Schulz, J., Hammond, EE., Haymon, M., Ramis, A., Martorell, J., and Aguilar, RF. (2003). Magnetic resonance imaging as a method of diagnosing leukoencephalopathy in a cheetah *(Acinonyx jubatus)*. Verh. ber. Erkrg. Zootiere 41: 1-6.

Keywords: Acinonyx jubatus/captivity/cheetah/diagnosis/leukoencephalopathy/zoo

Abstract: Leukoencephalopathy is a recently described disease of cheetahs characterized by white matter degeneration in specific areas of the brain. A 12-year-old male cheetah (Acinonyx jubatus) presented with progressive hind-limb ataxia and incoordination of 22-month duration. Magnetic resonance imaging was utilized as a diagnostic technique. The regions of interest were defined as brain and spinal cord. Images produced by magnetic resonance did not show changes in the intensity of the cerebral white matter consistent with a chronic degenerative process. The absence of clear lesions on the MRI implies a final diagnosis can not be made until the animals' signs worsen, and a follow up MRI shows unequivocal lesions, or until C.N.S. lesions can be detected postmortem by means of histopathology. The animal's chronic neurologic signs, apparent occasional blindness, and slow recovery from anesthesia, associated with severe neurologic signs during recovery, indicate it will remain a strong clinical suspect of leukoencephalopathy. Should the animal in this case be found positive, it would suggest that the disease may be suspected clinically before magnetic resonance imaging is a diagnostic option.

# MAGNETIC RESONANCE IMAGING AS A METHOD OF DIAGNOSING LEUKOENCEPHALOPATHY IN A CHEETAH (ACINONYX JUBATUS)

Schulz J<sub>1</sub>, Hammond EE<sup>1</sup>, Haymon M<sub>2</sub>, Ramis A<sub>3</sub>, Martorell J<sub>3</sub>, Aguilar RF<sub>1</sub>

<sup>1</sup>Audubon Zoo-Audubon Nature Institute, 6500 Magazine Street, New Orleans, LA 70118, USA <sup>2</sup>Children's Hospital of New Orleans-Magnetic Resonance Unit, 200 Henry Clay Avenue, New <sup>2</sup>Orleans, LA 70118, USA

<sup>3</sup>Departament de Medicina i Cirugia Animal, Facultat de Veterinària, Universitat Autònoma de <sup>1</sup>Barcelona, 08193 Bellaterra, Catalunya, SPAIN

### Su mmary

Leukoencephalopathy is a recently described disease of cheetahs characterized by white matter degeneration in specific areas of the brain. A 12-year-old male cheetah (Acinonyx jubatus) presented with pro gressive hind-limb ataxia and incoordination of 22-month duration. Magnetic resonance imaging was utilized as a dia gnostic technique. The regions of interest were defined as brain and spinal cord. Images produced by magnetic resonance did not show changes in the intensity of the cerebral white matter consistent with a chronic degenerative process. The absence of clear lesions on the MRI implies a final dia gnosis can not be made until the animals' signs worsen, and a follow up MRI shows unequivocal lesions, or until C.N.S. lesions can be detected postmortem by means of histopathology. The animal's chronic neurologic signs, apparent occasional blindness, and slow recovery from anesthesia, associated with severe neurologic signs during recovery, indicate it will remain a strong clinical suspect of leukoencephalopathy. Should the animal in this case be found positive, it would suggest that the disease may be suspected clinically before magnetic resonance imaging is a dia gnostic option.

### Introduction

Leukoencephalopathy is a recently described disease of cheetahs (*Acinonyx jubatus*) characterized by white matter degeneration in specific areas of the brain (MUNSON, 1999a). Since 1997, leukoencephalopathy has been confirmed in at least 60 cheetahs in North America. Most of the cheetahs diagnosed post mortem in the US have been over 9 years old (MUNSON, pers. comm., 2003). At present, the only available techniques for antemortem diagnosis in suspected cases are magnetic resonance imaging (MRI) and computerized tomography (CT). Of these two, MRI is the most reliable (DE LAHUNTA, pers. comm., 2003).

