert AVP (ZM), Dipl ACZM, Edward C. Ramsay, DVM, Dipl ACZM, and Linden E. Craig, DVM, PhD, Dipl ACVP

Abstract: This retrospective study identified and characterized brain lesions in captive nondomestic felids from a large cat sanctuary. Necropsy reports from January 2002 through December 2018 were examined, and gross images and microscopic slides were reviewed from individual cats, where available. In total, 255 cats met the following inclusion criteria: complete necropsy report available, brain examined grossly or microscopically, and age of >1 mon. Of the 255 cats, 49 cats (19%) were determined to have brain lesions. Eleven different felid species,

as well as one captive-bred hybrid (liger), were included in the study, with tigers (Panthera tigris) (55%) and lions (Panthera leo) (18%) being the most common species. Lesions were grouped into six etiologic categories: neoplastic (32%), vascular (26%), inflammatory or infectious (20%), congenital (9%), idiopathic (7%), and metabolic (6%). Not included in these categorized lesions were previously undescribed amphophilic globules in the cerebral cortex of many cats with and without other brain lesions; these were in 95% of lion and 93% of tiger brains where the cerebral cortex was available for histologic examination. These globules were not associated with clinical disease. The histopathologic and gross brain changes documented in this study provide insight into specific diseases and pathologic processes that affect the brains of captive large cat populations.

* Gender if affected animals that had lesions was evenly distributed
* Neoplastic lesions were the most common followed by vascular lesions and then lesions caused by inflammatory or infectious disease
* 14/17 of the neoplasms were primary brain neoplasms (meningioma being the most common)
* 7/12 had neoplasms that could only be seen microscopically and though to be incidental
* No animal with ischemic/infarction lesions had neurologic clinical signs
* Inflammatory: most common meningitis and encephalitis of unknown origin
* Pathogen: most common Blastomyces dermatitis
* The smallest category was metabolic lesions 6%: due secondary to renal disease (uremic encephalopathy)
* Amphophilic globules in the cerebral cortex were seen in 95% lions, and 93% tigers
  + Also found in liger, serval, cougar, leopard, snow leopards, and caracal
* Lymphoma is the most common secondary brain neoplasm in domestic cats- this was not seen in any of the felids in the study (including a few that had been diagnosed with lymphoma antemortem)
* Chiari-like formations have been reported in lions with association with hypovitaminosis A
* Alzheimer type II astrocytes were IDed in two of the cases evaluated- exact pathology unknown

Photomicrographs of two tigers with Blastomyces dermatidis infection of the brain. (a) In the cerebellar white matter of a 10-yr-old male tiger, pyogranulomatous inflammation surrounds medium-walled yeast organisms measuring 10–15 lm in diameter (arrows). 360 objective, H&E. (b) In the same tiger, the yeast walls are silver stain positive, and broad-based budding is identifiable (arrows). 360 objective, GMS. (c) Within the medulla oblongata of a second adult male tiger, pyogranulomatous inflammation surrounds a large thick-walled yeast organism measuring .30 lm in diameter (\*). 360 objective, H&E. (d) In the same tiger, the yeast wall is silver positive (\*). 360 objective, GMS.A collage of different cells

Description automatically generated

A microscope view of a cell

Description automatically generated

Photomicrograph of the cerebral cortex of a

15-yr-old spayed female lion. Multiple irregularly

round amphophilic globules (arrows) measuring 10–

15 lm in diameter are within the superficial cortex.

360 objective, H&E.

EXOCRINE PANCREATIC INSUFFICIENCY-LIKE SYNDROME IN FOUR CAPTIVE TIGERS (PANTHERA TIGRIS)

Lauren M. Mulreany, DVM, Edward C. Ramsay, DVM, Dipl ACZM, Andrew C. Cushing, BVSc, Cert AVP (Zoological Medicine), Dipl ACZM, Jan S. Suchodolski, Dr med vet, PhD, Dipl ACVM

(Immunology), Jonathan Lidbury, BVMS, MRCVS, PhD, Dipl ACVIM, Dipl ECVIM-CA, and Joerg

