

Dzieduszycki, A. M., Zlamal, A., Ryba, M. S., Grieb, P., Taraszewska, A., Kruszewicz, A. G., and Jakucinski, M. 2004. Myelopathy in cheetah (*Acinonyx jubatus*) cubs treated with citidinediphosphocholine (CDP-Choline). European Association of Zoo- and Wildlife Veterinarians (EAZWV), 5th scientific meeting, May 19-23, 2004. 1-3. Ebeltoft. Denmark, European Association of Zoo- and Wildlife Veterinarians (EAZWV). 19-5-2004.

Keywords: *Acinonyx jubatus*/ataxia/CDP-choline/cheetah/myelopathy/neuropathology/veterinary

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## MYELOPATHY IN CHEETAH (*Acinonyx jubatus*) CUBS TREATED WITH CITIDINEDIPHOSPHOCHOLINE (CDP-CHOLINE)

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### Extended abstract

Cheetah status: two adult male and one 6 years old female "Giza", who gave birth to 7 kittens on 29<sup>th</sup> Feb 2003 in her 3<sup>rd</sup> brood. In one of the 10 weeks old cubs there was observed ataxia for the first time. Preliminary diagnosis based on bacteriological, parasitological and neurological methods. All found pathogens were treated adequately. Additionally, antiviral drug was administered for several days. In order to stop the progressive development of ataxia a neuroprotective drug (CDP-choline) was introduced orally. Neurological reflexes were controlled daily until the improvement of the animals' mobility was achieved.

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**Key words:** *Acinonyx jubatus*, ataxia, neuropathology, Citidinediphosphocholine (CDP-choline), myelopathy.

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### Introduction

Out of a seven new born cheetahs in the Warsaw Zoo, one of the females developed gait disorder in her sixth week of life. Within few weeks the disease spread over the whole litter. Symptoms observed in this group resembled those, described already under term of "ataxia". It consists in a range of gait disorders from slight sway-back to the degree when the animal can't walk and is unable to stand up at all. Ataxia itself is not a disease – it is only a symptom, however the aetiology remains unknown. Many various factors are suspected such as: metabolic (copper deficiency), infectious (viral or protozoan). The disease concerns certain structures within the Central and Peripheral Nervous System (1,2,3,4,5,).

### Materials and Methods

On 27<sup>th</sup> February 2003 there were seven cheetah cubs (*Acinonyx jubatus*) born in the Warsaw Zoological Garden in Poland: four females and three males. They were the third litter of the same parents couple (International Studbook numbers: female – 3902, male - 3668). Two previous litters were brought up with no problems whatsoever. The mother, together with the whole litter was kept in grassy outdoor enclosure of approximately 1000 m<sup>2</sup>. They had the direct access to one heated pen. Animals were fed a diet of rabbits and beef with vitamin and mineral supplements. Due to ascariasis they were regularly dewormed (pyrantelium). The first cub showed slight ataxia in sixth week with progressive course. Following weeks ataxia appeared in the rest of the litter. Due to evident neurological background the Citidinediphosphocholine (CDP-choline) was introduced. After death of four cheetah cubs, which wasn't related to primary disease, their cerebellum, brainstem and spinal cord were taken and fixed in 4% buffered formalin. For light microscopic study the transverse sections from many levels of spinal cord and the coronal sections from cerebellum, pons and medulla were taken embedded in paraffin and stained with standard methods.

## **Results**

### ***Clinical history***

In their seventh week of life cubs became listless and body weight gain slowed down. The body temperature remained normal. Just several days later first bilateral watery ocular and then mucopurulent nasal discharge occurred. The signs subsided within 10 days. In their second month first symptoms of disease were observed (ataxia). Due to suspected viral background cubs were treated with acyclovir (5). There was no improvement whatsoever.

