Amyloidosis in cheetahs (Acinonyx jubatus), transmissible?

Kanyon M. McLean, BS,1* Rebecca B. Garabed, VMD, MPVM, PhD,1 and Barbara A. Wolfe, DVM, PhD, Dipl ACZM2,2
1College of Veterinary Medicine, The Ohio State University, Columbus, OH 43210 USA; 2The Columbus Zoo and The Wilds, Columbus, OH 43065 USA

ABSTRACT
Amyloidosis causes pathology through the accumulation of misfolded amyloid A protein in visceral organs, often leading to death of the animal. The increase of amyloidosis in captive cheetahs is of grave concern for the species, yet nothing is definitively known about its mechanism of transmission. One hypothesis is that amyloidosis is transmissible. Cheetah demographic and disease data were analyzed to determine the likelihood that amyloidosis is infectious. While our analysis does not disprove the infectious transmission route, simple transmission is not supported based on our findings.

INTRODUCTION
Acinonyx jubatus
The wild cheetah (Acinonyx jubatus) population is thought to have declined over 30% in the last 18 years, with an estimated 10,000 total cheetahs remaining.1 Poor genetic diversity has been proposed to be the cause of increased disease susceptibility, increased juvenile mortality, and low reproductive fitness in captivity.2,4 Thus, preservation of the species is important, and any diseases affecting cheetahs could be devastating to the remaining populations.

Amyloidosis
Systemic AA amyloidosis is considered to be a major cause of morbidity and mortality among captive cheetah populations with an estimated prevalence of 70% in 1995, increased from 20% pre-1990.2,3,5 Amyloidoses are chronic, protein misfolding diseases, caused by the deposition and aggregation of the protein in visceral organs such as the liver and kidney, resulting in organ failure and death.3,5 Despite the high prevalence and fatal consequences of amyloidosis in cheetahs, little is known about the etiology and transmission of AA amyloidosis.

Hypothesis
One hypothesis for the disease etiology is that amyloidosis transmits amongst cheetahs, similar to the way chronic wasting disease is thought to transmit in cervids. Zhang et al. (2008) found AA amyloid fibrils in cheetah feces that were infective in mule deer. Ecol Appl 16: 2208–2214.

METHODS
Six zoos were included in this study: Cincinnati, Columbus, Fossil Rim, White Oak, WildLife Safari, and The Wilds.

Odds Ratio Calculations
The risk of transmission among cheetahs co-habiting in a zoo for different lengths of time was quantified using odds ratios. Levels of exposure to known infected cheetahs were: high (>30 cheetah days), medium (10 to 30 cheetah days) and low (<10 cheetah days). Exposure data were based on the 2012 International Cheetah Studbook, and disease data were based on records on cheetahs dying between 1990 and 2010 retrieved from the species survival plan’s official pathologist.

Model Development
• Metapopulation models were designed for a homogeneously mixing and a heterogeneously mixing population and were then compared to infection data.
• Each model included three main disease states – susceptible (S), sub-clinically infected (Ih) and clinically infected (Ic) – as well as an environmental component (E).
• Figure 1 represents the model for all six zoos as a homogeneously mixing population.
• Figure 2 represents all six zoos as sub-populations within a metapopulation, producing an overall heterogeneously mixing population.

RESULTS
Odds Ratios Calculations
Table 1. Odds Ratios Calculations

<table>
<thead>
<tr>
<th>Odds Ratio</th>
<th>Confidence Interval</th>
<th>P-value</th>
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<tbody>
<tr>
<td>High</td>
<td>0.603</td>
<td>0.159-1.787</td>
</tr>
<tr>
<td>Mid</td>
<td>0.695</td>
<td>0.203-3.230</td>
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Odds ratio for mid-level exposure was 0.603 (p=0.362, CI: 0.194-1.787) and for low-level exposure was 0.695 (p=0.555, CI: 0.203-3.230), so there was no significant effect of exposure to infected cheetahs on development of amyloidosis.

Model Simulations
Figure 3 represents the simulation of a homogenous population. This model estimates a significantly higher number of clinical amyloidosis cases than those seen in necropsy reports.

CONCLUSIONS
Simple transmission is not supported based on initial odds ratio calculations.

The heterogeneous model fits observed data better than the homogeneous model. More complex hypotheses include a genetic component or the need for another inflammatory process to activate the disease.

REFERENCES

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