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A Longitudinal View of Primate Life in Two American Laboratories

Jonathan Balcombe
Independent Scientist and Author

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White Paper

Jonathan Balcombe, PhD

EXECUTIVE SUMMARY

If laboratory experiments weren't painful, stressful, harmful and lethal,
we would be performing them on human patients.

Six thousand pages of detailed records from two National Primate Research Centers were analyzed to document the potential hardships faced by the three populations of monkeys kept there (146 rhesus macaques, 37 chacma baboons, and 22 crab-eating macaques). These records were obtained by a US citizen concerned for the wellbeing of primates in labs.

Data were organized under several categories, including: demographic and mortality, housing history, environmental enrichment, experimental procedures, handling and other non-experimental manipulations, chemical agents, illness and injury.

The records spanned three decades. On average, macaques at Institution 1 died at seven years of age, while baboons at Institution 2 averaged nearly nine years of age. Roughly half of the monkeys at Institution 1 were killed as part of an experiment; most of the remainder were killed for non-experimental reasons, though often due to the effects of experiments.

On average, monkeys from both facilities were subjected to seven experiments during their lives. Among the more common procedures performed on macaques were catheter insertion and removal, surgical removal of the ovaries, and surgical insertion and removal of implants (e.g., minipumps implanted into the parascapular region). Procedures commonly performed on baboons were whole body irradiation, bone marrow biopsy with aspiration, and fetal stem cell transplantation.

Monkeys were regularly subjected to painful non-experimental procedures performed routinely in labs as part of clinical care, including: blood draws, injections, force-feedings or dosing, and tuberculin tests (which involve the injection of tuberculin into the upper eye-lid). These and other procedures (e.g., physical exams, experimental protocols) require handling and restraint of the animal, both of which are known to cause stress. Handling events were common for both populations: 113 times per year (nearly 3x per week) and 42 times per year (once every 9 days) for macaques and baboons, respectively.

Perhaps the greatest (and least appreciated) hardships these highly social animals face are the social disruptions of being moved from one cage to another, and the added trauma of being housed alone. The macaques at Institution 1 averaged 22 moves during their lifetimes and were caged alone cumulatively for more than half of their lives (on average four and a half years). Baboons at Institution 2 were moved an average of 31 times, and spent 41% of their lives living alone.

Chronic stress is a well-recognized risk factor for chronic illness (Elliott & Eisdorfer 1982, Manuck et al. 1991, McEwen & Stellar 1993). Illnesses were rampant at Institution 1, where the monkeys were afflicted with 1,440 separate infections involving 30 different types of pathogenic bacteria, viruses and parasites. Diarrhea was an especially persistent problem at Institution 1, afflicting nearly three-quarters of the monkeys there; half of these monkeys suffered chronic cases with five or more separate diagnoses. About a third of the monkeys suffered significant weight loss (10% or more, average 20%) at least once during their lives.

Injuries were also common at Institution 1. Amputations or avulsions (in which a body structure is forcibly detatched) were especially disturbing; most involved fingers and thumbs, and most appear to have been self-inflicted. Illnesses were less common among the baboons (Institution 2), with 15 individuals (40%) afflicted. The most common injuries in this population were lacerations and puncture wounds (75 incidences) and amputations (14).

Though there is no evidence that macaques and baboons are any less sensitive to pain than humans, we found pain relief to be severely lacking. An analysis of post-surgical pain relief at Institution 1 found that the monkeys typically got pain medication on the day of, and day after surgical procedures (e.g., Caesarean section, surgical removal of the ovaries) for which human patients typically receive 1-2 weeks of pain relieving drugs. We also assessed the possibility that many of the injections given at Institution 1 and 2 were for pain relief, but most (95% and 94%, respectively) were not pain relieving medications.

Environmental enrichment (EE), the provision of which was mandated by the 1985 amendment to the Animal Welfare Act that came into effect in 1991 (9 C.F.R. § 3.81), was minimal at both facilities according to the records. EE usually took the form of adding a toy or a food puzzle to the cage, or providing something other than the processed monkey chow routinely given as food. A few of the macaques at Institution 1 were paired with another individual, which would be considered a type of enrichment.

At Institution 1, the earliest EE record is dated February 1993, which indicates that this lab took eight years to implement a primate EE program from the time the amendment was passed. Furthermore, only three monkeys' records (out of a possible 23) include any EE provision after year 2000. Average duration of EE was three years, and the average proportion of time that a given monkey received EE was 30% of her/his lifespan. At Institution 2, the record for 32 of the 37 baboons indicates "no psychological wellbeing program records." Two of the remaining five baboons' records indicate that they were given a toy.

If representative of other facilities, our findings uncover serious welfare concerns for the wellbeing of primates kept in American research facilities. These animals face regular or chronic sources of pain and distress including noxious experimental and non-experimental events and illness and injury; and severe and prolonged social disruptions. Pain relief is meager by comparison to that normally provided to humans, despite legislative requirements to minimize pain and distress and assume similarity to humans in terms of ability to experience pain and distress. Living environments are usually confinement indoors to a metal cage, often alone, and often with a minimum of physical or mental stimulation.

I INTRODUCTION

I.1 Background

This report is based mainly on primate records from two NIH-funded National Primate Research Centers (hereafter: Institution 1, and Institution 2). The records were obtained using the Freedom of Information Act (FOIA) by a US citizen with a background in biomedical communications, and with no official connection to The Humane Society of the United States (HSUS). It took persistence by this citizen to successfully obtain these records. In all, the citizen requested records from ten US institutions that conduct experiments on primates. All ten initially denied her requests. Two of the responses were hostile, and four came from a legal representative of the institution. Eventually, three institutions complied when the citizen promised not to seek to identify them publicly.

This person also used these records to produce a detailed 328 page summary document (anonymous 2010), which was an important source for the current analysis. The citizen complainant is not seeking to vilify any particular research facility, but rather wishes to draw attention to systemic welfare problems with primate research and with laws intended to minimize pain and distress and to promote psychological wellbeing. Legitimate debate surrounds whether or not primates ought to be used at all in harmful experiments. However, few would disagree that, while they are being used, every effort should be made to minimize their pain and suffering.

The United States is by far the world's biggest user of primates in harmful research and testing. According to the United States Department of Agriculture (USDA), over 124,000 primates were used for research, testing and education, or bred or held for such purposes in the United States in 2009 (USDA 2010)—more than ten times the number of primates used in the rest of the world combined (Balcombe et al 2011).

Because they are intensely social, intelligent, and long-lived, the welfare of primates is an area of special concern. Among the chief concerns with regard to the wellbeing of primates in laboratory settings are:

- failure to address their pain and distress
- poor veterinary care
- lack of environmental enrichment
- inconsistent record-keeping
- use of animals who are sick and stressed and subsequent impact on scientific results

Two sets of government regulations pertain to the welfare of primates used in US laboratories. The Animal Welfare Act (AWA) simply stipulates transport, husbandry, and minimum housing requirements, and a provision "to develop … an appropriate plan for environment enhancement adequate to promote the psychological well-being of nonhuman primates" (9 C.F.R. § 3.81) (see Section III.4). Institutions that receive Public Health Service (PHS) funding to conduct research on primates are required to follow the PHS care and standards of NIH's Office of Laboratory Animal Welfare (OLAW) (OLAW 2002). OLAW stipulates compliance with the Institute of Laboratory Animal Research's 1996 *Guide for the Care and Use Laboratory Animals* (*Guide*) (ILAR 1996). The *Guide* makes non-binding recommendations that primates be housed socially as much as possible, and gives recommendations on primate restraint, minimum space requirements, noise levels, and diet (ILAR 1996).

In part because obtaining and analyzing detailed records of primate use in labs is arduous and difficult, there has been little examination of longitudinal data on these animals. The current document is a rare exception. It is based on close to 6,000 pages of detailed records of the lives of over 204 individual animals. This data set provides the opportunity to examine the long-term welfare status of these animals—albeit with the limitations imposed by records that only mention medical and research-related events. In addition to providing insight into the wellbeing of representative populations of primates in a laboratory setting, this analysis also provides a more biographical view of individual animals whose lives usually come and go in complete anonymity.

I.2 Natural behavior

Many of the problems inherent in primate research stem from the artificiality of the animals' existence, and the inability of a laboratory setting to meet the animals' psychological and physical needs (Balcombe et al. 2011). Adapted for climbing and running, monkeys kept in cages are thwarted of opportunities to engage in these basic behaviors. USDA regulations allow rhesus macaques to be kept in cages measuring 2x4x3 feet, and adult baboons in cages measuring 5x5x7 feet (USDA 2005). These deficits are exacerbated by the social deprivation that comes from being housed alone. The vast majority of primates—including rhesus macaques and baboons—are intensely social creatures. Interdependent, they live long lives among familiar individuals with many of whom they form close alliances and bonds (Smuts et al. 1987, Dunbar 1988).

I.2.a Macaques

Rhesus macaques range from Afghanistan to south and Southeast Asia, occupying the widest geographic range of any nonhuman primate. They are found in grasslands, woodlands and in mountainous regions up to 2,500 m (8,200 ft) in elevation. Crab-eating macaques also range through Southeast Asia. Both species are regular and capable swimmers (Lindburg 1980).

Macaques live in groups, or "troops" ranging in size from less than 30 to 140 or more individuals. In the wild they have a potential lifespan of three to four decades: 29 years for rhesus macaques, 33 years for Japanese macaques, and 37 years for crab-eating macaques (Ross 1991). In a study of wild macaques in Nepal, the four activities that the monkeys spent the most time doing were: locomotion, feeding, looking and grooming (Teas et al. 1980). Weaning begins at about four months of age, and is usually complete by the time the next infant is born. Mothers sometimes pick up and carry their offspring for up to a year (Fooden 2000). Communication in macaque societies involves vocalizations, body postures, gestures and facial expressions (Partan 2002). Macaques show individual recognition by voice (Hansen 1976).

Macaques are very active and mobile. Wild populations studied in Nepal had home ranges of from 2.5 to 24 hectares (Teas et al. 1980).[1] A wild troop of 42 crab-eating macaques in Indonesia had a home range of 125 hectares (1¼ square kilometers), passed through approximately 20 hectares per day. Though they spent almost all of their time (97%) in trees, only rarely did they spend more than an hour in a single tree (Wheatley 1980). Their diverse diet in the wild includes a wide variety of fruits, flowers, insects, leaves, fungi, grasses, and clay (ibid).

[1] 100 hectares = 1 square kilometers = 0.39 square miles.

I.2.b Baboons

In the wild, chacma baboons are more terrestrial than macaques, though they are still reliant on trees for evading predators and for sleeping. They occupy open grasslands in a wide geographic swath of north-central Africa extending nearly from coast to coast (Cheney & Seyfarth 2007).