M. Steiner, Dr med vet, PhD, Dipl ACVIM, Dipl ECVIM-CA

Abstract: Exocrine pancreatic insufficiency (EPI) is a condition characterized by a decreased synthesis and secretion of pancreatic enzymes, which results in weight loss, poor hair coat, and diarrhea. The diagnostic test of choice for EPI in domestic cats is feline serum trypsin-like immunoreactivity (fTLI). This paper details four tigers (Panthera tigris) with clinical signs compatible with EPI. On the basis of domestic cat reference ranges, fTLI assays for all four clinically affected tigers were diagnostic for EPI (median 1.0 lg/L; range 0.5–1.2 lg/L). All four tigers had a rapid clinical response to pancreatic enzyme supplementation. Serum from 10 clinically healthy tigers was submitted for the fTLI assay, for comparative purposes. The healthy tigers’ fTLI assays were also within range for a diagnosis of EPI in domestic cats (median 3.1 lg/L; range 1.9–4.5 lg/L); however, clinically affected tigers had significantly lower serum fTLI concentrations than healthy tigers (P 1⁄4 0.0058). Serum cobalamin was below the detection limit in both the affected and healthy tigers (,150 ng/L). Measuring fTLI appears to be a useful tool in the diagnosis of EPI-like syndrome in tigers. As in other species, EPI-like syndrome in tigers may also be associated with cobalamin deficiency.

* Exocrine pancreatic insufficiency syndrome in domestic cats- develops secondary to chronic pancreatitis; EPI: insufficient synthesis and secretion of digestive enzymes from the exocrine pancreas
* Clinical signs of EPI: steatorrhea, undigested food in feces, increased appetite and poor haircoat
* Pancreatic function test= fTLI (feline serum trypsin-like immunoreactivity): measuring trypsinogen as well as trypsin; Treatment: exogenous enzyme supplementation and if deficient- cobalamin supplementation
* Affected tigers had a significantly lower fTLI concentrations than healthy tigers (the fTLI assay results were in diagnostic range for EPI in domestic cats)
* Serum cobalamin concentrations were below the detection limit in all affected and healthy animals
* All four affected tigers had improved hair coat and stool quality within a week of starting pancreatic enzyme supplementation
* Hypocobalaminemia is a common diagnostic finding in domestic cats with EPI: which can cause primary GI inflammation
* Serum folate concentrations were significantly greater in affected tigers compared to healthy ones (folate can increase due to intestinal dysbiosis and increased folate synthesis, increased folate absorption from lowered duodenal pH, or decreased activation to a useable form because of hypocobalaminemia)
* Interesting Note: Tigers did not like the taste of powdered pancreatic enzymes so tablets were needed

**MOUNTAIN LIONS (PUMA CONCOLOR) RESIST LONG-TERM DIETARY EXPOSURE TO CHRONIC WASTING DISEASE** – Lisa L. Wolfe, Karen A. Fox, Karen A. Griffin, Michael W. Miller. *Journal of Wildlife Diseases, 58(1), 2022, pp. 40–49.*

Abstract: For nearly 18 yr, we evaluated susceptibility of captive mountain lions (Puma concolor) to chronic wasting disease (CWD) in the face of repeated exposure associated with consuming infected cervid carcasses. Three mountain lions with a monomorphic prion protein gene (PRNP) sequence identical to that described previously for the species had access to parts of >432 infected carcasses during 2,013 feeding occasions, conservatively representing >14,000 kg of infected feed material, during May 2002 to March 2020. The proportion of diet in infected carcass material averaged 43% overall but differed from year to year (minimally 11–74%). Most infected carcasses were mule deer (Odocoileus hemionus; ~75%). We observed no clinical signs suggestive of progressive encephalopathy or other neurologic disease over the ~14.5–17.9 yr between first known exposure and eventual death. Histopathology revealed no spongiform changes or immunostaining suggestive of prion infection in multiple sections of nervous and lymphoid tissue. Similarly, none of 133 free-ranging mountain lion carcasses sampled opportunistically during 2004–20 showed immunostaining consistent with prion infection in sections of brainstem or lymph node. These findings align with prior work suggesting that CWD-associated prions face strong barriers to natural transmission among species outside the family Cervidae.

