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The Influence of Quarantine on Reproductive Cycling in Wild-Caught Baboons (*Papio anubis*)

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Keywords

Perivulvar tumescence; menstrual cycle; stress

Introduction

Adaptive suppression of the hypothalamic-pituitary-gonadal axis in response to acute or chronic stress is associated with disruption of the menstrual cycle in human [4] and nonhuman primates [5]. Perturbations of the menstrual cycle have been observed following transport [2], alterations in housing [8, 13], and chronic restraint [3] in baboons and macaques. Due to a close approximation of reproductive tract anatomy and physiology, wild-caught baboons are successfully utilized in models of human female reproductive tract disease [1] [7]. The use of wild-caught animals necessitates a prolonged quarantine period to avoid introduction of disease to established captive populations. In cases where these baboons are used in studies of reproductive pathophysiology, experiments may be affected by alterations in cycling associated with quarantine. Here we retrospectively evaluated veterinary medical records of wild-caught female baboons following capture in order to better characterize the impact of quarantine on menstrual cycle.

Materials and Methods

Humane care guidelines

Wild-caught olive baboons (*Papio anubis*) trapped with permission of the Kenyan Wildlife Service were housed at the Institute for Primate Research (IPR; Karen, Kenya). *In vivo* work

was approved by the IPR Institutional Review Committee (IRC) and received an off-site exemption from the University of Michigan's University Committee on Use and Care of Animals (UCUCA). The IRC at IPR adheres to humane animal use principles in accordance with the three R's [10], Kenyan law (Cap 360: Prevention of Cruelty to Animals Act) and the International Guiding Principles for Biomedical Research Involving Animals (CIOMS, ICLAS 2012). The latter is consistent with the American Society of Primatology's Principles for the Ethical Treatment of Non-Human Primates.

Study population and inclusion criteria

A retrospective evaluation of veterinary records was performed for wild-caught female olive baboons quarantined at IPR from January 2009 until July 2013. Records from 143 animals were available. Records meeting the following four criteria were included for evaluation: (1) Animals were reproductively mature, (2) No evidence of pregnancy was observed on physical examination, (3) Unexpected death or euthanasia did not occur during or immediately following completion of quarantine, and (4) Collection of cycling data began within 50 days of capture and continued for at least 120 days. Animals with records not meeting these criteria were excluded from the analysis, leaving a remainder of 31 baboons (28 adults; 3 subadults).

Quarantine protocol

Following capture at one of three sites within Kenya (Ngurumani, Laikipia, and Olorbototo Ngomongo) baboons were transported to IPR within three days. Upon arrival, baboons were acclimated to group housing for two weeks at which time animals were anesthetized for veterinary evaluation followed by a quarantine of at least 90 days.

Reproductive cycle analysis

Reproductive cycle stage was recorded daily via cageside examination of perivulvar skin tumescence [11]. Cycle length was measured from the last day of maximal tumescence [9]. Total time in quarantine (TT_{Qu}) was calculated as the number of days from capture to exit from quarantine. Total time observed (TT_{obs}) was calculated as the number of days from the first to last observation (including time observed after quarantine). Percent time cycling was determined by $[1 - (\text{number of days to first day of first observed cycle} / TT_{obs})]$. Irregularity of each cycle was calculated as a deviation from the median observed cycle length (31 days): $[\ln(\text{observed}/31)]$ [9]. All data not normally distributed were log transformed and analyzed using unpaired t-test, one-way ANOVA and Tukey's multiple comparisons test where appropriate. Additionally, a series of linear mixed models were used to assess cycle length and cycle irregularity as a function of cycle number while controlling for repeated measures. Values are reported as median (range). For all analyses, $p < 0.05$ was considered significant. All statistical analyses were performed using GraphPad Prism version 6.0 (GraphPad Software, La Jolla, CA) or SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results

Records from 31 baboons were evaluated. Cycle and quarantine data are presented in Table 1. A total of 87 cycles were observed with a median length of 31 days (20–62 days) and 2

(0–9) complete cycles observed per animal. Median time to first observed cycle was 94 (19–181) days (see Table 1). 58% of baboons took greater than 71 days to begin cycling. Linear mixed models of the impact of cycle number on cycle irregularity and length suggested that for each additional cycle observed, a significant decrease in cycle length by 1.25 days was predicted ($p=0.006$). Predicted cycle length was 33.1, 31.9, and 30.7 days for the fourth, fifth, and sixth cycles, respectively. Predicted cycle irregularity was not significantly greater than zero for the fourth observed cycle and all subsequent cycles.

The impacts of initial observed weight and TT_{Qu} on time to first observed cycle, length of the first cycle, and percent time cycling while under observation were evaluated. Baboons greater than 11 kg at the onset of observation spent a significantly greater percent of time cycling than those weighing less than 11 kg ($p < 0.0001$). A quarantine length of greater than 100 days was associated with significantly greater percentage of time spent cycling during observation ($p = 0.01$) and a longer time to begin cycling following capture ($p = 0.02$).

Discussion

The median observed cycle length of 31 days reported here is consistent with previously documented cycle lengths of 30–35 days in captive baboon populations [6] and 32 days in wild troops [13]. In our study, cycling initiated in 94 (19–181) days and normalization of cycle length required approximately 4–6 cycles. This corroborates work on chronic stress in captive nonhuman primate populations. For example, in a study assessing menstrual cycle length as a toxicological endpoint, new housing resulted in prolongation of cycle length for up to 5 months in 8 of 24 cynomolgus macaques [2]. Similarly, in a study of 18 baboons moved from social to single housing, cycle length was prolonged for 4–5 cycles post-move [8]. The association of prolonged quarantine with a greater percent time spent cycling observed here may indicate that environmental and social stability is associated with regularity of reproductive cycling. In summary, the impact of quarantine on reproductive cycling is significant and should be taken into consideration when planning for use of wild-caught nonhuman primates on reproductive study.

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Table 1

Reproductive cycling parameters observed.

Parameter	Median	Range
Initial weight (kg)	11	8.5–15.6
Total time in quarantine (days)	140	89–164
Total time observed (days)	196	121–288
Complete cycles observed per animal	2	0–9
Percent time cycling	55	0–88
Time to first observed cycle (days)	94	19–181
First cycle length (days)	33	20–57
Second cycle length (days)	37	22–59