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Socialization Strategies and Disease Transmission in Captive Colonies of Nonhuman Primates

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Abstract

In captive research environments for nonhuman primates (NHP), social housing strategies are often in conflict with protocols designed to minimize disease transmission. This is particularly true in breeding colonies, and is especially relevant when attempting to eliminate specific pathogens from a population of primates. Numerous strategies have been used to establish such specific pathogen free (SPF) breeding colonies (primarily of macaques), ranging from nursery rearing of neonates to single housing of socially-reared yearlings to the rearing of infants in large social groups. All of these strategies attempt to balance the effects of the chosen socialization strategy on parameters related to disease transmission, including the ultimate elimination of the target pathogens. Such strategies may affect the overall disease states of NHP breeding colonies through selective breeding processes. This can occur either by creating subpopulations of animals that do not have target diseases (SPF colonies), but may have other issues; or by creating situations in which the ‘best’ animals are sold and the breeding colony is stocked with animals that may be more disease susceptible than those that were sold. The disease states of NHP research colonies also may be affected by selective utilization programs, in which animals removed from the breeding colony for health/behavior reasons, are preferentially chosen for use in scientific investigations. Such utilization criteria raise the question of whether ideal subjects are being chosen for use in research. Finally, captive primate colonies, where both socialization and disease states are intensely managed, may provide opportunities for those testing predictions from models of the interactions of socialization and disease transmission in the evolution of wild populations of NHP. This would be especially true for some extreme conditions of these disease ecology models, given the exceedingly high social densities and levels of pathogen control that exist in many captive nonhuman primate colonies.

Keywords

Disease transmission; Social density; Specific pathogen free; Colony management; Captivity; Disease ecology

INTRODUCTION

Many captive colonies of nonhuman primates (NHP) are purposefully managed to achieve at least two critical goals: 1) to minimize the transmission of disease in the colony [Morton et

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al., 2008; Roberts & Andrews, 2008] and 2) to maximize the social opportunities available to the animals that comprise the colony [Schapiro et al., 1994]. While these two goals can often be pursued using a single integrative strategy [Schapiro & Bushong, 1994; Schapiro et al., 1994], in certain instances, the provision of ‘additional’ social opportunities may create additional disease transmission opportunities, placing the attainment of the two goals in conflict with one another. In fact, single housing, the strategy that absolutely minimizes the probability of NHP-to-NHP disease transmission, simultaneously minimizes both the probability of the development of species-appropriate social behavior and the usefulness of natural social groupings. Additionally, inappropriate, but still social, housing can result in changes in disease susceptibility and/or progression, as Capitanio and colleagues have reported in their studies of SIV-infected rhesus living in unstable social groups [Capitanio et al., 1998]. It is obvious that compromise management strategies must be developed; ones that enhance social opportunities while maintaining disease transmission concerns well below acceptable thresholds [Mansfield, 2003; Schapiro et al., 1994].

Several such strategies exist, and have been effectively implemented, with the goal of the colony significantly influencing the particular strategy chosen [Morton et al., 2008]. For example, when attempting to develop a self-sustaining breeding colony of specific pathogen free (SPF) macaques, young subjects prosper most when housed in groups that provide considerable opportunities to be parented, to observe appropriate parenting, and to alloparent [Schapiro et al., 1995a; Schapiro et al., 1995b]. On the other hand, experiences related to learning parental behavior are much less important for the production of young subjects for short-term toxicological experiments. In general, the probability of disease transmission is likely to be the determining factor in the overall management of captive primates, especially social management, as there are likely to be limits to maximum acceptable risks for transmission of disease [Morton et al., 2008], while there are fewer limits to the amount of socialization that is desirable.