Background:

* Chronic wasting disease (CWD) = infectious prion disease = spongiform encephalopathy
  + Naturally infects deer (*Odocoileus*), elk (*Cervus canadensis*), and other cervids
* Humans and predators i.e. mountain lions could be exposed to CWD by eating infected deer meat
* Felids with BSE reported – CS included ataxia, tremors, hypermetria, falling, lameness, behavioral changes
* Domestic cats infected with CWD via intracerebral injection - stilted gait, weight loss, anorexia, polydipsia, patterned motor behaviors, head and tail tremors, ataxia
* Domestic cats orally challenged with brain tissue from a CWD-infected mule deer failed to contract prion disease over a 1.5–7-yr period

Methods: n=3 orphaned mountain lions were intermittently fed CWD infected meat (at least 20% of diet was infected) for 18 years

* Additionally screened 133 wild mountain lion samples with IHC of brainstem (obex of medulla oblongota) and retropharyngeal LN over same time period

Key Points:

* 3 lions that were deliberately exposed to CWD infected carcasses as diet items for 18 years never developed neurologic signs consistent with disease
* Histopath and IHC of these 3 mountain lions and additional 133 sampled carcasses of free-ranging mountain lions did not show evidence of prion disease or spongiform changes (neuronal vacuolation or neuropil spongiosis)

**TLDR:** Mountain lions unlikely to be susceptible to CWD through natural routes of exposure (ingestion)

**PSEUDORABIES (AUJESZKY’S DISEASE) IS AN UNDERDIAGNOSED CAUSE OF DEATH IN THE FLORIDA PANTHER (*PUMA CONCOLOR CORYI*)**. *JWD, 57(4), 2021.* Cunningham MW, Onorato DP, Sayler KA, Leone EH, Conley KJ, Mead DG, Crum Bradley JA, Maes RK, Kiupel M, Shindle DB, Wisely SM, Subramaniam K, Wise AG, Clemons BC, Cusack LM, Jansen D, Schueller P, Hernández FA, Waltzek TB.

Abstract: Feral swine (Sus scrofa), an important prey species for the endangered Florida panther (Puma concolor coryi), is the natural host for pseudorabies virus (PRV). Prior to this study, PRV had been detected in just three panthers. To determine the effect of PRV on the panther population, we prospectively necropsied 199 panthers and retrospectively reviewed necropsy and laboratory findings, reexamined histology, and tested archived tissues using real-time PCR from 46 undiagnosed panther mortalities. Seven additional infections (two prospective, five retrospective) were detected for a total of 10 confirmed panther mortalities due to PRV. To further evaluate the effect of PRV, we categorized radio-collared (n=168) and uncollared panther mortalities (n=367) sampled from 1981 to 2018 based on the likelihood of PRV infection as confirmed, probable, suspected, possible, or unlikely/negative. Of 168 radio-collared panthers necropsied, PRV was the cause of death for between eight (confirmed; 4.8%) and 32 (combined confirmed, probable, suspected, and possible categories; 19.0%) panthers. The number of radio-collared panther mortalities due to PRV was estimated to be 15 (95% empirical limits: 12–19), representing 8.9% (confidence interval: 4.6–13.2%) of mortalities. Gross necropsy findings in 10 confirmed cases were nonspecific. Microscopic changes included slight to mild perivascular cuffing and gliosis (primarily in the brain stem), lymphoplasmacytic meningoencephalitis (cerebral cortex), and intranuclear inclusion bodies (adrenal medulla). The PRV glycoprotein C gene sequences from three positive panthers grouped with the sequence from a Florida feral swine. Our findings indicate that PRV may be an important and underdiagnosed cause of death in Florida panthers.