### **Case Report**

A 12-year-old male cheetah weighing 52 kg presented with progressive hind-limb ataxia of 22-month duration. Keepers reported that the animal occasionally acted "blind" and appeared unable to locate its food. Frequent staggering and moderate to severe incoordination with hind-limb dragging were also reported to occur. The animal's 1 5-year-old dam died in 1997 of suspected leukoencephalopathy. Based on characteristic clinical signs and recent reports (MUNSON and TERIO, 2002) of a high incidence of this disease, a decision was made to obviate preliminary testing and perform an MRI of the affected animal.

The cheetah was chemically restrained with 210 mg tiletamine hydrochloride and zolazepam hydrochloride (Telazol®, Fort Dodge Laboratories, Fort Dodge, Iowa, 50501, USA) intra muscular (IM) delivered by means of a blowdart. The animal was intubated for ventilation support. Blood samples were drawn through an intra-venous (IV) catheter placed at the time of induction, and all values were within normal parameters for the animal's age-group (ISIS-MedArks- Reference Ranges for Physiological Values in Captive Wildlife - International Species Information System (ISIS). 2002. Apple Valley, Minnesota, USA). Anesthesia was maintained with IV propofol (PropoFlo®, Abbott Laboratories, North Chicago, Illinois, 60064, USA) in a continuous drip at a rate of 0.4 mg/kg/min.

The MRI was performed with a 1.5 Tesla closed field Horizon GE magnet. The regions of interest were defined as brain and spinal cord. Fluid-attenuated inversion recovery (FLAIR),  $T_1$  weighted, proton density, spectrum inversion recovery (SPIR), and  $T_2$  weighted images were taken as a baseline. The animal received 10.0 ml of a gadopentate dimeglumine solution (469.01 mg/ml) IV for tissue contrast and the entire series was repeated. Sagittal and transverse views of the regions of interest were captured over a two-hour period.

The animal recovered fully from anesthesia over a period of 96 hours. During this time it exhibited severe neurologic clinical signs of decreasing magnitude. By the fourth day, the neurologic signs had decreased to their pre-anesthetic level.

## **Resu Its**

Images produced by magnetic resonance were read by two experienced neurologists. They did not confirm any form of bilateral symmetrical changes in the intensity of the cerebral white matter nor any dilatation of the ventricles. These signs would have been consistent with a chronic degenerative process.

### Discussion

Ataxia, incoordination, and progressive hind-limb paresis in adult cheetahs are associated with numerous pathological processes. Spinal cord demyelination (WALZER and KÜBBER-HEISS, 1995), degenerative spinal disease (KOLMSTETTER et al., 2000; ROTHSCHILD et al., 1998), spongiform encephalopathy (BARON et al., 1997; KIRKWOOD et al., 1995), and leukoencephalopathy (MUNSON et al., 1999) have all been associated with the clinical signs observed in this animal. Cases of acute onset of hind limb ataxia-paresis have been described in young cheetahs (WALZER et al., 1998; PALMER et al., 2001). Blindness, abnormal responses to the environment, and incoordination are clinical signs of leukoencephalopathy (MUNSON et al., 1999). Clinical suspicion in this animal was heightened by intermittent upper motor neuron signs.

In cases of progressive hind-limb paralysis, adult cheetahs have had extensive demyelination of the spinal cord white matter from T6 to L3 (WALZER and KÜBBER-HEISS, 1995). These lesions have only been diagnosed postmortem to date. Degenerative spinal disorders include intervertebral disc disease and spondylosis. Most commonly affected is the lumbar area, but cervical and thoracic vertebrae may also be involved (KOLMSTETTER et al., 2000). Cheetah cubs with acute hind limb ataxia-paresis showed demyelination of the spinal cord (WALZER et al., 1998; WALZER et al., 2003) and cerebellum (PALMER et al., 2001). European felids exhibiting similar clinical sings have been

reported to have spongiform encephalopathy, a prion-induced disease affecting the entire brain axis 12

(KIRKWOOD et al. 1995; BARON et al., 1997). The primary histopathologic lesions found in leukoencephalopathy are limited to the cerebral cortical white matter (MUNSON, 1999b).