It is possible then, that captive colonies of NHP may be removed from the natural selection pressures that typically influence wild groups of NHP. While there is considerable evidence to suggest that social groupings of wild primates are influenced by issues related to the transmission of diseases [Altizer et al., 2003; Bonnell et al., 2010; Chapman et al., 2005; Gillespie et al., 2008; Leendertz et al., 2006; Nunn, 2010; Nunn et al., 2008], captive primates may be less likely to experience similar influences. As mentioned above, the choice of social housing strategies in NHP colonies is typically driven primarily by the needs and requirements of the human managers of the colony [Rommeck et al., 2009]; not by those of the primates. The animals, and the pressures under which they evolved, have very little input into the social conditions with which they are managed. One possible exception to this might be the outbreaks of problematic intragroup aggression that occur in many captive macaque colonies [Oates-O’Brien et al., 2010] and the social group re-formations that result from such aggressive episodes.

Similarly, the health of primates is also closely managed by the humans in charge of captive colonies [Butler et al., 1995]. Considerable effort is devoted to programs to prevent the occurrence of physical and mental maladies, and should an animal become sick, substantial, and often heroic, efforts are devoted to the treatment of the animal. While infectious diseases and intestinal parasites 1) are important concerns for veterinarians and others who manage colonies of captive primates, and 2) may help determine the socialization system used in the colony, it seems unlikely that these factors are exerting evolution-like selective pressures directly on the animals.

Although the captive environment is likely to be an extremely unnatural one in terms of social grouping, disease prevalence, and on many other dimensions, captive colonies may

still provide an analytical opportunity for researchers developing and testing models of the effects of disease transmission on the social organization of wild primates [Altizer et al., 2003; Gillespie et al., 2008; Nunn et al., 2008; Nunn, 2010]. Specifically, captive colonies may provide opportunities to test such disease ecology models at the extreme points on several different continua; for example, extremely high social densities, extremely low pathogen prevalences, and extremely high levels of resources (i.e., food, water, sleeping sites) that are consistently available. Captive NHP are typically maintained at high densities; as many as 1000 animals per 0.016 km² for rhesus macaques or as many as 350 animals per 0.0008 km² for owl monkeys (see Table 1). At the same time, NHP are maintained in highly sanitary laboratory environments that are disinfected regularly with the goal of maintaining pathogen prevalence at minimal levels. Additionally, regulations require that ALL captive NHP be provided with access to resources (food, water, etc.) adequate to maintain their physical and psychological well-being.

METHODS

A brief presentation of the specific pathogen free ‘derivation strategy’ that was employed at The University of Texas MD Anderson Cancer Center’s Michale E. Keeling Center for Comparative Medicine and Research (KCCMR) during the late 1980s and early 1990s [Buchl et al., 1997] will serve as the methodological anchor for this paper. All animals in the KCCMR colony entered the SPF program at the same time and comparable control data from non-SPF animals are not available. The derivation strategy was chosen specifically to address the interaction between social housing conditions and disease transmission, especially transmission of Herpes B virus (*Macacine herpesvirus 1*). Previous publications have described the KCCMR derivation strategy in detail [Buchl et al., 1997; Schapiro, 2002; Schapiro et al., 1994]; what follows is a brief summarization of the aspects of colony management that are relevant to the current discussion of 1) the relationships among socialization strategies and disease prevalence, and 2) the potential utility of captive colonies in tests of models of disease ecology. The KCCMR has been continuously accredited by AAALAC International since 1979. All procedures were approved by the UTMDACC IACUC and conformed to all local, state, and national laws regulating research on nonhuman primates. In addition, the research reported adhered to the ASP Principles for the Ethical Treatment of Non Human Primates.

Derivation strategy

Beginning in 1989, six-month-old, Indian-origin rhesus macaque infants, living in unimale-multifemale breeding groups (one adult male, four-six adult females, and their most recent offspring) were tested for the four target pathogens for the SPF program (*Macacine herpesvirus 1*, Simian Immunodeficiency Virus (SIV), Simian Retrovirus (SRV), and Simian T-Cell Lymphotropic Virus (STLV). SIV, SRV, and STLV were virtually nonexistent in the colony from the start. Therefore, the derivation strategy addressed Herpes B virus almost exclusively). Testing was conducted every eight weeks and those individuals that continued to test negative for the four pathogens were sequentially housed: 1) in single cages for the year between one and two years of age; 2) in pairs for the year between two and three years of age; and 3) in unimale-multifemale breeding groups or all-male groups for all subsequent years. If an animal tested indeterminate or positive for any of the pathogens, that individual was removed from the derivation strategy. Very few animals were removed from the program once they initially tested negative at six months of age.