Chacma baboons live in troops numbering between 8 and 200 individuals (typically 30-40). They have a potential lifespan of 45 years (Ross 1991). They are extremely mobile; a wild troop may walk 30 kilometers (ca. 20 miles) or more in one day (Stammbach 1987). Their omnivorous diet is widely varied, and includes plants, grass, bulbs, roots, flowers, fruit, seeds, twigs and bark, and various invertebrate and vertebrate animal prey (Rowe 1996).

Baboons can live up to 40 years. Infants are carried by their mother until 6 to 12 weeks of age, at which time they begin to ride on their mother's back. By one year of age, juveniles are foraging for themselves, but they rely on their mother for protection and guidance for another six months (Rowe 1996).

Female baboons form strong, equitable, and enduring relationships with specific female partners, especially close relatives and age-mates (Silk et al. 2010). Baboons have a range of emotions, including grief. Recent studies have demonstrated physiological and behavioral responses to the loss of an infant by mother baboons that parallel those of human females. A period of bereavement is marked by elevated blood levels of glucocorticoid hormones. These hormones, associated with grieving in humans, subside about a month following the infant's loss. Close associates of the bereaved mothers also show these chemical and behavioral responses, though to a lesser degree (Engh et al. 2006, Cheney & Seyfarth 2007).

II THE DATA

The records analyzed for this project comprise about 6,000 pages of animal medical and health records of 216 primates from three laboratories (Table 1).

Table 1: Numbers of animals by species at each of the three primate research facilities.

SPECIES	Rhesus macaque	Crab-eating macaque	Chacma baboon	Pig-tail macaque	Japanese macaque
Institution 1	146				1
Institution 2	1	22	37	1	
Institution 3			8		
TOTAL	147	22	45	1	1

The records date up to October 2009, and encompass animals born as far back as 1968. Most of these records are summary data from logs maintained by animal care staff during the course of the animals' lives in the institution. While records are incomplete for many of the animals, the data set permits the evaluation of trends and patterns of use. Moreover, because the records are longitudinal, in many cases spanning an animal's entire lifespan, these data provide a rare glimpse into the long-term tenor of life these animals led.

II.1 Data capture

Animal records were studied and tabulated into eight data categories: Demographic, Housing, Experiments, Manipulations, Chemical Agents, Illness and Injury, Reproduction, and Miscellaneous. Within each of these categories we defined a number of quantitative measures to allow calculation of means and evaluation of trends. Table 2 presents the full range of data categories and subcategories used, with definitions of terms used for capturing and summarizing the data set. Microsoft Excel was used to produce summary data and means for the categories presented in Table 2.

Table 2: Categories and definitions of terms used for capturing and summarizing the data set.

Demographic
Identification number
Species
Sex
Birth date
Birth location
Death date
Cause of death
Age at death
Time spent at institution: number of months the monkey spent at the institution
Housing
Moves: total number of times the monkey was moved into a different enclosure
Moves per year: average number of moves per year
Number of times alone: number of housing assignments where the monkey was housed alone
Number of days alone: cumulative number of days in which the monkey was housed alone
Percent of time alone: percentage of total time at institution that the monkey was housed alone
Days not alone: cumulative number of days the monkey was housed with at least one other monkey
EE (Environmental Enrichment) start: date on which the first EE record occurs
EE end: date on which the last EE record occurs
EE duration: cumulative time, in months, during which the monkey was provided with EE
EE % of total time in lab: percentage of total time at institution that monkey received EE
Experiments
Number of protocols assigned to: the number of studies to which monkey was assigned
Assignment descriptions: descriptions of studies to which monkey was assigned
Experimental procedures: a list and number of experimental procedures the monkey was subjected to as part of designated studies/protocols
Invasive experimental procedures: number of experimental procedures that pierce the skin or include the insertion of an instrument into a body orifice
Number experimental: total number of invasive and non-invasive experimental procedures
Manipulations
Number of blood collections
Number of TB (tuberculin) tests
Number of times weighed

Maximum weight loss: maximum recorded weight loss (not related to a birth) without any intervening weight gain
Other manipulations: a list and number of manipulations not included above (e.g., physical exams, palpations, dental exams)
Total manipulations: sum of above manipulations categories (except maximum weight loss)
Chemical Agents
Total chemical agents: total number of different types of chemical substances administered to the monkey
Total invasive doses: total number of invasive dosages the monkey received
Total noninvasive: total number of noninvasive administrations (e.g., oral, inhalation)[2]
Sum inv+noninv: total number of all invasive and noninvasive dosages combined
Illness and Injury
Pathogens and parasites: names of different pathogens (e.g., viruses, bacteria) and parasites the monkey was infected with (incidentally or experimentally)
Number of pathogens: number of different kinds of pathogens and parasites monkey was infected with (incidentally or experimentally)
Number of infections: number of separate pathogenic and parasitic infections[3]
Other illnesses and health problems: a list and number of any additional illnesses and medical conditions
Injuries: a list and number of separate injuries suffered by the monkey
Number of injuries: total number of injuries suffered by the monkey
Reproduction
Births: number of separate times a monkey gave birth
Births notes: birth outcomes (e.g., live vaginal, Cesarean section, stillborn)
Miscellaneous
Significant gaps in the record: any notably long periods between records
Potential Animal Welfare Act (AWA) violations: events that might indicate violations of the AWA
Abnormal behavior: behavior exhibited by the monkey that could indicate poor well-being not noted in other data categories
Summary data
Total handling events: Number of experimental procedures + Total manipulations + Sum invasive and noninvasive chemical dosing
Total invasive events: Blood collections + TB tests + Invasive experimental procedures + Total invasive doses

II.2 Data Analysis

Data were analyzed using simple measures—sums, percentages and means—available on Microsoft Excel. We used no statistical tests. Qualitative data were recorded in the Excel spreadsheets and used for summary tables presented in this document.

[2] Gavage (forced tube feeding) is treated as an invasive dose

[3] Recurrent diagnoses occurring less than a month apart were treated as a single infection

III RESULTS

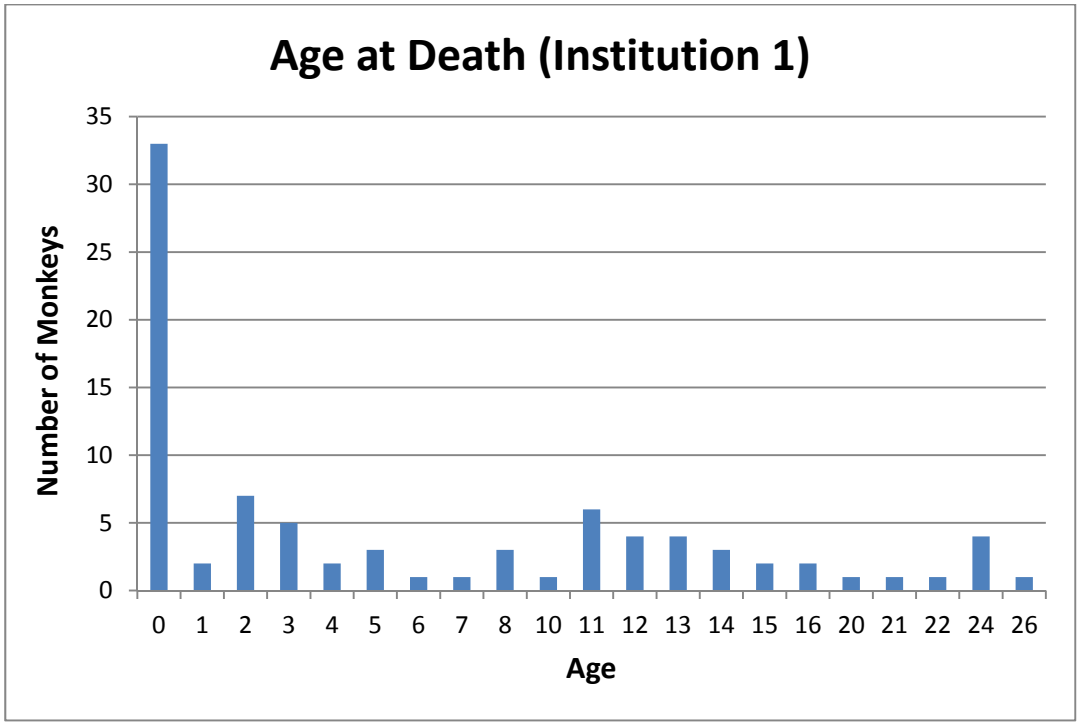
III.1 Demographics

Institution 1 (rhesus macaques)

A total of 147 rhesus macaques (*Macaca mulatta*) comprised the Institution 1 data set: 81 females, 63 males, and 3 whose sex was unrecorded. Of this population, 98 individuals were born at Institution 1; 9 were imported from India, one each from China and elsewhere in the USA, and for the remaining 38 monkeys there was no birth location data. Year of birth (n=137) ranged from 1968 to 2002.

The monkeys (n=102 with age records and/or who had died by the time the records were retrieved) lived to an average age of 7.1 years with a range of 0 to 25.8 years (Figure 1). For the 42 monkeys for which cause of death was given, 23 were "sacrificed for experiment" and 12 were "sacrificed for non-experiment." Two were "harvested" (meaning uncertain), two were terminated at birth, two died from fights and one died from pneumonia aspiration.

Figure 1: Age at death for macaques born at Institution 1.