Leukoencephalopathy has been found in approximately 10% of the captive cheetah-population of the United States (MUNSON, 1999b). Clinical signs in affected animals include blindness, disorientation, ataxia and behavioral changes, although many cheetahs do not have specific neurologic signs. Leukoencephalopathy affects older cheetahs of both sexes. All animals have belonged to North American facilities (MUNSON, 1 999a). Histopathologic findings include bilateral degeneration and necrosis of the cerebral cortical white matter. Characteristic of the disease are reactive astrocytes with abnormal nuclei (MUNSON et al., 1999). Magnetic resonance imaging is the most reliable method of diagnosing leukoencephalopathy in suspect cases (DE LAHUNTA, pers. comm., 2003). The correlation between the extent of white matter lesions seen histologically and clinical signs the animal presents seems to be small. There is little experience with MRI results in comparison to clinical signs in this particular disease process (MUNSON, pers. comm., 2003).

Magnetic resonance is accomplished through the response of nuclei with odd protons or neutrons in the nucleus (especially hydrogen) and a specific magnetic spin resulting from excitation from radio frequency electromagnetic waves. Unlike computed tomography (CT), MRI results largely reflect the behavior and position of protons within water molecules in the tissues. It therefore has a greater sensitivity in subtle soft tissue types than CT (SPAULDING and LOOMIS, 1999). Magnetic resonance imaging has been used as a diagnostic technique in domestic animals (HUDSON et al., 1995; PODELL et al., 1999), nonhuman primates, birds, reptiles (SPAULDING and LOOMIS, 1999), and marine mammals (VAN BONN et al., 2000). Symmetric degeneration in the cerebral white matter can be demonstrated antemortem using MRI. Unfortunately, the lesions may not be evident, or the technique may not be sensitive enough to make an unequivocal diagnosis. The cheetah examined exemplifies the difficulties of the use of this technique.

The etiology of cheetah leukoencephalopathy remains unknown. Various possibilities are being researched and remain tentative to date. Vitamin B deficiency and mycotoxins can cause similar lesions (MUNSON et al. 1999). Helicobacter gastritis has been the only consistent concurrent infection in affected animals. Autoantibodies incited by Helicobacter could cross react with astrocyte surface antigens such as proton pumps. The destruction of parietal cells of the stomach by Helicobacter sp. could result in a decrease in Vitamin B<sub>12</sub> absorption, leading to a deficiency (MUNSON, 1999b). A statistically significant association between the disease and a high lifetime number of rabies vaccines was found during a preliminary epidemiological study. Aluminum in vaccines is known to cause neurodegenerative disease in domestic cats. The etiology of this disease is under current investigation (MUNSON and TERIO, 2002). Chronic persistent infections with feline corona virus, canine distemper virus and JC polyoma virus can cause similar diseases in other species, but no virus could be found in affected cheetahs (MUNSON et al., 1999). Even though the lesions do not look like those in prioninduced diseases, several animals have been tested for prions and all were negative (MUNSON, pers. comm., 2003). Since all cheetahs in captivity in North America have been fed the same commercial diet based on cull horsemeat and slaughterhouse byproducts, food product contamination by infectious or mycotic agents is also a possibility for the origin of this disease (DE LAHUNTA, pers. comm., 2003).

The animal's chronic neurologic signs, apparent occasional blindness, and slow recovery from anesthesia, associated with severe neurologic signs during recovery, imply it will remain a strong clinical suspect of leukoencephalopathy. Should the animal in this case be found positive, it would suggest that the disease may be suspected clinically before magnetic resonance imaging is a diagnostic option. Other etiologies for the observed clinical signs are possible, but unlikely, since

spinal cord segments of the MRI, blood values, and radiographs were within normal limits. In advanced cases, magnetic resonance imaging might be a benign, noninvasive technique that allows for the antemortem diagnosis of leukoencephalopathy. Future epidemiological studies continue to depend on maintaining accurate and detailed life-time clinical and management records of each animal.

### Acknowledgments

The authors are grateful to staff of the MRI-Unit of Children's Hospital of New Orleans, Dr. C. N ata li n i of the Clinical Sciences Department/Veterinary Anesthesia of the Louisiana State University School of Veterinary Medicine, Dr. S. B. Citino of White Oak Conservation Center, and Dr. D. L. N ei ffe r of the Disney Animal Kingdom, for their kind and generous support.

# References

BARON T, BELLI P, MADEC, JY, MOUTOU F, VITAUD C, SAVEY M (1997): Spongiform encephalopathy in an imported cheetah in France. Vet. Rec. 141, 270-271.

DE LAHUNTA (2003): Pers. comm.