During this early phase of the SPF program, one-half of the subjects were maintained in normal (control) conditions, while the other half of the subjects were maintained in enriched conditions, and the effects of environmental enrichment were studied [Schapiro & Bloomsmith, 1994; Schapiro & Bloomsmith, 1995; Schapiro et al., 1996a; Schapiro et al.,

1996b]. To briefly summarize these findings, social enrichment was more effective than inanimate enrichment at decreasing time spent in abnormal activities, while both forms of enrichment increased the amount of time monkeys spent in species-typical behaviors [Schapiro, 2002]. Both control and enriched subjects were able to breed and parent adequately, even after their year spent housed alone [Schapiro et al., 1995a; Schapiro et al., 1995b].

The strategy described above was chosen for reasons directly related to the interaction between socialization and disease transmission. In the late 1980s, it was thought that young rhesus living with their Herpes B positive parents were most likely to contract the virus from bites, scratches, sexual behavior, and/or any other contact with bodily fluids from infected animals [Kessler & Hilliard, 1990; Weigler et al., 1990]. Additionally, as a latent virus, it was felt that Herpes B virus was most likely to be expressed by animals when they were severely stressed. Therefore, remaining in the natal group with potentially positive parents until one year of age and then living alone for the next year was determined to be a workable strategy that would balance the negative virological/disease transmission consequences of living with positive animals for a year, with the behavioral benefits of living in social groups that functionally simulated natural [Lindburg, 1971] rhesus monkey groups. It was well known that social deprivation early in the development of captive macaques, such as might result from the nursery rearing of infants obtained via C-section (very low probability of disease transmission), resulted in a number of persistent behavioral and physiological deficits [Harlow & Harlow, 1962; Laudenslager et al., 1985; Rommeck et al., 2009]; a situation to be avoided when attempting to build a production colony.

Once individuals had developed a normal behavioral foundation during the first year of life in their natal group, social conditions were changed to 1) minimize the potential for virus transmission and contamination of a large number of subjects, and 2) maximize the probability of virus expression, through single and then, pair housing. An appropriate foundation of social behavior, one that included exposure to proper reproductive and parenting behavior and appeared predictive of reproductive and parental competence, was deemed critical for these young animals that were destined to form the core (as founders) of the SPF breeding colony.

After the first five years of the derivation strategy presented above (natal group to single cage to pair cage to breeding group), it became obvious that animals were not converting from negative to positive status for Herpes B virus during the years of restricted socialization [Hilliard & Ward, 1999; Ward & Hilliard, 1994]. Therefore, it was decided to maintain the frequency of testing (every 8 weeks), while eliminating both the single and pair housing components of the strategy [Schapiro et al., 1996b]. Since approximately 1995, subjects have been removed from their natal groups and placed into groups comprised of newly weaned animals. They have remained in these groups until they reached three years of age. At age three, unimale-multifemale groups or all-male groups were formed as before. Weanling groups were initially formed when the monkeys reached one year of age, but for the last decade, the weaning age has been lowered, with monkeys being placed into weanling groups at seven months of age. Additionally, 12 years ago, the frequency of viral surveillance was reduced from biannually to annually, as the vast majority of animals within the SPF colony were several generations removed from any monkey that tested indeterminate or positive for Herpes B virus.

In the KCCMR rhesus colony, proper Personal Protective Equipment (PPE), including eye protection, masks/respirators, long sleeves, boots, and gloves, have always been required for those working with macaques [Cohen et al., 2002]. Additionally, all personnel must step in bactericidal/virucidal foot baths as they enter and exit animal holding areas. In the very early

days of the derivation strategy, both non-SPF and SPF sub-colonies were maintained within a single compound, requiring the implementation of traffic patterns (SPF buildings/animals first; non-SPF buildings/animals last) and PPE guidelines (green scrubs when working with SPF animals; blue scrubs when working with non-SPF) designed to minimize the transmission of the target pathogens by humans and/or handling procedures.