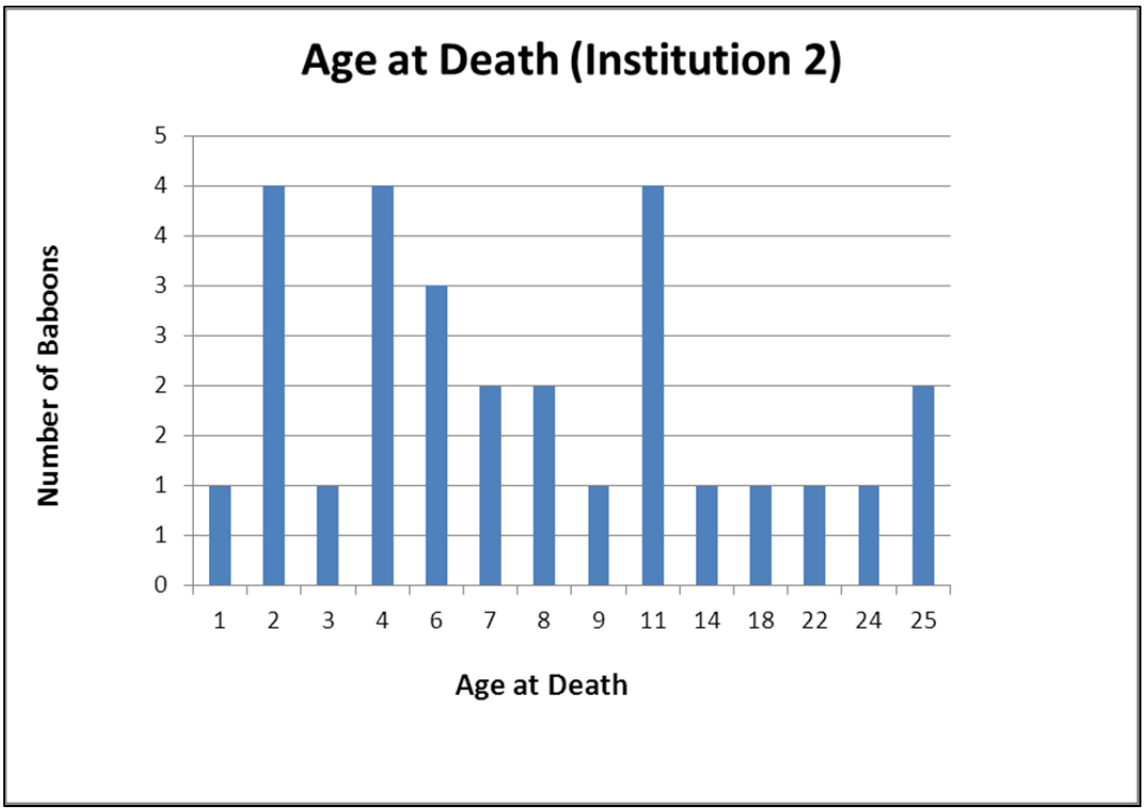


Institution 2 (chacma baboons)

This captive population of chacma baboons (*Papio cynocephalus*) numbered 37 individuals: 23 females and 14 males. Twenty-three of these baboons were born at the institution, five were imported from Africa, three from elsewhere in the United States, two from Russia, and three unknown. Year of birth ranged from 1982 to 2003.

Average age at death for these baboons (n=28) was just under 9 years (range: 0.5 to 24.9 years). Thirteen were killed as part of the experiment, four died spontaneously during the experiment, and ten died while not involved in an experiment.

Figure 2: Age at death for baboons at Institution 2.



III.2 Pain and Distress

Animals' capacity to experience pain and distress is the basis for the controversy over animal experimentation. The common assumption that feelings are more acutely felt by humans than by so-called "lower" species is not supported by data. With regard to pain there are no unequivocally "higher" or "lower" sentient species among mammals, all of which share the same physiological pain pathways (Silverman 2008). Stoicism is adaptive, but there is no sound evolutionary basis that a needle prick, an amputated finger, or recovery from surgery is less painful to a monkey than to a man (Balcombe 2010). The *US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Teaching* and USDA Policy state that procedures that cause pain and distress in humans should be assumed to cause pain and distress in other animals, unless the contrary is established (IRAC 1985 & USDA-APHIS 2011).

There is no controversy about the vulnerability of primates to psychological disturbance resulting from prolonged stress leading to distress. There is extensive documentation of the various manifestations of chronically stressed primates in labs, such as hair-pulling, repetitive behaviors, and self-biting to the point of serious injury (Kraemer *et al.* 1997; Reinhardt & Rossell 2001; Lutz *et al.* 2003; Novak 2003; Rommeck et

al. 2009). The 1985 Animal Welfare Act amendment explicitly acknowledges the importance *"… for a physical environment adequate to promote the psychological well-being of primates"* (USDA 1985).

Less recognized are the stressful effects of seemingly benign laboratory routines, such as handling, injections, and blood collections. Research on a wide range of laboratory animals indicates that physiological measures of fear and stress typically rise between 20% and 100% in response to these routine events (Balcombe et al. 2004). Studies of rhesus macaques have shown significant increases in heart rate, blood cortisol, growth hormones and leukocyte counts in response to various perturbations, including someone entering the room, cage changes (even within the same room), and blood collection from a leg vein (Meyer and Knobil 1967; Line 1989; Reinhardt et al. 1990; Capitanio et al. 1996). Common behavioral responses to blood collection in primates include fear-grinning, vocalizations, diarrhea and physical resistance (Vertein & Reinhardt 1989).

We examined the following sources of pain and distress:

- experimental procedures (e.g., surgeries)
- inadequate pain relief (routine and post-operative)
- non-experimental procedures (e.g., blood collections, tuberculin tests)
- handling events (e.g., physical exams, drug administrations)
- social disruptions (cage moves, single housing, transfers)
- illnesses and injuries

III.2.a Experimental procedures

It is axiomatic that experiments and other procedures performed on animals in research laboratories cause pain and distress and are intrinsically harmful. If that were not the case, they would be performed on human subjects.

Institution 1

On average, each rhesus monkey (n=75 with applicable data) in Institution 1 was subjected to 7.7 experimental procedures (range: 1 – 32), with an average of 1.1 procedures per year. Table 3 provides a sample of experimental procedures performed on this population.

Table 3: Sample experimental procedures performed on macaques at Institution 1.

Procedure	# of monkeys	# of procedures
Catheter insertion/removal	33	89
Surgical removal of ovaries	29	58
Surgical insertion and removal of implants	20	84
Biopsy	17	45
Fetus surgically removed, catheters inserted, then returned to womb	12	16
Caesarean section	11	21
Surgical obstruction or removal of blood vessels	3	13
Puncture and drainage of brain fluid	1	4
Implantation of a metal plate on the skull for electrode insertion	2	2

Puncture and drainage of urine from the bladder	1	2
Removal of portions of the colon	1	1

All of these procedures also involve handling, restraint, anesthesia and post-surgical recovery. The example below provides a more detailed description of one of these procedures, fetal surgery (which was performed a total of 16 times on 12 different pregnant mothers):

<u>Second fetal surgery on Josephine, aged 11*</u>
Sedated, removed from cage, taken to surgical room and anesthetized.
A 1.5 inch incision was made in the groin and the right femoral vein and artery were isolated.
Catheters were placed in the artery and vein, and then secured with silk.
The catheters were tunneled to the left abdominal region and exteriorized.
The incision was stitched closed.
The abdomen was entered via a 4 inch ventral midline incision.
The uterus, containing the fetus, was exteriorized.
A 2 inch incision was made in the uterus and the fetus delivered.
A 1.2 inch linear incision was made on the fetal neck.
The fetus's left internal jugular vein and left carotid artery were isolated.
Catheters were inserted into the vein and artery and secured with silk.
The incision was stitched closed.
Two electrodes were placed on the fetus: on the left shoulder and above the sternum.
Two additional electrodes were placed on the mother's uterus.
The fetus and uterus were returned and the abdomen was stitched closed in four layers.
All catheters and electrodes were tunneled to the mid-region and exteriorized.
Mother was maintained on terbutaline (a smooth muscle relaxant) for the next 10 days.
She was also partially restrained in a tether/vest.
Mother underwent three ultrasounds during the following weeks of her pregnancy; the fetus was determined to be normal in appearance.
Three weeks following fetal surgery, the fetus, a female, was born dead via C-section.
Catheters and electrodes were removed from the dead fetus and from the mother.

*Note: Josephine's previous fetal surgery was performed 11 months earlier. That fetus was also delivered dead by Caesarean section.
Institution 2

Experimental procedures conducted on baboons at Institution 2 included:

- whole body irradiation
- bone marrow biopsy/aspiration
- fetal stem cell transplantation
- fetal injection of stem cells using ultrasound
- embryo flush
- chronic catheter implantation
- restraint in a tethered vest

On average, each baboon (n=35) in Institution 2 was assigned to 5.2 experimental protocols (range: 1 – 18 protocols) during her or his lifetime, with an average of 1.2 protocol assignments per year. These baboons were subjected to an average of 7.1 experimental procedures (range: 1 - 32), with an average of 2.4 procedures per year.

III.2.b Pain relief

The administration of chemical agents is usually an invasive procedure that requires handling, and is stressful for primates (Reinhardt et al. 1990 & Balcombe et al. 2004) and the records from Institution 1 and 2 show that these animals were dosed often (see Table 4). However, because many of these invasive doses could be to administer pain-relieving drugs, we did an analysis to estimate the proportion of invasive doses that were for this purpose.

Institution 1

We randomly selected 15 of the rhesus macaques from Institution 1. These animals received a total of 1,171 invasive doses, involving three drugs with anesthetic properties: ketamine, Nubain, and Buprenex. Ketamine made up a significant portion (18%) of the invasive doses given to these animals. Nubain (2%) and Buprenex (0.3%) were quite rarely used. All uses of Nubain and Buprenex were for pain-relief, whereas only 10% of ketamine doses could have been associated with pain-relief. Most ketamine administrations (193 of 215 doses = 90%) were associated with handling procedures (e.g., physical exams, ultrasound exams) and thus used to render the animal calmer and more manageable. Overall, only 4.2% of invasive doses were administered to relieve pain in these animals.

Institution 2

We randomly selected 15 of the baboons from Institution 2. These animals received a total of 373 invasive doses, involving four drugs with anesthetic properties: ketamine, procaine, marcaine, acetaminophen, and isoflurane (delivered by endotracheal tube, which we treat as an invasive dose because of the restraint and stress it causes). Once again, ketamine was the most commonly used of these compounds, comprising 11% of all invasive doses given to these 15 animals. The other compounds were exclusively used for pain relief, but they were rarely used: isoflurane 2%, and the others less than 1%. No more than one quarter of ketamine doses could have been used for pain-relief; the other doses were used to make the animal easier to handle (mainly for tuberculin tests). Overall, only 6% of invasive doses were administered to relieve pain in these animals.

III.2.c Post-operative pain relief

> *Post-surgical pain relief for human patients typically lasts 1-2 weeks; in this lab, the monkeys typically got 0-1 day.*

In human medicine, the treatment of post-operative pain is more of an art than a science. Typically, pain relief is provided until the patient says s/he no longer needs it. One of the disadvantages of trying to treat pain in non-humans is that they cannot verbalize their pain. Another challenge is that animals may hide their pain; stoicism is adaptive because it reduces the chance of being singled out as more vulnerable by a

predator. Nevertheless, there are many ways that animals may express their pain, including vocalizations, favoring the affected body part, loss of appetite, and pained facial expressions (Langford et al. 2010).

U.S. Government policy holds that, in general, procedures that cause pain in humans should be assumed to cause pain in other animals (IRAC 1985 & USDA-APHIS 2011). Post-operative pain is an important concern in human medicine. According to the International Association for the Study of Pain, the overall incidence of chronic pain after major surgery is estimated at between 20% and 50% (Macrae 2008). Shorter-term pain is of course inevitable, and pain medications are routinely prescribed for human patients for a few days to weeks following minor or major surgery (Mayo Clinic 2009). A typical post-surgical pain relief regimen for a human patient is to provide substantial amounts of narcotics intravenously for 2-4 days, followed by orally for 1-2 weeks.