Background:

* Florida panther = endangered ssp. of puma/mountain lion/cougar (*Puma concolor*)
  + Only 20-30 panthers in 1980’s; >200 individuals today
* Feral swine = definitive host of suid alphaherpesvirus 1 (pseudorabies virus/PRV)
  + Causes Aujeszky’s disease (aka pseudorabies) in other mammals
  + No disease/latent/subclinical in naturally infected feral swine
    - Stressors such as concomitant disease, farrowing, breeding, can reactivate infection and lead to viral shedding and subsequent risk of transmission
  + Domestic swine → embryo resorption, abortion, stillbirths, fever, respiratory signs, neurologic disease, death in neonates
  + Other carnivores, ruminants, rodents → typically fatal

Methods: evaluated retrospective (n=336; 1981-2012) and prospective (n=199; 2013-18) necropsies and PRV tests to determine prevalence of PRV in Florida panthers between 1981 – 2018

Key Points:

* PRV was found as cause of death in 9% of radio collared panthers
  + Higher than previously suspected (2%)
  + 3rd leading cause of death (behind conspecific aggression and vehicle collision)
  + Telemetry data, gross and microscopic path suggest acute death in these animals
* Likely underdiagnosed in felids due to often focal and unilateral infection; missed in samples
  + Often focal and unilateral infection thus a negative real-time PCR alone does not necessarily rule out infection as sample collected may not contain the virus
  + Low sensitivity of rtPCR - two confirmed PRV cases in frozen tissues on virus isolation were negative on rtPCR >10y later
  + Recommend PCR on medulla oblongata just rostral to obex on fresh carcasses
* PRV panther prevalence was associated with higher swine density (in northern Florida) i.e. in and around game enclosures
  + Ingestion of infected swine is the likely source of transmission
* Absence of pathology does not rule out PRV infection
  + Gross: 10/15 confirmed positive animals had nonspecific findings
  + Histopath: mild perivascular cuffing and gliosis (brain stem), lymphoplasmacytic meningoencephalitis (cerebral cortex), intranuclear inclusion bodies (adrenal medulla)
* Management proposals
  + Increase white-tailed deer density to decrease panther reliance on swine as food
  + Feral swine management (vaccines, harvest, density reduction) to reduce PRV
  + Panther vaccination for PRV (safe and effective drug not available currently)
  + Determine epizootiology of PRV in feral swine specifically - PRV was eradicated in domestic swine but remains endemic in feral swine in the US

**TLDR: Aujeszky’s disease/pseudorabies (alphaherpesvirus 1 or PRV) may be a significant disease threat to Florida panthers (responsible for 9% of radio-collared panthers mortalities) and further research for management strategies of pseudorabies in feral swine (the reservoir) is needed**

**Mortality review for the North American snow leopard (Panthera uncia) zoo population from January 1999 to December 2019.** *Journal of Zoo and Wildlife Medicine* 52.1 (2021): 145-156.

Laura Martinelli

**Abstract:** The objective of this 20-yr retrospective study was to review and summarize causes of mortality in the North American (NA) snow leopard population to inform and enhance animal health and husbandry practices. **Pathology reports were requested from all NA zoological institutions housing snow leopards that died between 01 January 1999 and 31 December 2019.** Data were reviewed and cause of death (COD) and concurrent diseases were summarized and compared by age group, organ system, and disease process. The **241 snow leopards** in this report include 109 males, 130 females, and two of undetermined sex. Among them were 116 geriatric snow leopards (>15 yr), 72 adults (15–3 yr), 16 juveniles (3 yr to 2 mo), 32 neonates (2 mo to 0 days), and five fetuses (<0 days). **Overall, noninfectious diseases were the most common COD across all age groups (73%). In** **adult and geriatric snow leopards, chronic renal disease (CRD) (38.8%) and malignant neoplasia (19.7%), including oral squamous cell carcinoma (6.4%), were a common COD.** **In juveniles and neonates, perinatal death and congenital diseases, including ocular coloboma (15.6%), were a common COD.** Individuals with CRD were 13.5 and 4.36 times more likely to have veno-occlusive disease and cardiac fibrosis, respectively. Snow leopards with urolithiasis were 5.27 times more likely to have CRD. Infectious (14.1%) and inflammatory diseases (8.7%) for which no specific etiology was identified were less common overall and more common in juveniles and neonates (25% and 21%, respectively). Neoplasms not previously reported in snow leopards or that are generally uncommon in the veterinary literature included transitional cell carcinoma of the urinary bladder (n = 7) and mesothelioma (n = 1).