HUDSON LC, CAUZINILLE L, KORNEGAY JN, TOMPKINS MB (1995): Magnetic resonance imaging of the normal feline brain. Vet Radiol Ultrasound 36, 267-275.

- KIRKWOOD JK, CUNNINGHAM AA, FLACH EJ, THORNTON SM, WELLS GAH (1995): Spongiform encephalopathy in another captive cheetah (Acinonyx jubatus): Evidence for variation in susceptibility or incubation periods between species? J. Zoo Wildl. Med. 26, 577-582.
- KOLMSTETTER C, MUNSON L, RAMSAY EC (2000): Degenerative spinal disease in large felids. J. Zoo Wildl. Med. 31, 15-19.

MUNSON L (1999a): Cheetah (Acinonyx jubatus) Species Survival Plan. In: AZA Annual Report on Conservation and Science 1998-99. Vol. I: Conservation Pro grams Reports. <u>http://www.aza.org/-</u> <u>conscience/consciencepubs/documents/ARCS9899Vol1.pdf</u> (virtual publication). Pp. 116-118.

MUNSON L (1999b): Necrotizing Leukoencephalopathy in Cheetahs (Acinonyx jubatus): Etiologic and

*Epidemiologic Investigations, AZA Conservation Endowment Fund. <u>http://www.aza.org/-</u> <u>ConScience/Documents/CEFExample 1.pdf</u> (virtual publication).* 

- MUNSON L, DE LAHUNTA A, CITINO SB, RADCLIFFE RW, NEIFFER DL, MONTALI RJ, STALIS I (1999): Leukoencephalopathy in cheetahs. Proc. Am. Assoc. Zoo Vet., 69.
- MUNSON L, TERIO K (2002): Update on Felid Diseases. In: WILD T DE, MELLEN JD (Eds), North American Felid Taxon Advisory Group (TAG) Annual Report and Action Plan 2002. <u>http://www.felidtag.org/pages/Reports/Action%20Plan%202002/2002midyear\_report.htm</u> (virtual publication).

MUNSON L (2003): Pers. comm.

- PALMER AC, CALLANAN JJ, GUERIN LA, SHEAHAN BJ, STRONACH N, FRANKLIN RJM (2001): Pro gressive encephalomyelopathy and cerebellar degeneration in 10 captive-bred cheetahs. Vet. Rec. <u>149</u>, 49-54.
- PODELL M, WACK R, VANDEWOUDE S (1999): Neurologic complications of feline immunodeficiency virus (FIV) in lions. Proc. Am. Assoc. Zoo Vet., 256-258.
- ROTHSCHILD BM, ROTHSCHILD C, WOODS RJ (1998): Inflammatory arthritis in large cats: an expanded spectrum of spondyloarthropathy. J. Zoo Wildl. Med. 29, 279-284.

SPA ULDING K, LOOMIS MR (1999): Principles and applications of computed tomography and magnetic resonance imaging in zoo and wildlife medicine. In: FOWLER ME, MILLER RE (Eds),

Zoo and Wild Animal Medicine. Current Therapy 4. Ed., Philadelphia, USA, Saunders Company. *Pp.* 83-88.

- VAN BONN WG, JENSEN ED, MILLER WG, LANG HM, RIDGWAY SH (2000): Clinical magnetic resonance imaging reference anatomy of Turicops truncatus, Proc. Am. Assoc. Zoo Vet. and Int. Assoc. Aqua. Anim. Med. Joint Conference, 558-560.
- WALZER C, URL A, ROBERT N, KÜBBER-HEISS A, NO WO TNY N, SCHMIDT P (2003): Idiopathic acute onset myelopathy in cheetah (Acinonyx jubatus) cubs. J. Zoo Wildl. Med. 34,in press.
- WALZER C, KÜBBER-HEISS A, GELBMANN W, SUCHY A, BA UDER B, WEISSENBOCK H (1998): Acute hind limb ataxia-paresis in cheetah (Acinonyx jubatus) cubs. Proc. Am. Assoc. Zoo Vet. and Am. Assoc. Wildl. Vet. Joint Conference, 79-82.

WALZER C, KÜBBER-HEISS A (1995): Pro gressive hind limb paralysis in adult cheetahs (Acinonyx jubatus). J. Zoo Wildl. Med. 26, 430-435