Institution 1

We examined post-surgical pain relief in a random sample of 15 monkeys. The total number of surgeries across the 15 monkeys was 12 (average: 1 procedure per monkey, range: 0 - 6). Ten of these monkeys had no surgeries. For the remaining five monkeys, in cases where surgical procedures were combined in one session—for example, bilateral oophorectomy (surgical removal of the ovaries) and bilateral salpingectomy (surgical removal of the fallopian tubes), we counted these as a single surgery.

The surgical procedures performed on these five animals were as follows:

1. ovarian resection: removal of part of the ovary
2. fetal surgery: fetus surgically removed, manipulated, then returned to the uterus
3. Cesarean section: delivery of baby by incision through abdomen and uterus
4. bilateral oophorectomy: surgical removal of both ovaries
5. bilateral salpingectomy: surgical removal of both fallopian tubes
6. insertion of implants into the shoulder-blade region
7. hysterectomy: surgical removal of the uterus
8. lymph node biopsy: removal of a small tissue sample from the armpit or groin area

The amount of post-surgical pain relief given for these procedures ranged from no pain relief to two days of pain relief. In three instances the monkey received no pain relief following surgery (one fetal surgery, Cesarean section, ovarian follicle aspiration). In seven instances the monkey received one day of pain relief, and in one instance (a fetal surgery), two days of pain relief were provided (Appendix 1). In the case of Rangana, a pregnant 5-year-old female, two significant abdominal surgeries were performed on the same day (16 July 1984): fetal surgery in the morning (08:00 – 08:29) and a Cesarean section in the afternoon (13:43 – 13:44). The infant was terminated at birth, and no post-surgical pain relief was given following these procedures. With the exception of one female monkey, Padma, who in October 1997 received four intravenous doses of ketamine (an anesthetic with analgesic qualities) over two days following fetal surgery, none of the other monkeys received more than one day of pain relief following the procedures listed above. These levels of pain relief are dramatically less from those given to human patients following similar procedures, and even less than the 24-72 hours recommended by Flecknell (1996) for laboratory animals.

Institution 2

None of the baboons were subjected to abdominal or other major surgery.

III.2.d Non-experimental procedures

Laboratory routines that cause pain and/or stress to animals may be of greater welfare significance than experimental and surgical procedures. Procedures such as blood collections, injections and force-feedings are known to cause stress in laboratory animals (Balcombe et al. 2004). That these procedures also require that the animal be handled compounds the problem, for handling is also aversive in the laboratory context where it so often accompanies noxious events (ibid).

Institution 1

Of 98 rhesus monkeys with data, the average number of blood collections during an individual's lifetime was 34, with a range of between 1 and 224. The average rate of blood collections was 6 per year, with a range of 0.4 to 30/year.

Of 100 monkeys with data, the average number of injections during an individual's lifetime was 95, with a range of between 0 and 918. The average rate of injections was 13 per year, with a range of 0 to 76/year, or one injection every five days.

Of 46 monkeys with data, the average number of tuberculin (TB) tests during an individual's lifetime was 30, with a range of between 1 and 141. The average rate of TB tests was 2.5 per year, with a range of 0.1 to 6.5/year.

Combining blood collections, injections, TB tests and invasive experimental procedures provides us with an estimate of the total number of painful procedures (excluding invasive experimental procedures). For the 92 monkeys with complete data, the average number of painful procedures during an individual's lifetime was 156, with a range of between 2 and 1,184. The average rate of painful procedures (n=63) was 20 per year, with a range of 1 to 98/year.

Institution 2

Of 33 baboons with data, the average number of blood collections during an individual's lifetime was 33, with a range of between 2 and 98. The average rate of blood collections was between 10 and 11 per year, with a range of less than one to 36 per year.

Of 32 monkeys with data, the average number of injections during an individual's lifetime was 47, with a range of 2 to 313. The average rate of injections was just under 14 per year, with a range of < 1 to 149 per year, or one injection every four days.

Of 35 monkeys with data, the average number of tuberculin (TB) tests during an individual's lifetime was just below 19, with a range of between 1 and 53. The average rate of TB tests was 3.3 per year, with a range of 1.7 to 13.3/year.

Combining blood collections, injections, TB tests and invasive experimental procedures provides an estimate of the total number of painful procedures (excluding invasive experimental procedures). For the 36 monkeys with complete data, the average number of painful procedures during an individual's lifetime was 95, with a range of between 1 and 346. The average rate of painful procedures (n=32) was 28 per year, with a range of 2 to 165/year.

III.2.e Handling

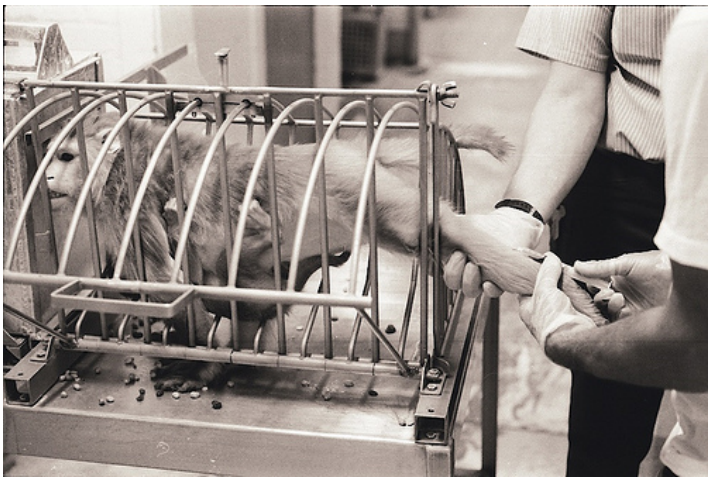


Figure 3: Macaques show behavioral and physiological stress reactions to being removed from the familiar home environment and being forcefully restrained/immobilized during handling procedures. Here, a mother macaque with a baby clinging to her belly is injected while in a squeeze cage (note vertical bars). (Photo courtesy Viktor Reinhardt)

Handling is typically stressful for animals confined in laboratories, where many handlings are accompanied by aversive events such as an injection, a blood collection, or forced-feeding (Balcombe et al. 2004). Handling events such as being moved to another cage, or being weighed often cause significant increases of 200% or more in blood levels of the "stress hormone" corticosterone in rats and mice (ibid). Heart rates of six rhesus macaques increased 46% from resting rates in response to a cage change, and remained elevated for two hours after the intrusion (Line et al. 1989). Growth hormone, which may be influenced by many factors including stress, increased abruptly in two of three female rhesus macaques in response to room entry by unfamiliar persons, and in all three monkeys in response to the onset of a telephone ringing (Meyer & Knobil 1967).

Institution 1

Macaques at Institution 1 were regularly subjected a wide range of procedures that require handling and physical restraint and often pain. These included: blood draws, injections, palpations, rectal or vaginal swabs, ultrasound exams, dental procedures, force-feedings, dosings, x-rays, wound treatments, tattoos, and tuberculin tests (see section III.1.d).

These monkeys were handled often (Table 4). For the 45 individuals with complete handling data, the average number of handling events (experimental procedures + total manipulations + sum invasive and non-invasive doses) was 805, which averages to 113 per year (nearly 3x per week). Roxanne, an 8-year-old female who was still living at the time the records were obtained, had been handled 4,630 times (1.5 per day). Administrations of drugs and other compounds made up a significant portion of handling events (see Table 4 and Figure 3).

Table 4: Administration of drugs and other substances at Facility 1.

Metric	N	Average	range
Number of different substances (per monkey)	100	14	1 – 49
Number of invasive administrations (per monkey)	100	95	0 – 918

Number of invasive doses per year	68	12	0 – 77
Number of non-invasive administrations	100	198	0 – 3,465
Sum of all administrations	100	293	1 – 4,004

Institution 2

At Institution 2, baboons were also handled often, though less so than the macaques at Institution 1. For the 34 baboons with complete handling data, each individual was handled an average of 191 times (average 42 handlings per year, or once every 9 days), with a range of 29 – 480 total handling events.

III.2.f Social disruptions

Macaques and baboons are highly social creatures. For the first year or more, an infant's mother is the epicenter of her/his world. As the youngster gains independence, s/he befriends others and learns proper social etiquette. The evolutionary imperative for genetic mixing impels some individuals to migrate from their natal community; this is usually a one-time event in the individual's lifetime—and it is a highly stressful and destabilizing one. Otherwise, these monkeys spend their entire lives living among familiars. All group members know all others, and strong social ties are forged with other preferred individuals. These relationships provide safety and emotional stability (Lindberg 1980, Cheney & Seyfarth 2007).

Figure 4: Social isolation is arguably the greatest hardship of all for highly social primates in labs. This hardship is exacerbated by chronic lack of stimulation and frequent painful and/or stressful events. (Photo courtesy Viktor Reinhardt)

Laboratory settings present a strong contrast to these animals' natural social milieu. Common social disruptions include forced weaning from the mother, sometimes at a very young age. It is self-evident that removing a still-suckling infant monkey from its mother is a severely emotionally stressful event for both animals, and early weaning has been used to model stress, immune deficiency and depression (Reinhardt 2002). Cage moves are another source of stress. Animals have no idea when they will be moved, no control over who they may be paired with, or if they will have any social company at all. Caging itself thwarts important activities in a primate's life, such as walking, running, climbing, playing and foraging.

Being caged without others is a harder fate. Single housing is known to cause prolonged stress, anxiety, psychological disturbance, and suppressed immunity in social primates (Lilly et al. 1999, Balcombe et al. in press). Single housing also restricts or curtails physical contact with others. Grooming, for example, is an important social lubricant and general wellbeing-enhancer. Some primate species, including macaques and baboons, spend between ten and twenty percent of their time grooming one another (Dunbar 1988). The International Primatological Society (IPS) stipulates that *"single caging on experimental grounds should always be avoided if possible,"* and that it *"should be for as short a time as possible"* (IPS 2007, p 16). The USDA Code of Federal Regulations stipulates that housing *"must include specific provisions to address the social needs of nonhuman primates of species known to exist in social groups in nature"* (USDA 2008, p 108).

Figure 5: Physical contact, such as grooming, is an important social lubricant in primate societies. (Photo courtesy Jonathan Balcombe)

Institution 1

At Institution 1, monkeys were moved often from one cage to another. Of the 115 monkeys with complete housing history data, the average number of moves was 22 times, with a range of 0 to 74 moves. On average, a monkey was moved twice per year, with a maximum of 15 moves in one year for a female who was weaned at 3.5 months, suffered from chronic diarrhea and died shortly before her second birthday.