RESULTS

Since the inception of the SPF colony, a variety of statistics, including morbidity, mortality, production, serology tests performed, and animals sold have been regularly recorded. Data from 2000–2010 are presented below. A major change in data collection and organization techniques was implemented in 2000. Although we have data from the early years of the SPF program, when the colony contained both non-SPF adult and SPF infant and juvenile monkeys, these data are not directly comparable to the more recent data set and are not included in this paper. The SPF program is now 22 years old, it is quite productive, and most of the animals from the colony that are available for use in research are four or five generations removed from any monkeys that ever tested positive for any of the target pathogens (primarily, Herpes B virus).

Each animal in the colony is tested annually (at a minimum) for Herpes B virus and the three retroviruses. Since 2000, there have been six indeterminate Herpes B tests and 10 positive tests (from 8,436 tests; 0.07% indeterminate and 0.12% positive, see Table 2). The actual number of animals that have tested indeterminate or positive is smaller, as any animal that tested indeterminate or positive was immediately tested again. There were essentially no indeterminate or positive test results for the other three target pathogens during this period or during the earlier phases of SPF colony development. Therefore, the results of these tests are not included in Table 2.

Gastrointestinal problems are the most frequent cause of morbidity in the SPF rhesus colony. Since 2000, on average, approximately 173 veterinary interventions per year for gastrointestinal problems have occurred (see Table 3). Again, the number of individuals treated per year is lower than that, as some animals require multiple diarrhea-related interventions during, and across, the year(s). Mortality (from all causes) is fairly low in the SPF colony, as seen in Table 4.

All of the breeding parameters (see Table 5) in the SPF colony are indicative of successful reproduction, resulting in the availability of a substantial number of Indian-origin, SPF rhesus macaques for use in research each year (1862 have been sold since the year 2000). Production statistics and the number of animals (by age class) made available for research each year are shown in Tables 5 and 6.

DISCUSSION

The data suggest that we have successfully achieved the dual goals that drive the establishment of most primate breeding colonies, especially those that are intended to eliminate a set of pathogens from an initially non-SPF population [Mansfield, 2003; Schapiro et al., 1994]. The SPF rhesus colony at the KCCMR is comprised of socially, reproductively, and parentally competent animals and has negligible incidences of Herpes B virus and the three simian retroviruses (SIV, STLV, and SRV) that were targeted for elimination in 1989.

While it is reasonably clear that we have successfully selected for animals that were negative for the target pathogens, it is somewhat less clear whether we have selected for (or against) other traits/characteristics that might be beneficial (disease resistance) or

detrimental (disease susceptibility) to the animals. This may seem like a minor problem in the time frame of just a few generations, but such artificial selection may have important implications for colonies in which the primary goal is to provide subjects for biomedical research projects. In general, enhancing the definition of subjects can have positive consequences for the power of experiments, but reductions in interindividual variation may also diminish the validity of certain experiments [Capitanio, 2010].

Artificial selection issues may be particularly important when considerable, and sometimes heroic, veterinary efforts are devoted to maintaining the health and utility of sick animals, either as breeders or as research subjects. Such efforts can include multiple multi-day, multi-antibiotic treatments for animals experiencing diarrhea [Bernacky et al., unpublished data]. Due to lower levels of scrutiny and higher thresholds for veterinary interventions, many of these animals would not have been diagnosed with, or treated for, diarrhea if they had lived in the natural environment. Similarly, they would have been unlikely to survive or reproduce in the wild and/or in the absence of veterinary care, and the possibility exists that reliance on these types of veterinary interventions in captivity may be artificially selecting for individuals that would have failed the test of natural selection. This is often considered problematic, however, several colonies of ‘unhealthy’ animals have been developed, specifically to study the disease processes involved in conditions that have important implications for human health (Krabbe’s disease [Borda et al., 2008] and Huntington’s disease transgenics [Yang et al., 2008]). Within the KCCMR SPF rhesus colony, several family groups prone to intestinal adenocarcinomas have been fortuitously identified and protected (Bernacky et al., unpublished data).

