Dresser,B.L.; Gosselin,S.J.; Setchell,K.D.R.; Kramer,L.W.; Johnston,O.J.; Tarr,M.J.; Balistreri,W.F.1985. Possible cause of infertility in captive cheetah. Proceedings of the American Association of Zoological Parks and Aquariums; 558-559.

Keywords: Acinonyx jubatus/captive breeding/captivity/cheetah/diet/exogenous estrogens/health/infertility/veterinary/zoo

Abstract: High levels of estrogen were found in commercial exotic feline diet. These exogenous estrogens were determined to be biologically active. The estrogenic effects on the liver and female reproduction observed in the cheetah appear to be reversible after a change in the diet.

Proceedings of the American Association of Zoological Parks and Aquariums, pgs. 558-559, 1985.

## Possible Cause of Infertility in Captive Cheetah

B.L. Dresser<sup>1,2,3</sup>, S.J. Gosselin<sup>1,5</sup>, K.D.R. Setchell<sup>4</sup>, L. Kramer<sup>1</sup>,
O.J. Johnston<sup>5</sup>, M.J. Tarr<sup>6</sup>, W.F. Balistreri<sup>4</sup>
Cincinnati Zoo<sup>1</sup>; Kings Island Wild Animal Habitat<sup>2</sup>;
University of Cincinnati College of Medicine, Dept. Ob/Gyn<sup>3</sup>;
Children's Hospital Medical Center<sup>4</sup>; Merrell-Dow Research Institute<sup>5</sup>;
Ohio State University<sup>6</sup>

It is well known, that cheetah populations are diminishing in the wild due to poaching, habitat destruction and possibly to the lack of genetic variation (O'Brien et al, 1985). Captive animals often exhibit reproductive failure as well as shortened life spans. The number of offspring born in North American zoos has decreased annually since 1981 (1984 Cheetah Studbook) and the average adult age of reproductively active females in the captive population is 8.4 years. Most females only reproduce until approximately age 10 so the female breeding population, as a whole, is older and less likely to produce as many cubs.

Observations since the later 1960's, have indicated that captive cheetah were being lost due to liver failure of unknown causes. In 1970 (Dinnes and Henrickson, 1970) and in 1981 (van den Ingh et al, 1981), studies in cheetah demonstrated that the liver failures were due to veno-occlusive disease but the cause remained undetermined. The present study is the first to characterize veno-occlusive disease in captive cheetah as well as determine its association with infertility in sexually mature cheetah.

The livers and/or reproductive organs from more than 100 cheetah were evaluated histologically. The incidence of veno-occlusive disease was 60-65% in adults and most of these animals were known to be infertile before death. This population was compared to a known fertile population in South Africa (De Wildt Cheetah Research and Breeding Centre) that produced 230 cubs in less than 10 years (Bertschinger et al, 1984). No clinical signs of liver failure or hepatic vascular lesions were observed in the DeWildt cheetah. These animals, in contrast to most cheetah in North American zoos, were not fed a commercial diet or horsemeat.

Since the diet was a major difference between these two populations, comparisons of several parameters were made before and after the diet was changed in a group of cheetah at the Cincinnati Zoo. The change was from a commercially prepared feline diet to boneless chicken with vitamin and mineral supplement.

After three months there was improvement in several parameters evaluated (liver function, coagulation time, abnormal mitochondria...). All of these abnormalities, including veno-occlusive disease, have been previously associated with the effects of estrogen used in oral contraceptives in women during 1960-1970's (Alpert, 1976; Heldin, 1975; Perez et al, 1969).

The commercially prepared feline diet was analyzed by gas chromatography-mass spectrometry, allowing the definitive identification of compounds present in the diet. By this method, at least two estrogens derived from plants have been fully identified in large amounts as well as the presence of other estrogens, probably derived from horsemeat. However, even though these estrogens were identified at high levels, it does not necessarily follow that they are biologically active. Therefore, an extract of the diet was subsequently injected into immature female mice as a bioassay. This resulted in a dose

related increase in uterine weight within three days which confirmed that the extract was estrogenic and, therefore, could have a similar effect in cheetah. This would also explain the estrogenic lesions observed histologically in the uterus of the female cheetah.

In conclusion, high levels of estrogen were found in commercial exotic feline diet. These exogenous estrogens were determined to be biologically active. The estrogenic effects on the liver and female reproduction observed in the cheetah appear to be reversible after a change in the diet.

## Acknowledgements:

The authors would like to thank the following zoological institutions for their contributions to this project: Baltimore; Baton Rouge; Brookfield; Cheyenne Mountain; Columbus; Detroit; Gladys Porter; Houston; Kansas City; Lincoln Park; Louisville; National; St. Louis; San Antonio; San Diego; Toledo; Toronto; Fossil Rim Ranch; Wildlife Safari (Oregon); Institute of Zoology, London, England; Sydney, Australia and DeWildt Cheetah Research and Breeding Centre, South Africa.

## References:

Alpert, L.L., 1976. Veno-occlusive disease of the liver associated with oral contraceptives: Case report and review of literature. Hum. Pathol. 7:709-718.

Bertschinger, H.J., Meltzer, D.G.A., van Dijk, A., Coubrough, R.I., Soley, J.T. and Collett, F.A., 1984. Cheetah life-line. Nuclear Active 30:2-7.

Dinnes, M.R. and Henrickson, R., 1970. Liver disease in cheetahs: A preliminary report. AAZV Annual Proceedings, pp. 110-117.

Heldin, A.M., 1975. The effect of oral contraceptive estrogen on blood coagulation and fibrinolysis. Thrombos. Diathes. haemorrh. (Stuttg.) 33:370-378.

North American Regional Cheetah Studbook, 1984.

O'Brien, S.J., Roelke, M.E., Marker, L., Newman, A., Winkler, C.A., Meltzer, D., Colly, L., Evermann, J.F., Bush, M. and Wildt, D.E., 1985. Genetic basis for species vulnerability in the cheetah. Science 227:1428-1434.

Perez, V., Godosdisch, S., De Martire, J., Nicholson, R. and Di Paola, G., 1969. Oral contraceptives: Long-term use produces fine structural changes in liver mitochondria. Science 165:805-807.

van den Ingh, T.S., Zwort, P. and Heldstab, A., 1981. Veno-occlusive disease (VOD) of the liver in cheetahs and snow leopards. Schweiz. Arch. Tierheilk 123:323-327.