One monkey—a female born in 1993 and still living at the time of document retrieval (August 2009) had been moved 74 times during her 16 years there (4.6 moves per year).

For the 113 monkeys with data, average time spent caged alone was 4½ years. On average, a given monkey spent more than half his or her life (53%) without direct social companionship (112 monkeys, range 0% - 100%). One male, born at Institution 1 in 1968, spent 20 years housed alone before he died there in December 1993.

Institution 2

Levels of social disruption were similar for the baboons housed at Institution 2. Individuals were moved from one cage or enclosure to another an average of 31 times during their lives (n = 34, range 3 – 91). On average an individual baboon was moved every 73 days (range every 37 - 214 days). One male was moved 25 times before he died at 2½ years of age. He was removed from his mother at birth and caged alone for most of his life.

Overall, baboons spent an average of 41 percent of their lives, or nearly two years, caged by themselves at Institution 2. One female, Dalmar, who died in an experiment at age 11, spent 78% of her life (more than three thousand days) housed alone.

To put these numbers in perspective, in their natural state these species typically spend their entire lives in a rich social setting—usually one or two stable social networks. They spend 100% of the time living freely in the open air.

III.2.g Illness and Injury

Institution 1

A variety of pathogens and parasites afflicted the captive rhesus monkey population at Institution 1. In all, 81 (55%) monkeys were infected at least once, and the records contained 1,440 separate infections involving 15 different types of pathogenic bacteria and viruses and another 15 species of parasites. The average number of different types of pathogens and parasites per infected animal was four (range: 1 - 16). The average number of separate infections per infected animal was 18. One male, who died in 1997 at age twelve, had had 201 infections during his twelve years of life, including chronic diarrhea (117 separate diagnoses). This population also suffered a wide range of other illnesses, averaging 17 per animal (n=94) and ranging from 1 – 154. These included: inflammation, enlarged organs, anorexia, emaciation, prolapse (uterus, rectum, colon, vagina), periodontal disease, abscess, spinal deformation, and depression.

Diarrhea is a common and persistent problem in laboratories housing primates (Henrickson 1984). Prolonged confinement with or near other caged individuals and away from fresh air and exercise combine with chronic stress to create an environment conducive to such illness. Of 103 animals with pertinent records, 75 (73%) suffered at least one diarrhea diagnosis. The average number of separate diarrhea diagnoses per animal for these 75 macaques was 7.8 (range: 0 - 117). The number of animals with chronic diarrhea—which we arbitrarily defined as five or more separate diagnoses, or whose records noted “persistence,” ”chronic,” or some similar term in conjunction with diarrhea—was 37 (49%). Nineteen animals suffered at least one bout of bloody diarrhea.

Thirty-three monkeys experienced significant weight loss (unrelated to births) of greater than ten percent of their body weight. The average weight loss for these monkeys was 20%, and the range was from 10 – 50 percent. The female who lost half her weight did so during the last fifteen months of her life. She was born at Institution 1 and was sacrificed there for non-experiment, aged 19. Among her many ailments recorded during this period were diarrhea (six diagnoses, two bloody), anorexia, curved spine, muscle atrophy with non-use of legs, abnormal cardiac rhythm, mass on head, inflammation, arthritis, severe pain, emaciation, and depression. She was moved 45 times and singly caged 27 times for a total of six years.

Injuries were noted in the records for 49 monkeys (48% of the total who had adequate records). Injuries among these 49 individuals totaled 182, averaging just under four per injured animal (range: 1 – 12). Twenty monkeys (41% of those with injuries) suffered at least one amputation or avulsion (in which a body structure is forcibly detatched). Amputations usually involved fingers and thumbs, and three of seven avulsions involved the tongue.

- Esme, a female at Institution 1 lost her left ring finger at age 10 and her left thumb two years later; both were bitten off while she was housed alone. She died as a non-experimental sacrifice two months before turning 13. This macaque was moved 26 times and spent over 3,900 days caged by herself.

- Padma, a female at Institution 1 bit off both her thumbs and two fingers over a span of nine years. She was fifteen years old at the time her record ended, at which point she had been moved 40 times and had spent cumulatively nearly four years caged alone.

- Kajri, a female born at Institution 1 in 2001 and still living at the time records were obtained suffered four puncture wounds, finger wounds, facial abrasions, and an avulsed tongue. At the time of record acquisition she was 8 years old, had been moved 72 times, and had been singly caged for a total of 2,092 days (84% of her life).

- Ekanga, a male at Institution 1 suffered self-inflicted wounds to his arm, forehead and finger. He was moved 13 times, spent 2,790 days (97% of his life) caged alone, and was sacrificed for an experiment shortly before turning eight years old.

- Wafiya, a female originating from China, who was sold to another institution at age 15, had a pellet gun missile in her forearm.

Of 91 monkeys with relevant records, total health problems (infections, illnesses and injuries) averaged 35 per animal (range 1 – 333).

Institution 2

Although 17 different kinds of pathogens and parasites infected the baboons at Institution 2, this population was less susceptible to infection than were the macaques at Institution 1. Most of the baboons (22, 59%) suffered no pathogenic or parasitic infections. The remaining baboons seemed markedly more susceptible, with an average of three infections per individual (range 1 – 7). While not absent, diarrhea was not as serious a problem for the baboons as for the macaques in Institution 1. Six animals (16%) were afflicted with a total of nine reported bouts of diarrhea.

In all, the baboons at Institution 2 suffered 108 injuries (Table 5). The average number of injuries sustained by the 21 animals (57%) with injury data was 4.8 per animal (range 0 – 15). The average number of all health problems (infections, illnesses and injuries) was 6 per baboon (range 0 – 30).

Table 5: Injuries sustained by the baboons at Institution 2

Type of Injury	Number of Occurrences
Laceration, puncture wound	75
Abrasion	11
Amputation (finger): surgical traumatic	7 (4) (3)
Infected wound	5
Dental fracture	4
Avulsion (finger)	2
Hematoma	2
Fracture	1
Dislocation	1
TOTAL	108

III.3 Veterinary Care

Failure to comply with federally mandated animal care standards is not a rare event. The NIH's Office of Laboratory Animal Welfare received 160 reports of significant failures from animal research facilities during a three month sample period alone in 2005. These reports revealed that over 1,000 animals were affected, the great majority of which either died or experienced pain and/or distress (Gomez et al. 2010). If this randomly selected three-month period is representative, then approximately 640 incidents are reported per year or 1.8 per day (ibid). Moreover, the actual numbers of animals affected is probably much higher because many of the reported incidents withheld the number of animals affected, and such reporting is at the discretion of the research facility (ibid).

The following brief examples illustrate serious welfare problems faced by the monkeys in this study. Most of these animals' case histories are available in expanded form in the Case Studies (see section III.5).

Institution 1

Mabel: In her last of six pregnancies (2 live births, 2 terminated at birth, 2 stillborn), Mabel's fetus died in the womb and was discovered dead via ultrasound exam on October 5th 1992. The mummified fetus was noted as still present by ultrasound six weeks later. Another two weeks were allowed to elapse before the fetus was removed by C-section on December 9th.

Melinda was chronically sick with diarrhea during her short life. She also suffered from anorexia, dehydration, an enlarged pancreas, and depression. She was still subjected to experimental procedures (electroretinography) and died at agethree.

Meredith was subjected to repeated abdominal surgeries until the vet requested that she be flagged as surgery exempt. The principal investigator (PI) disregarded the flagging and ordered another surgery. As a result, Meredith's wound dehisced (opened up after surgical closure) and another open abdominal surgery was required to close the abdominal wound. Meredith was then put into a protocol where her shoulders were repeatedly (at least five times) tunneled open for implants.

Chitra's cause of death (at age 8) was listed as a fight, but wounds noted were on extremities; lab record indicates a chronic infection of multiple organisms, including *Shigella*, confirmed the day before she died; also, preventable physiological measures at death include 14 blood metrics outside normal ranges (many wildly so).

Kajri had chronic infections and displayed self injurious behavior, excessive drinking, and aggression towards other animals. She was identified by an animal technician as having a small, red inflamed mass on her jaw and then her wrist, which went untreated (and without relief) for two weeks, by which time she was carrying her head at a tilt. Lab tests showed it to be a *Staphylococcus* infection. After multiple attempts to get Kadri some relief, the tech recorded observations of her distress but did not contact the PI again.

Millie was subjected to major surgery (cholecystectomy) when she was just 7 months old. She was used in a taurine deficiency study and also placed in a retinography protocol while suffering from numerous parasitic and microbial infections. She was sold while still an infant (at age one year) to another institution after chronic infections.

Raj was chronically ill with parasitic and microbial infections, yet he was sold at age three to a corporation that makes tissue and fluid products for biomedical research, at which time the Institution was not licensed for the sale of live animals. The concerned citizen who obtained these records (through FOIA) inquired with the USDA and learned that the purchasing corporation was never licensed to receive live animals. The last note in Raj's chart was that he had been designated as a "vet cull." Nevertheless, he was re-sold in 1997 to a commercial company and not a research institution.

Wafiya was imported from China before being subjected to multiple surgical protocols for 15 years. She had multiple microbial and parasitic infections and was repeatedly bred, with her infants surgically altered or removed by C-section. Despite several chronic health problems, including liver enlargement and a constricted esophagus, her condition was described as "status quo" and she was sold while pregnant to another institution in 1997.

Before being sold at age 16, Lilly was assigned to multiple surgical procedures involving opening her abdomen, intensive care stays totaling 7 times and isolation caging twice. She had a history of curvature of the spine, an abnormal heartbeat and a prolapsed uterus. Yet she was sold in 1994 for further experimentation on the basis of a limited exam which declared her of normal appearance.

Lionel was placed in multiple protocols his whole life. He suffered repeat infections with bacteria and parasites, and in 1999 was noted as having possible carcinoma as well as mild liver enlargement. His 2002

record includes “ongoing enteritis” and bladder abnormalities that included bloody urine. Nonetheless, just two weeks after an open abdominal surgery he was put in a vest and assigned to a geriatric study. Lionel also suffered from alopecia (hair loss), and amputation of a portion of his tail. In November 2002, a technician complained he was having difficulty breathing, with harsh, moist chest rales, and he recovered slowly (nearly 90 mins) from a procedure requiring sedation. He was left untreated for three months to suffer from diffuse pulmonary edema and labored breathing until he died from pneumonia aspiration on January 10th.

Institution 2

Dalmar was scheduled to be euthanized for illnesses and self injurious behavior after she was experimentally exposed to whole body radiation. Instead, she was moved into a protocol studying self-injurious behavior, which she continued to exhibit for nearly two more years until she died at age ten.