The initial stages in the development of a primate breeding colony (either SPF or conventional) would typically follow a pattern in which the ‘best’ available animals are used as the founders of the colony. This could include either wild-caught [Stanley, 2003] or captive-bred animals [Capitanio et al., 2006], depending on the type of colony being formed. Again, in the initial stages of colony development, the animals that are chosen for distribution to clients would more than likely be the ‘best of the best’ animals available in the colony (to impress investigators with the quality of the animals from this new source; Houghton, personal communication), leaving less desirable animals behind as replacement breeders for the continuation of the colony. Once such a pattern is established, the breeding colony could continue to be developed/replenished using these less than best animals, potentially adversely affecting the disease susceptibility and social competence of the colony, including those monkeys available for future sales.

Although the goal of many captive colonies is to maintain the monkeys in conditions in which pathogen prevalence is virtually zero, this is impossible [Baze & Bernacky, 2002; Elmore et al., 1992; Gibson, 1998]. In the KCCMR SPF colony, *Campylobacter spp.*, *Shigella flexneri*, *Escherichia coli*, *Balantidium coli*, *Entamoeba histolytica*, *Yersinia enterocolitica*, *Trichomonas spp.*, and several types of *Staphylococcus* and *Streptococcus* have all been documented to exist. KCCMR animals are also maintained with considerable access to the outdoors (central Texas, USA), bringing them into contact with the following potentially pathogenic animal vectors and/or their products: opossums, armadillos, skunks, raccoons, deer, rats, mice, cats, bats, squirrels, vultures, grackles, other songbirds, snakes, mosquitoes, flies, and other insects. Additional potential vectors include people and/or animal care products (enrichment devices [Bayne et al., 1993]) and procedures.

The effects that natural selection exert on primates in captive breeding colonies are likely to be overwhelmed by the effects exerted by captive management strategies (artificial selection). While captive selection is occurring with several conscious goals in mind (elimination of target pathogens), it has yet to be determined whether other traits are also

potentially affected by selection. Of current interest are those traits that might be selected for in animals that are destined to be distributed for research projects. It is unclear whether one should attempt to enrich the population with monkeys that appear to prosper in indoor, caged environments or attempt to choose those animals that prosper in outdoor, breeding colony environments. Alternatively, one could simply choose those animals that appear to look the best or those animals that possess particular genetic traits that make them valuable for certain investigations (e.g., MHC Class I alleles, [Mudd et al., 2011]). Different subsets of primates within a large breeding colony would be likely to satisfy these different criteria.

Captive NHP colonies and disease ecology

Captive colonies of NHP may provide useful insights into the understanding of disease ecology [Nunn, 2010; Nunn et al., 2008] in wild populations of NHP. Clearly, there are numerous fundamental differences between captive NHP colonies and wild populations of their conspecifics (described below and listed in Table 7), and many of these differences diminish the utility of captive colonies in assessments of disease ecology.

Differences between captivity and the wild that may prevent the use of captive data to test disease ecology models

Many captive colonies of NHP are located outside of the species', the pathogens', and the vectors' natural home range, reducing the validity of pathogen prevalence studies at many facilities. This would include most macaque breeding colonies in Europe and the United States.

Captive colonies are constructed with physical barriers that are specifically designed to prevent 1) disease transmission from one unit to another and 2) physical contact between subpopulations of primates. Buildings/enclosures are built a minimum distance from one another; subpopulations of monkeys are housed in separate indoor rooms; and individual cages are constructed and spaced to prevent contact between animals.

The enclosures, structures, and furnishings in captive colonies are frequently sanitized in order to prevent the development of conditions that might promote disease transmission. Similarly, active vermin control measures are used to control vectors that might contribute to the transmission of various diseases.