Key Points

* Snow leopards are the largest carnivore to specialize in high-altitude mountain regions
* Snow leopards range across 12 Asian countries
* Noninfectious disease most common COD in all age groups
  + Geriatric + Adult 🡪 degenerative and neoplastic
  + Juvenile 🡪 anesthesia-related or other
  + Neonate 🡪 perinatal – maternal neglect, rejection, or trauma
* Juveniles + neonates more likely to die of infectious cause than other age groups
* Juveniles + neonates 3x more likely to die of respiratory disease than other age groups
* Most common COD by organ system was the urinary system (most often chronic renal disease-CRD), males 2.3x more likely to die of urinary system disease
  + Urolithiasis was common and associated with CRD
  + Most uroliths calcium-containing
  + Snow leopards with CRD more likely to have veno-occlusive disease (13.5x more), cardiac fibrosis (4.36x more), and enteritis (2.91x more)
    - Veno-occlusive disease specifically means subendothelial fibrosis with partial to complete occlusion of central or sublobular hepatic veins
* Euthanasia in neonates due to multiple ocular coloboma were reported (most commonly agenesis of one or both upper lids)
* The digestive system (including oral cavity + liver) was most common site for malignant tumors (SCC in oral cavity most common, sublingual most common location), suspect *Panthera uncia* papilloma virus 1 (PuPV-1) associated with SCC but not yet proven
* DJD most common at coxofemoral joint

**Take Home Point:** Major preventative health monitoring should include routine assessment of oral cavity to screen for SCC and bloodwork to screen for renal disease. Overall, this study provides useful information on Snow Leopard managed care populations.

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**A retrospective study of neoplasia in nondomestic felids in human care, with a comparative literature review.** *Journal of Zoo and Wildlife Medicine* 52.2 (2021): 413-426.

**Abstract:** This retrospective study of neoplasia in nondomestic felids in human care presents the cases diagnosed at Northwest ZooPath (NWZP), Monroe, Washington, from 1998 to 2017 in conjunction with a scoping literature review. The 554 neoplasms identified in 20 species in the NWZP archive were combined with the 984 neoplasms identified in those same species in the published literature. Some of the cases identified in the literature were from the NWZP archive. **Based on this review, mammary adenocarcinoma (183/1,483, 12.3%), lymphoma (89/1,483, 6.0%), squamous cell carcinoma (85/1,483, 5.7%), pheochromocytoma (57/1,483, 3.8%), and thyroid adenoma (57/1,483, 3.8%) are the most frequently reported neoplasms in nondomestic felids in human care.** Apparent species predilections for neoplasia include mammary adenocarcinoma in tigers, jaguars, lions, and jungle cats; lymphoma in lions and tigers; squamous cell carcinoma in snow leopards; pheochromocytoma in clouded leopards; ovarian adenocarcinoma in jaguars; cholangiocarcinoma in lions and tigers; multiple myeloma in tigers; bronchoalveolar adenocarcinoma in cougars and lions; hemangiosarcoma, hepatocellular carcinoma, and gastrointestinal adenocarcinoma in lions; mesothelioma in clouded leopards, lions, and tigers; myelolipoma and cutaneous mast cell tumor in cheetahs; soft tissue sarcomas in tigers; and transitional cell carcinoma of the urinary bladder in fishing cats.

Key Points:

* Mammary neoplasms are the most frequently reported neoplasm in nondomestic felids in human care
  + Malignancy rate of mammary neoplasms is high (97.4% in this study) and rapid metastasis to multiple sites frequent
  + Prolonged exposure to progestin contraceptive (MGA) linked to development of mammary adenocarcinoma in nondomestic felids
    - AZA Repro Mgmt Center recommends GnRH agonists, early ovariohysterectomy or ovariectomy and warns against long-term use of MGA
* Lymphoma second most frequently reported neoplasm
  + Common clinical signs – hyporexia, anorexia, lethargy, weight loss, splenomegaly, and lymphadenopathy
  + Multicentric distribution in lions and tigers, with it never involving GI in lions (contrary to domestic feline presentation)
  + Prognosis grave but clinical remission can be achieved

**Take Home Point:** Neoplasia is a common problem for nondomestic felids in managed care and understanding the species predilections can guide preventative medicine.