Derek arrived from Tanzania at age three. In the two years he was at Institution 2 he was moved 25 times, exposed twice to whole body irradiation, and spent three-quarters of his life there caged alone. He received 337 administrations of 23 different chemical agents and was confined to a vest for repeated intravenous doses for 98 consecutive days immediately following irradiation and bone aspiration. He lost one-fifth of his body weight following the first radiation exposure.

Vera was moved 30 times and spent 1,341 days (62% of her life) caged alone. She was subjected to whole body irradiation, three bone marrow blood draws, and insertion of a catheter and implant in the thigh. She had many illnesses and injuries, and she bit off two of her fingers. She lost nearly a third of her weight in the months leading up to her death. Vera stopped breathing during a procedure and couldn’t be resuscitated. She was six years of age.

Althea was moved 70 times and spent more than six years caged alone. She suffered 18 reported bite wounds to the head, lips, hips, tail, and thigh, and two fingers which resulted in surgical amputations. She lost nearly a third of her body weight during her ninth year, and died in an experiment at age eleven.

III.4 Environmental Enrichment

The psychological well-being of non-human primates is a subject of special interest and concern (European Commission-SCHER 2009; Banner *et al.* 2002). Today, there is no longer any debate about the importance of providing physical and mental stimulation to a normally curious and highly active animal confined to a cage (NRC 1998). That importance was enshrined into US law with enactment of the 1985 amendment to the AWA *“to promote the psychological well-being of primates”* (AWA 1985). It should be added that EE is a palliative, not a panacea, and that the ravages of prolonged confinement, social isolation and pain and distress make animals vulnerable to psychological illness (see Pain and Distress section, above).

Institution 1

It is fairly certain that many of the macaques at Institution 1 were provided with no EE, especially those who died before the 1985 AWA amendment for primate psychological well-being took effect in 1991. EE records at Institution 1 were listed under “Environmental and Social Enhancement Diagnosis,” and most of these records reported “No Data.” However, because we couldn’t be sure (lack of a record may not mean

lack of EE), we took the conservative approach of excluding these animals' records (n=103) from the EE analysis. For the 44 monkeys with EE data, most of the records describe a typicalmonthly regime of replacing one toy (e.g., "Ring," "Kong," "Ball," "Tug") with another. The earliest record is dated February 1993, which indicates that this lab took an additional two years to implement a primate EE program after the 1985 AWA amendment took effect in 1991. The most recent EE record is dated September 2009 (ongoing at time of records retrieval), but only two other monkeys' records (out of a possible 23) include any EE provision after year 2000. Average duration of EE (n=44) was three years (range 0 to 6.6 years), and the average proportion of time that a given monkey received EE was 30% of her/his lifespan. It should be noted that the 1985 AWA amendment made no concrete stipulations for providing EE to primates, instead leaving it up to the discretion of the research institution.

"No psychological well-being program records" are indicated for 30 of the 37 baboons at Institution 2. Of the remaining seven animals, four received sporadic toy provisions; the other three records make no mention of EE at all.

Institution 2

For 32 of the 37 baboons at Institution 2 the record indicates "no psychological wellbeing program records." However, it is apparent from the extended records of a handful of these animals that some enrichment items were given. For example, the record for female baboon Yusra mentions a suspended perch (April 2000), a forage board (May /2000), and her being given treats such as marshmallows and peanuts (June 2000). So it is not clear from the record just how much or how little EE the baboons received. We do know that these animals spent a lot of time in cages, often alone (see section III.2.f Social Disruptions). Two of the remaining five baboons' records indicate that they were given a toy.

III.5 Population #3 – Macaques at Institution 2

It is important to note that this study was not the result of a whistleblower, and that the data summarized above from two separate federally-funded national primate research centers are probably representative, not exceptional. To further support this claim, we briefly present here a summary of findings from a third population of animals—macaques housed at Institution 2.

This population comprised 23 monkeys: 22 crab-eating macaques and one rhesus macaque. Most of these animals were imported from Indonesia and they lived on average only 2.4 years at the Institution. All died there, either killed as part of the experiment (83%) or they died spontaneously from its effects (17%). Average age at death was 4.7 years. Eleven monkeys (46%) died while in a vest and tethered by a catheter inserted into their back. Experimental procedures included cutting off the blood supply to the major (femoral) leg artery, injection of complete Freund's Adjuvant (a toxic compound that stimulates a painful immune response), and biopsies. The lone rhesus macaque was inoculated with syphilis.

Of 370 total invasive doses recorded at Institution 3, at most between 21 and 70 of these (6% to 19%) could have been used for the relief of pain. These monkeys were subjected to 9.7 blood collections (range: 2 – 50) and 7.5 tuberculin tests (1 – 12) per year. Five individuals lost at least 20% of their weight as a result of the experiments, and all but four lost at least 10% of their weight at some point. Each monkey was handled an average 98 times (range: 35 – 324) during their 2.4 years at Institution 3 (average 41 handling events yearly, or once every 9 days).

As in the other labs, monkeys were moved often from one cage to another. Average number of total moves for this group was 13 (range: 4 – 80), and on average, a monkey was moved over 8 times per year. The average time spent caged alone was 547 days, or 1.5 years. On average, a given monkey spent well over half his or her life (62%) caged alone (range 25% -- 100%). One male spent all but 135 days of his nine years at the lab caged by himself, and one female had social company for only 3 days during her 8 years there. She suffered many self-inflicted bite wounds.

Illnesses were diverse and widespread in these monkeys, with 46 different afflictions appearing in the record. These included: lung congestion and swelling, enlarged heart, dysfunctional uterine bleeding, liver degeneration, intestinal inflammation, meningeal hemorrhage, purulent discharge at catheter insertion or surgical site, diarrhea, candidiasis, measles, anemia, anorexia, and rectal prolapse.

Each of the animals in this population had "no psychological wellbeing program records," suggesting that no efforts were made to comply with the 1986 Animal Welfare Act amendment to promote psychological wellbeing in laboratory primates. In sum, this lab's record paints a picture of life comparable to that of the other two laboratory populations analyzed.

III.5 Case examples

Because each of the animals who unwittingly find themselves in a research laboratory is an individual with a biography, it is inadequate to view them merely as anonymous, numbered subjects. Here we present one-page summaries of the lives of selected individual monkeys in an attempt to give a better idea of the tribulations they faced.

Case 1.1
Name: Mabel (# 12234)
Species: Rhesus Macaque
Origin: Born at Institution 1 (1 June 1982)
Time with her mother: Unknown
Age at death: 10 years and 359 days
Cause of death: Sacrificed for experiment
Number of times moved: 34
Days spent caged alone: 1,613 (30% of her life)
Total times handled: Approximately 450
Number of times dosed: 388
Number of different drugs/medications/compounds administered: 24

Injuries: When Mabel was nine years of age, an x-ray detected a wire in her abdomen (probably a materials count oversight during an earlier surgery). Eighteen months later, five weeks before her death, Mabel suffered a traumatic finger amputation on her right hand. Ten days later, another finger on her right hand was surgically amputated due to fracture and swelling. Mabel was caged alone and these wounds were almost certainly self-inflicted.

Illnesses (experimental and unintentional):
At age ten, Mabel's fetus was determined to be dead in utero by ultrasound with its head thickness increased. Seven weeks later, the mummified fetus was still present inside of her. Four days on, a "daily bleed" was started, which continued until a C-section was performed twelve days later. Mabel lost weight (amount not given in record). The finger amputations and subsequent death occurred 3-4 months later. Other problems included: two gingival inflammations; scoliosis of vertebral column (age nine); mouth infection of *Shigella*; and an abdominal *Staphylococcus* infection (age nine) the same day an inflammatory abdominal fistula was noted.

Surgeries: Two Cesarean sections; uterine biopsy; vascular catheterizations and electrode implantations of two fetuses during pregnancy; vascular catheter removals (a separate surgery); EMG electrode removals (a separate surgery); amniotic catheterization; implants into lower abdomen; laparoscopy; exploratory laparotomy.

Overall Summary: Despite documented evidence of scoliosis in 1991 and a fistula following an operative procedure, Mabel was kept in surgical protocols involving repeated abdominal incisions (C-sections and laparotomy). Mabel was again taken to surgery for exploratory laparotomy a week after wire was detected in the region of her uterus. During her life in the institution Mabel was infected with four different types of microbes and three different types of parasites. She was given telazol and estradiol E-2 for bleeding during the time the mummified fetus was left inside from October 5th (date of documented fetal death) to December 9th, 1992 (date of C-section). However, no indication of pain meds is given in the record. After the C-section, she was given Nubain for one day and Chloromycetin for 3 days. Mabel had six pregnancies. Of these, two were born alive, two were terminated at birth and two were born dead.

Case 1.2
Name: Bonnie (# 16014)
Species: Rhesus Macaque
Origin: Born at Institution 1 (30 November 1989)
Time with mother: Removed from mother (Mabel) on day of birth
Age at death: 6 years
Cause of death: Not provided
Number of times moved: 21
Days spent caged alone: 2,179 (93% of her life)
Total times handled: 188
Number of times dosed: 92
Number of different drugs/medications/compounds administered: 12

Illnesses: Bonnie suffered from mental illness during her short life. Her record reports 17 instances of self-biting. She was also observed drinking her own urine on seven occasions (probably many more unwitnessed), hair plucking until her arms were bare, stereotypy (repetitive, functionless behaviors), and threatening own reflection. Bonnie was also diagnosed as "mildly depressed."

Bonnie had diarrhea for two months as an infant, and again at age 21 months. Other ailments and symptoms included: inflammation around the eyes, runny nose, abnormal respiratory sounds, hypothermia, lethargy, inflammation (unspecified), anorexia, rash, and alopecia.

Surgeries: Removal of ovaries, insertion of parascapular implants x3, surgical removal of the uterus and uterine tubes, and removal of the parascapular implants x3 (different surgeries than the implant surgeries).