Captive animals are routinely scrutinized for symptoms of illness or injury. Minor symptoms, which are unlikely to be noticed, and are less likely to be treated, in wild populations, may be extensively treated in captive colonies. Additionally, primates in many colonies receive vaccinations to prevent outbreaks of specific diseases (measles, rabies, etc.).

Most of the humans encountered by captive nonhuman primates wear a variety of PPE to prevent human-to-NHP and NHP-to-human disease transmission. Such zoonotic processes have been problematic in the habitats of some wild NHP populations [Fedigan, 2010; Jones-Engel et al., 2008].

And finally, most captive NHP colonies have non-natural population pyramids that typically contain relatively small numbers of males and juvenile animals of both sexes. This is primarily due to the utilization of social groups that functionally simulate, but do not match natural groups (unimale-multifemale groups of macaques [Schapiro et al., 1994]), and the preferred distribution of younger animals for use in research.

Differences between captivity and the wild that may be valuable when using captive data to test disease ecology models

On the other hand, there are differences between captive colonies and natural populations that may be useful in certain types of tests of disease ecology models. These apply primarily to conditions at the extreme ends of certain continua.

Captive colonies of NHP are usually maintained at extremely high population densities; situations that, in the wild, might be conducive for the occurrence of epizootics. For instance, chimpanzees may be maintained in captivity at population densities that are 700–38,000 times those in the wild, and squirrel monkeys may be maintained at as many as 12,000 times natural population densities (see Table 1).

The health status of individuals within captive colonies is regularly and closely monitored, allowing for the accurate identification of animals with even minor health issues. As part of this process, health records in captive colonies are usually quite detailed, providing considerable opportunities to identify procedures/techniques/strategies that were successful (or unsuccessful) at addressing issues related to disease transmission.

Captive NHP are likely to be maintained in similar or the same environments throughout their lives in captivity, allowing for analyses in which habitat degradation, a potential influence on disease ecology for wild populations [Chapman et al., 2005], can be held constant. In a similar vein, captive primates must be provided with resources (food, water, sleeping sites, etc.) adequate to maintain their physical and psychological well-being. The average captive primate will, therefore never experience the types of resource fluctuations that occur frequently in wild habitats [Bonnell et al., 2010].

While aspects of the captive environment are likely to remain fairly consistent across captive colonies, and even within a single facility, several different levels of management practices related to disease transmission may be available for inclusion in disease ecology models. These may range from the strict conditions necessary for maintaining super-SPF colonies, to those appropriate for SPF colonies, and to the more relaxed requirements for maintaining conventional colonies [Kanthaswamy et al., 2010; Mansfield, 2003; Morton et al., 2008]. In addition, a variety of social grouping strategies may be available for assessment, within and across facilities. These can include large multimale-multifemale groups in outdoor field cages, smaller unimale-multifemale groups in indoor-outdoor runs, weanling groups in play cages, male-female pairs in indoor timed-mating laboratories, and single or paired animals in indoor research laboratories. Variations in aspects of the physical environment may also be available and relevant for analysis, including diet, flooring materials (dirt, concrete, or mesh); lighting schedules (natural vs. artificial); and/or climate control.

Captive colonies are typically physically isolated from one another, and many are closed and do not accept animals from other facilities. This virtually eliminates the possibility of any contact or disease transmission between populations, allowing for analyses of ‘isolated’ populations. The closest macaque colonies to Bastrop, TX are located in San Antonio, Dilley, and Alice, TX; 92, 163, and 197 miles away, respectively.

Human-NHP interactions occur frequently in captivity, and typically involve closer contact with NHP bodily fluids than would be encountered in more natural settings. In macaque colonies, whether SPF or conventional, humans wear considerable Personal Protective Equipment, to provide infection control from human-to-NHP, from NHP-to-people, and from NHP-to-NHP through people and handling procedures.