As the response to cases described in world resources (particularly results of pathology), the group of scientists from Polish Academy of Science [Polish abbreviation: PAN] has proposed therapy with new drug Citidinediphosphocholine (CDP-choline). The drug has a neuroprotective action and was administered orally. First three of cheetah cubs with the disease symptoms were treated with CDP-choline. Because animals were touched by disease at a different time and the progress of symptoms differed from one to another, at the moment of the drug introduction the two of cubs were falling over and the third was in a state of sway-back. During following weeks the four others developed gait disorders of different degrees. The decision was made to introduce the drug to the rest of the litter. In order to monitor the therapy impact on ataxia, animals were constantly neurologically examined. Examinations consisted of: sense of pain in fore and hind fingertips, examination of radicles sensitivity, knee reflex, abdominal lower reflex and muscle strength of hind limbs as well as evaluation of the ataxia degree. All of that allowed to objectively observing progress in the treatment.

In 22<sup>nd</sup> week of their life, cheetahs developed another disease which was not related to the primary one (with ataxia). Its course was so acute, that in spite of almost immediate pharmaceutical intervention four animals were lost in deep generalised shock. However, with the great devotion of involved staff, three other were resuscitated. After recover from that unfortunate episode, increase of ataxia was observed. Again CDP-choline was introduced. Gradual and nearly constant gain of the gait ability was clearly seen until complete recover of two of cheetah cubs was achieved. The third one, that suffered the longest from the disease, has recovered up to the degree that allowed ceasing the treatment.

### ***Post mortem***

The most distinct changes of cerebellum appeared in cortex and white matter of paramedian and ansiform lobuli but the archicerebellum was less affected. Changes consisted of demyelination of white matter, predominantly in cortical folia, severe Purkinje cells loss and rarefaction of granule cells in cerebellar cortex with axonal swellings and formation of torpedoes in the granular layer or nerve fiber degenerations in the cortex, white matter and cerebellar nuclei associated with hyperplasia and hypertrophy of astroglial cells.

Mudulla and pons showed spongineous changes and demyelination of white matter in spino-cerebellar tracts, inferior cerebellar peduncles and focally in middle cerebellar peduncles. Dorsal funiculi and pyramids were unchanged. Inferior olivary nuclei were rather small and showed chromatolysis with loss of nerve cells.

Spinal cord lesions: myelinated fibers degeneration, vacuolation and mild astrogliosis of lateral and ventral columns, especially in ascending spinocerebellar tracts and in paramedian parts of ventral funiculi (peripheral parts of lateral funiculi). In one case changes occupied whole of lateral and ventral columns. Dorsal funiculi were less affected than lateral and ventral columns. The changes in white matter were pronounced mainly at the thoracic level of spinal cord. Chromatolysis of nerve cells of gray matter was present in ventral horn and thoracic Clarke's nucleus. Additionally, there was nerve fibers degeneration and vacuolation of myelin in spinal roots. There were also alterations and lack of ganglion cells with concomitant increase of satellite cells in ganglia of the dorsal root. The changes in spinal roots and ganglia were most prominent at the lumbar level of spinal cord.

## **Discussion**

As already mentioned above, ataxia is not a disease – it is a symptom. In fact the aetiology remains unknown. Certain authors suspect copper deficiency to be responsible for the condition (1). It doesn't seem to be likely because copper is involved in many co-enzymes and supportive substances in an organism. That is why its deficiency leads to multiple pathologies such as: disturbed erythropoiesis, collagen and myelin production and so on. As the result, copper

deficiency should be clinically manifested by multiple syndromes and not only by isolated one - that is ataxia. Moreover, copper, together with other minerals and vitamins supplemented Warsaw cheetahs. Two previous litters (free of ataxia) were fed the same way, with exactly the same supplementation. Other authors claim viral background with Herpes virus involved (5). Following those suggestions the cubs were medicated with acyclovir for 12 days. Nevertheless, the progress of the disease was not inhibited. Also neuropathology reveals no inflammatory lesions – so typical for viral diseases. Because aetiology remained unknown, symptomatic treatment drug (neuroprotective) was introduced. The drug in short is called CDP-choline.

Young cheetahs were medicated for 96 days. Neurological condition of all seven cubs was improving. Two ones with so heavy ataxia that they couldn't walk at all, with time passing under introduced treatment, have reached quite satisfactory condition – they become able to cover a distance of twelve meters. Other five were recovering too but unfortunate additional disease prevented from doing further observations in whole lot. Today, of three living animals the gait disorder in form of ataxia persisted only in one individual and yet it is so slight, that remains unnoticeable for visitors. What's even more: after caesurae of CDP-choline there is no symptoms escalation.

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