Case 1.3
Name: Bangles (# 14520)
Species: Rhesus macaque (female)
Origin: Born at Institution 1 (Oct 1986)
Time with her mother: Weaned at 4 months
Age at death: 11 years
Cause of death: Sacrificed for experiment
Number of times moved: 35
Days spent caged alone: 3,216 (77% of his life)
Total times handled: 402
Number of times dosed: 115
Number of different drugs/medications/compounds administered: 18

Injuries: Incisor tooth fracture; displaced left hand ring finger digit 4 while fighting; mutilating wounds to right ankle, (at this time Bangles's infant was removed, with reason noted as "maternal neglect," though she was dealing with serious injury and a threatening social milieu); the following day she suffered additional wounds of her left hand; her fracture and right ankle continued to need treatment; three days later she suffered a broken middle finger that required amputation; the wounds to her leg and her ankle were evaluated and showed infections of *Staphylococcus epidermis* and *S. aureus.*

Illnesses: Excessive alopecia and thin hair; diarrhea; fecal parasites with several bouts of rectal prolapse; lymph node enlargement; gingiva inflammation; enlarged liver. In January 1996 Bangles's daily record indicates a strep infection but a day later (1-2-1996) it states "monkey in labor ok to C-section." This implies that she was taken for an open abdominal surgery with an active infection present, which is further documented by tests run afterwards which clearly show infections requiring treatment. Despite a large abdominal mass and abnormal uterus shape, she was bred again and became pregnant. Inflammation and swelling of left eye; In August 1997 she was gavage fed due to anorexia and diagnosed a month later with an endometrial mass 8x8 cm in size. She was taken to surgery for a biopsy. On 3-9-1998 she was vomiting and with anorexia but she was approved three days later for another protocol and taken to surgery to have her carotid artery and right femoral artery catheterized. The same day post-operatively she had hematomas at the inguinal site with next day swelling noted at her neck and groin area. No other notes were given until her death. Infections included *Campylobacter fetus; Staphylococcus epidermis; S. aureus; Trichomonas, Balantidium,* and *Giardia* on more than one occasion.

Surgeries: Fetal surgery performed in December 1995 involved catheterization of femoral vein and artery; amniotic catheterization; vascular catheterization; placement of electrodes; and removal, catheterization and replacement of fetus in the womb. A month later she was C-sectioned to remove the catheters and electrodes and perform a uterine biopsy. Biopsy of abdominal mass via open abdominal laparotomy and removal of both ovaries. Carotid artery and right femoral artery catheterizations. Bangles was surgically restricted from June 1997 through March 1998 (15 days before her death).

Environmental enrichment program: Record shows a toy rotated through her cage from 3-10-1993 to 5-31-1996 (a year before her death). There are no further EE notes past this point.

Case 1.4
Name: Cecelia (# 10417)
Species: Rhesus Macaque
Origin: Born at Institution 1 (April 1979)
Time with mother: Unknown
Age at death: 20 y/o
Cause of death: Sacrifice for experiment
Number of times moved: 47
Days spent caged alone: 3,489 (46% of her life)
Total times handled: 746
Number of times dosed: 346
Number of different drugs/medications/compounds administered: 35

Protocols:
Cecilia was in a total of 6 protocols including the final terminal protocol, which began 9 days before her death. She had two C-sections, two vascular catheterizations, two EMG electrode implantations, two fetal surgeries, two amniotic catheterizations, one uterine biopsy, an exploratory laparotomy, a minipump implant, a minipump removal, and a laparoscopy. She spent time in a "suit" (vest) for intravenous administration.

Injuries:
In 1989 she was seen for a wrist lesion due to a *Staphylococcus* infection and body weight loss. On June 20, 1997 she suffered multiple traumas with multiple injuries to her left foot, fourth toe, mutilating wounds requiring amputation and right hand mutilating wounds requiring middle finger digit amputation. On 6-23-1997 she was seen again for left hand mutilating wounds and necrosis requiring digit amputation and again follow-up was done on June 26th where hydrotherapy was given. Nine months later she was seen for a lacerated lip with moderate hemorrhage (bleeding).

Illnesses:
Cecilia suffered multiple infections of *Balantidium, Entamoeba coli*, *Trichomonas* and *Giardia*, and numerous infections of microbes: Staphylococcus aureus (including a tissue infection of *Staph* at the wrist and vagina as well as *Strep* in the vagina), *Streptococcus alpha hemolytic*, *Campylobacter fetus jejuni*, and *Escherichia coli* (found in her pericardial fluid and kidney at death). She was diagnosed with degenerative spondylosis of the lumbar vertebrae at age 15. At age 20 she was noted as cachexic (wasting syndrome) with multiple pelvic peritoneal cysts and endometriosis. Cecilia's record contains multiple instances of dehydration, diarrhea, vaginal prolapse, anorexia, and cachexia. Other notes include an abnormal gait, enlarged uterus (not connected to pregnancy), enlarged liver, left corneal ulcer, abdominal distention, "unthrifty" condition, and "body condition thin." In January 1993 she was recommended for a cull (sacrifice) but she was kept in protocols for another 6 years. She was prone to overgrooming and her neck and legs were at times mostly bare.

Case 1.5
Name: Lilly (# 10006)
Species: Rhesus Macaque
Origin: Born at Institution 1 (15 May 1978)
Time with mother: Probably 1 year (housed in "corral," presumably with mother)
Age at sale: 16 years (sold to a medical school)
Number of times moved: 48
Days spent caged alone: 2,661 (45% of her life)
Total times handled: 503
Number of times dosed: 156
Number of different drugs/medications/compounds administered: 17

Illnesses: Lilly had a difficult birth and was flagged as having compromised stature and exempt from multiple surgeries. She was moved back and forth between three experiment protocols during her 16 years at the institution. Among Lilly's health problems were four separate incidents of a prolapsed uterus, two infections with *Trichomonas* (a parasitic microorganism) and one *Shigella* bacterial infection. There are three separate diarrhea diagnoses in her record, as well as poor appetite. A pre-protocol assignment exam at age 12 diagnosed Lilly with spinal kyphosis and partial mobility of her right hip. Nevertheless, she was approved for the protocol and taken to surgery requiring intensive care twice. Bradycardia (depressed heart rate) was noted just before she was approved for sale.

Environmental Enrichment: Lilly's enrichment startedin February 1993 (age 15). A single toy was rotated in and out of her cage until the time she was sold.

Surgeries: Removal of both ovaries; para-scapular implants (on three occasions); removal of uterus and uterine tubes; removal of parascapular implants (three times). She was in intensive care 7 times for a total of 70 days.

Offspring: Lilly had four babies, all live births. Female Aysha was sold to another institution at 8 y/o after being in multiple surgeries at this institution and with a history of multiple bouts of infection. Female Jwala was also sold at 8 y/o to another institution. She too had multiple surgeries and several bouts of infections as well as stays in intensive care. Male Ishan died at the institution at age 12, and male "Jack" was sold at 1 y/o to another institution after bouts with loose stool and infections.

Overall summary
Despite multiple surgeries, bradycardia, infections and multiple prolapses, she was approved for sale with documented bradycardia on the basis of a "limited exam" where she was deemed of "normal appearance" and sold to a medical school.

Case 1.6
Name: Ishan (# 13684)
Species: Rhesus macaque
Origin: Born at Institution 1 (May 1985)
Mother: Lilly (age at weaning unknown)
Age at death: 12 years

Cause of death: Not provided
Number of times moved: 49
Days spent caged alone: 1,475 (33% of his life)
Number of times handled: 2,702
Number of times dosed: 2,266
Number of different drugs/medications/compounds administered: 35

Illnesses: Ishan suffered chronic diarrhea (noted 117 times in his record), sometimes with bloody mucus. He also experienced many bouts of dehydration, two rectal prolapses; decreased appetite; dry chapped abdominal skin; body weight fluctuations, and many persistent infections of one or more of the following pathogens: *Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis, Citrobacter, Campylobacter* sp., *Morganella morganii, Shigella flexneri, Balantidium, Trichomonas* (occurs 104 times in his record)*, Entamoeba coli*, *Entamoeba histolytica*, *Entamoeba butschellii, Dientamoeba fragillis*, *Iodamoeba butschellii*, and *Giardia*. Ishan was listed as sick 180 times. At time of death he was infected with *Giardia* and *Trichomonas*.

Experiments and other procedures: Exploratory laparotomy; blunting of all four canines, and pulp capping of eight teeth. At one point he was on intravenous hook-up for 14 days, which likely involved him being placed in a vest and tethered. Ishan died two weeks following the surgical insertion of implants (unidentified) into the left parascapular region for a coronary reactivity study.

Environmental Enrichment Program: There is a single note in his daily record on 2-10-1997: “quiet”

Case 2.1
Name: Althea (# T94433)
Species: Chacma baboon
Origin: Institution 2
Time with mother: 5 months
Age at death: 10 years
Cause of death: Sacrificed for experiment
Number of times moved: 70
Days alone: ca. 2,280 days (60% of her life)
Number of times handled: 330
Number of different medications: 29
Number of times medicated: 154

Injuries: Fractured femur; abrasion of right wrist; tear of left forearm; laceration and hematoma of lefteyelid; bite wound of right thigh resulting in abscess; puncture wounds of upper lip, tibia, tail; multiple abrasions; laceration of 4th left finger requiring sutures; laceration of 2nd right finger resulting in surgical amputation of finger and limited motion in hand.

Illnesses: When she was five years old, Althea lost 30% of her body weight over the course of 11 months. In the last 4+ months of her life, Althea suffered from chronic inflammation of her sex skin. This resulted in a chronic abscess and infection described in her record as "a deep pocket of pus and discharge,” “offensive, smelly, scabby, purulent discharge,” and “necrotic with bloody spots scattered all around." The necropsy

report following Althea's death revealed eight additional problems, including active inflammations of the liver, heart, brain, kidneys and pancreas.

Experiments: Included: insertion of catheter into the left femoral vein so that she could be tethered; bone marrow biopsy (humerus) with tissue aspiration three times; bone marrow smear; drug administration via the periosteum (tissue layer covering the bone).

Overall summary
Althea spent the last 3¼ years of her life caged alone. She fared poorly in social housing, sustaining many injuries; so she was kept alone. She conceived five pregnancies and birthed four infants, whose fates are unrecorded. Althea experienced three bone marrow biopsies with tissue aspiration.

Case 3.2
Name: Vera (# F97059)
Species: Chacma baboon
Origin: Born in April 1997 (Institution 2)
Time with mother: Weaned at birth
Age at death: 6
Cause of death: Stopped breathing while under anesthesia and could not be resuscitated
Number of times moved: 30
Days spent caged alone: 1,341 (62% of her life)
Total times handled: 360
Number of times dosed: 191
Number of different drugs/medications/compounds administered: 28

Protocols: Whole body irradiation, three bone marrow blood draws, humeral biopsy/aspiration, femoral catheter insertion and implant.

Injuries: Vera lost two fingers: an amputation of her right fifth finger and an avulsion of her right 4th finger. Other injuries included a puncture wound of the right shoulder, abrasions on her chest, tail, thigh and wrist, hematomas on her arm and armpit, and lacerations on her finger, arm, and eyelid. Most bite injuries and amputations occurred when she was housed alone, so these are most likely self-inflicted. Her extended report also indicates "self inflicted superficial bite wounds to both knees" (10/18/99).