Using data from captive colonies to test disease ecology models

Although there are many important differences between the ecology and environments experienced by captive and wild groups of nonhuman primates, there may be enough useful information available from the plethora of data from captive colonies to justify preliminary tests of wild disease ecology models using captive populations. Across several relevant continua, the most fertile test conditions for assessing disease ecology models may be provided by the extremely high population densities, the extremely low pathogen prevalence, and the relatively high and consistent availability of resources in captive NHP colonies. However, there is a certain amount of circularity involved in arguing for the value of the captive data – disinfection and sanitation prevent disease transmission/outbreaks in groups of primates that are housed at extremely high densities. According to disease ecology models, such population densities might be thought to result in epizootics in natural conditions. In other words, disease prevalence is low in captive colonies, even though population densities are quite high, because active measures are taken to minimize the exposure of the animals to pathogens. Epizootics typically do not occur, even though animals are brought into, and spend long periods, in very close contact with one another and their potentially infectious excretions. This occurs in small areas where resources (feeders, water sources, sleeping sites) and pests (flies, mosquitoes, etc.) may be concentrated. While resources and pests may be concentrated in a small area, competition for resources [Bonnell et al., 2010] is unlikely to be as severe as in the wild, given that captive management procedures require the provision of adequate resources for all animals.

SUMMARY/CONCLUSIONS

The provision of social opportunities that are critical for the proper behavioral development of nonhuman primates makes it more difficult, but not impossible, to minimize disease transmission and/or the adverse effects of certain pathogens in captive primate colonies.

It is as yet unclear what other disease-related effects are associated with the artificial selection involved in the development of SPF primate colonies. Of particular interest is the potential for the co-selection of susceptibility (or resistance) to diarrhea-inducing pathogens.

The high quality of veterinary care in captive colonies allows primates, which probably would not have survived, to not only live, but also to reproduce. This raises several questions including 1) whether this type of heroic veterinary effort is selecting for suboptimal animals and 2) whether sick animals that have been saved are optimal, or even appropriate, models for biomedical investigations.

Captive colonies could serve as useful test systems for disease ecology models, especially at the extreme ends of certain continua (high social density, low pathogen prevalence, high resource availability, high habitat consistency), and when successful or unsuccessful disease control procedures/techniques/strategies have been identified.

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Table 1

Population Densities of Captive Primate Colonies at the Michale E. Keeling Center for Comparative Medicine and Research

Species	Number of animals in 'compound'	Area of 'compound' (km ²)	Density in captivity (animals/km ²)	Density in nature (animals/km ²)
<i>Macaca mulatta</i>	~1000	0.0158	~17,241	9.3 ^a
<i>Aotus spp.</i>	~350	0.0008	~437,500	14–40 ^b
<i>Saimiri spp.</i>	~500	0.0008	~625,000	50–80 ^c
<i>Pan troglodytes</i>	~175	0.0457	~3,829	0.09–5.0 ^d

^a[Melnick & Pearl, 1987]

^b[Robinson et al., 1987]

^c[Robinson & Janson, 1987]

^d[Nishida & Hiraiwa-Hasegawa, 1987]

Table 2 Serological Tests for the Specific Pathogens in the KCCMR SPF Rhesus Colony^a

Fiscal Year	# Herpes B and Retrovirus Tests	Indeterminate Herpes B	Positive Herpes B
2000	1396	0	3
2001	1466	3	0
2002	1430	0	0
2003	1488	1	4
2004	1586	1	1
2005	1590	0	0
2006	1628	0	0
2007	1906	0	2
2008	1940	1	0
2009	1922	0	0
2010 [*]	520	0	0

^aThere were no indeterminate or positive tests for SIV, STLV, or SRV during this period^{*}Sept. 1, 2010 – March 31, 2011 only

Table 3

Veterinary Interventions Due to Gastrointestinal (GI) Problems in the KCCMR SPF Rhesus Colony^a