Illnesses: Inflammation of the colon, fluid-watery diarrhea (x3), blood in feces, failure of normal weight gain, fibrous thickening of the pulmonary artery and vein, abnormal crackling sounds in the lungs, and anorexia. Vera lost a quarter of her weight when she was three, and nearly a third during the year leading up to her death. Her pathology report indicates a brain tumor.

Environmental Enrichment: Despite her record of apparent self-injury, her record contains "no psychological wellbeing records."

Case 3.3
Name: Dalmar (# F97069)
Species: Chacma baboon
Origin: Born in April 1997 (Institution 2)
Time with mother: 3 months
Age at death: 10
Cause of death: Sacrificed for experiment
Number of times moved: 83
Days spent caged alone: 3,074 (78% of her life)
Number of times handled: 480
Number of times dosed: 246
Number of different drugs/medications/compounds administered: 20

Protocols: Dalmar was assigned to nine experimental protocols. She had total body irradiation, insertion of catheter, insertion of implant, 18 injections of an experimental drug, and 21 punch biopsies.

Injuries: Fingertips bitten on her right third and fourth fingers requiring amputation; laceration ofright second finger; abrasive sticky wound on left arm; avulsion of left third finger; lesion (small) on left second finger; left foot injury with discharge

Psychological illness: Dalmar engaged in self-injurious behavior. She lost four fingers to self-inflicted bites, and it is disingenuous that her record states: "etiologic agent unknown." She had numerous records of self-biting and floating limb; also, she was reported as hunched/inactive, inactive/lying down, and with whole body spasms.

Environmental Enrichment: There are only a couple of mentions of toys in Dalmar's supplementary records. On September 21st, 2005, she "got new green dino toy today, really seemed to like it."

Summary: Dalmar was singly-caged from age 22 months old onward. She was moved often and so had tremendous physical and social instability. She showed repeated, severe bouts of self-injurious behavior, losing at least 4 fingers to traumatic injury.

Case 3.4
Name: Derek (# 00040)
Species: Chacma baboon
Origin: Born in Tanzania (July 2000)
Time with mother: Unknown
Age at death: 5 y/o
Cause of death: Sacrifice for experiment
Number of times moved: 25
Days spent caged alone: 584 (77% of his life)
Total times handled: 433
Number of times dosed: 337
Number of different drugs/medications/compounds administered: 28

Protocols: Derek was subjected twice to whole body irradiation (October and November 2000). He also was given a gene transfer into hematopoietic stem cells, and an arterial graft, which failed. On three occasions his left femoral vein was surgically cannulated.

Derek was placed on intravenous administration of drugs for 98 consecutive days immediately following bone marrow aspiration and whole body irradiation. Over a hundred day stretch, he received over 300 doses of eight different compounds. His death was initially recorded on July 15th, 2002, but procedures are reported through July 30th, 2002.

Injuries: He sustained a traumatic injury to his left knee from hair clippers which needed debridement and suturing.

Illnesses: Diarrhea, severe oral lesions.

IV CONCLUSION

Most people have only a vague, if any, impression of primate research. Few ever have direct contact with these animals or the environments they are kept in. It is easier and more convenient to forget who they really are. In truth they are no less than their free-living counterparts in the wild: cognitive, emotional individuals with biographies, psychologically vulnerable beings whose pain is as real as ours.

The information contained in this document provides a rare—albeit incomplete—glimpse into the daily existence of monkeys in government-funded American national primate research centers. It is important to reiterate that the data captured here were not the focus of a sensational whistleblower account. These are randomly acquired records, and the conditions they reflect can be considered fairly representative of the 100,000 or so other primates currently in American laboratories.

These animals spend most of their lives in metal cages, often alone for long periods of months or years. If they are placed with other monkeys, they have no choice in who they are housed with, and they are moved frequently, which disrupts the potential to form stable social relationships. In addition to the chronic stresses imposed by these conditions, the monkeys are regularly subjected to acute stressful episodes that require handling and restraint, and often needles or other invasive procedures (e.g., catheter insertions, surgeries, gavage tubes, orifice swabs). To these hardships we must add the effects of experimental procedures (e.g., recovery from surgery, radiation exposure), illnesses that are often long-lasting, and injuries many of which cause lasting pain (e.g., finger amputation) but which typically receive only a single dose of pain medication. We found pain medication sorely wanting for all painful events, be they experimental, accidental, or self-inflicted. Finally, these animals' living environments appear to remain relatively barren, with minimal enrichment provided, and for only a fraction of their lives.

The reason that people worry about animal experimentation—the reason that a private citizen acquired, and then spent hundreds of hours poring through lab records, and the reason for this report—is that animals are sentient. Monkeys' capacity to suffer makes them subjects of moral concern. Scientific studies show that monkeys have complex inner lives. Wild and captive macaques cooperate and show restraint in social settings, and they adjust their expectations and show patience towards an individual who is afflicted by physical or mental handicap (de Waal 2005). In one such case, a wild Japanese macaque named Mozu lived a long and productive life, successfully rearing several young despite her being born without hands or

feet. She couldn't have done it alone; she succeeded with the help of others in her social network (ibid). Baboons experience lasting emotional states, like grief. The long term study of baboons mentioned in the Introduction (section I.2.b) not only documented signs of bereavement at the loss of an infant, but also that the grieving mothers sought therapy by expanding their social networks and engaging in more grooming with other baboons (Cheney & Seyfarth 2007).

In light of the evidence from the labs, and the emotional capacities of the victims, we conclude that the quality of life for the typical laboratory primate is very poor. It is, for all intents and purposes, a miserable existence. Clearly, reforms are needed. The question might be: What reforms can make the use of laboratory primates more humane? Or perhaps the question should be: Ought we to use monkeys in harmful experiments at all?

<u>Appendix 1:</u> Post-surgical pain relief for 12 surgical procedures performed on a random sample of monkeys from Institution 1

ID	Surgical procedure	Peri-surgical drugs (analgesics in UPPERCASE and boldface)
6524	ovarian resection at 08:59	quelicin: 08:59, IV, 20 dextrose: 08:59, IV, 110 detamine: 08:59, IM, 15 atropine: 08:59, IM, 0.3 Pen G, Pricaine & Benzathine Pen G (Flocillin): 08:59, IM, 900,000 **NUBAIN: 08:59, IM, 5; 13:30, IM, 5mg SID 1 day**
10589	Concurrent: fetal surgery at 08:25 hysterotomy at 08:27 catheter insertion into left femoral vein and artery and utero-ovarian vein at 08:28	kanamycin: 08:00, IM, 37.5mg BID 6 days; 08:25, IM, 75 nafcillin: 08:00, IM, 62.5mg BID 6 days; 08:25, IM, 125 ketamine: 08:25, IM, 50 atropine: 08:25, IM, 0.3 dextrose: 08:25, IV, 300 whole blood: 08:25, IV, 100
10589	Cesarean section at 13:43 vascular catheter removal at 13:44	oxytocin: 13:43, IV, 5; IM, 5 dexamethasone: 13:43, IM 6; IV, 12 penicillin G, Potassium: 13:43, IRR 550,000, IP 300,000 ketamine: 13:43, IM, 30,000 dextrose: 13:43, IV, 140,000 vit B complex: 13:44, IM, 2
10589	bilateral oophorectomy at 10:02 bilateral salpingectomy at 10:03	vitamin B complex: 10:02, IM, 1 imferon: 10:02, IM, 50 Quelicin: 10:02, IV, 20 dextrose: 10:02, IV, 150 atropine: 10:02, IM, 0.3 ketamine: 10:02, IM, 50 chloromycetin: 10:02, IP, 500 **NUBAIN: 10:02, IM, 5; 15:00, IM, 5 SID 1 day** chloromycetin: 14:00, IM, 125 TID 3 days
11283	oophorectomy bilateral at 08:56	atropine: 08:56, IM, 2 flocillin: 08:56, IM, 300,000 dextrose: 08:56, IV, 100 ketamine: 08:56, IM, 40 **NUBAIN: 08:56, IM, 5; 15:00, IM 5, SID 1 day**
11283	implant insertion R parascapular at 09:50	**KETAMINE: 09:50, IM, 60mg, SID 1 day** atropine: 09:50, IM, 2mg, SID 1 day

11283	hysterectomy at 09:00 oviduct catheterization at 09:01 lymph node biopsy at 09:02 skin biopsy at 09:04	**NUBAIN: 10:18, IM, 5; 18:30, IM 5mg SID 1 da**y ketamine: 10:18, IM, 40 dextrose: 10:18, IV, 210 atropine: 10:18, IM, 4 flocillin: 10:18, IP, 500 chloromycetin: 20:00, IM, 250mg BID 3 days
11283	parascapular implant removal at 09:04	**KETAMINE: 08:55, IM, 60mg SID 1 day** atropine: 08:55, IM, 0.2mg SID 1 day
11283	implant insertion R parascapular at 08:10	**KETAMINE: 08:10, IM, 65mg SID 1 day** atropine: 08:10, IM, 0.2mg SID 1 day
12541	Ovarian follicle aspiration at 09:54	flocillin: 09:54, IM, 600,000 ketamine: 09:54, IM, 35 atropine: 09:54, IM, 0.3 dextrose: 09:54, IV, 130 quelicin: 09:54, IV, 20
13377	fetal surgery at 09:00: cath insertion femoral artery + fem vein; 10cm abdom incision; catheters inserted into jugular vein and artery of fetus and electrodes placed on L deltoid muscle and sternum; fetus returned to uterus; 2 electrodes placed on uterus; incision closed; catheters tunneled to midscapular exit vascular catheterization insertion, removal; ACTH infused to fetus;	**KETAMINE: 09:00, IM, 130; 15:37, IV, 10mg BID 2 days** atropine: 09:00, IM, 0.2 kefzol: 09:00, IM, 500; 10/12/97: 09:27, IV, 250mg BID 30 days dextrose: 09:00, IV, 250; 11:30, IV, 150mg SID 1 day; 10/12/97: 09:27 IV 150mg BID 30 days terbutaline: 11:30, IV, 2mg SID 1 day; 14:45, IV, 3.25mg SID 1 day; 10:00, IV, 6mg SID 1 day; 10/11/97: 11:00, IV, 2mg SID 1 day; 21:00, IV, 5mg SID 1 day; 10/12/97: 09:27, IV 5mg SID 1 day oxytocin antagonist: 13:00, IV, 0.94mg SID 1 day indocin: 15:37, IV, 50mg BID 2 days
13377	Caesarean section w/ laparotomy at 10:45	pitocin: 10:45, IV, 5 NaCl: 10:45, IV, 125 atropine: 10:45, IM, 0.2 ketamine: 10:45, IM, 100 **NUBAIN: 10:45, IM, 5; 16:00, IM, 5mg SID 1 day** kefzol: 10:45, IV, 175mg; 20:00, IM 175mg BID 3 days

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