Fiscal Year	GI: Adult	GI: Juvenile	GI: Infant	Total GI	Total Population	Approximate Average GI Interventions per Animal ^a
2000	94	54	25	173	698	0.25
2001	73	63	32	168	733	0.23
2002	38	33	15	86	715	0.12
2003	67	58	18	143	744	0.19
2004	73	42	22	137	793	0.17
2005	70	37	19	126	795	0.16
2006	121	94	15	230	814	0.28
2007	95	83	9	187	953	0.20
2008	145	126	0	271	945	0.29
2009	134	93	3	220	961	0.23
2010 [*]	97	61	1	159	914	0.17

^a Some animals received multiple interventions during a single fiscal year

^{*} Sept. 1, 2010 – March. 31, 2011 only

Table 4 Mortality in the KCCMR SPF Rhesus Colony^a

Calendar Year	Adults	Juveniles	Infants [*]	Total
2000	7	0	21	28
2001	49 [@]	0	18	67 [@]
2002	3	1	13	17
2003	11	5	20	36
2004	13	1	23	37
2005	14	7	19	40
2006	5	5	15	25
2007	12	8	23	43
2008	13	2	25	40
2009	15	4	28	47
2010	6	5	27	38

^aThe primary causes of death in the SPF rhesus colony are complications resulting from diarrhea or trauma

^{*}Includes abortions, stillbirths, and neonatal deaths prior to one year of age.

[@]A heating accident resulted in the deaths of 49 adult monkeys.

Table 5

Production Statistics from the KCCMR SPF Rhesus Colony

Calendar Year	Total Population	# Births	% Breeding Age Females that Conceived	# Stillbirths or Abortions	# Live Births	% Live Births	# Deaths	Lived to > 1 year of age	% Infant Survival
2000	699	210	84.0	17	193	91.9	5	188	97.4
2001	726	217	81.6	10	207	95.4	8	199	96.1
2002	733	230	90.4	10	220	95.7	7	213	96.8
2003	726	243	85.0	11	232	95.5	10	222	95.7
2004	837	261	90.1	11	250	95.8	12	238	95.2
2005	858	249	82.1	9	240	96.4	11	229	95.4
2006	879	246	83.6	9	237	96.3	6	231	97.5
2007	969	255	82.7	16	239	93.7	7	232	97.1
2008	886	238	76.0	13	226	95.0	13	213	94.2
2009	952	258	79.0	19	239	93.0	9	230	96.2
2010	972	255	80.4	20	235	92.1	7	228	97.0

Table 6

Animals Made Available for Research from the KCCMR SPF Rhesus Colony

Fiscal Year	Adults	Juveniles	Infants	Total
2000	24	74	31	129
2001	42	121	44	207
2002	8	139	10	157
2003	17	163	12	192
2004	6	163	0	169
2005	10	171	11	192
2006	17	87	14	118
2007	15	78	29	122
2008	90	143	35	268
2009	90	23	36	149
2010 *	11	144	4	159
TOTAL	330	1306	226	1862

* Sept. 1, 2010 – March 31, 2011 only

Table 7

Comparison of the Advantages and Disadvantages that Captive NHP Colonies may Provide for the Evaluation of Disease Ecology Models

Disadvantages of studying captive colonies	Advantages of studying captive colonies
Typically exist outside of the normal range of primates and their diseases	Extremely high population densities are used
Constructed with barriers designed to prevent disease transmission	Health records are rigorously maintained
Structures are frequently sanitized	There are variations in management practices across facilities
Vermin control measures are used	There are variations in management practices within facilities
Interactions between subsets of animals are prevented	There are typically large distances between captive facilities
Vaccinations and veterinary treatments are used to minimize morbidity	Environmental quality is likely to remain consistent over long periods
Population pyramids are non-natural	There is relatively little variation in the availability of resources (food, water, shelter) across individuals and/or groups
Personal protective equipment (PPE) is used routinely	Human-NHP interactions involving bodily fluids occur regularly
Artificial selection is probably overwhelming natural selection	Selection criteria can be controlled and/or manipulated
Animal health status is closely monitored allowing for the identification of subclinical problems	Animal health status is closely monitored allowing for the identification of subclinical problems