USDA

United States
Department of
Agriculture

Animal and
Plant Health
Inspection
Service

Legislative and
Public Affairs

Freedom of
Information

4700 River Road
Unit 50
Riverdale, MD
20737-1232

SEP 14 2008

Ms. Jean Barnes
Post Office Box 1623
Fayetteville, Georgia 30214

Dear Ms. Barnes:

This is the final response to your May 7, 2004, Freedom of Information Act (FOIA) request for Annual Reports (Reports) on Emory University for the last three years and any additional reports or other information about Yerkes Primate Center. Your request was received in this office on May 11, 2004, and assigned case number FOIA 04-468 We apologize for the delay of this response.

Enclosed are 30 pages consisting of the Reports for Emory University. However, information has been withheld under Exemption 4, 5 U.S.C. § 552(b)(4). This exemption protects confidential business information from disclosure when release would cause substantial harm to the competitive position of an individual, a partnership or a corporation from whom the information was obtained.

You may appeal our denial determination. If you choose to appeal, your appeal must be in writing and must be received at the following address within 45 days of the date of this letter:

Administrator
Animal and Plant Health Inspection Service
Ag Box 3401
Washington, D.C. 20250-3401

Please refer to FOIA 04-277 in your appeal letter and add the words "FOIA Appeal" to the front of the envelope. To assist the Administrator in reviewing your appeal, provide specific reasons why you believe modification of the determination is warranted.

Because the cost to process your request is less than $25.00, the fees have been waived. If you have questions, please contact Ms. Janice Shipman of my staff at (301) 734-0490.

Sincerely,

TGWoods

Tonya G. Woods
Director
Freedom of Information & Privacy Act Staff
Legislative and Public Affairs

Enclosures

DEC 0 1 2003

This report is required by law (7 U.S.C. 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150

See reverse side for additional information

Interagency Report Control No. 0180-DOA-AM

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. CERTIFICATE NUMBER: 57-R-0003
CUSTOMER NUMBER: 896

FORM APPROVED OMB NO. 0579-0036

2. Headquarter Research Facility *(Name and address, as registered with USDA.)*
Emory University
Div. Of Animal Resources
615 Michael St.
Atlanta, GA 30322
Telephone: (404) 727-7428

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS (*Sites*)

See Attached	

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (*Attach additional sheets if necessary or use APHIS FORM 7023a).*

A. Animals Covered By the Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments or tests were conducted involving no pain, distress or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surger or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report).*	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
4. Dogs	0	16	118	0	134
5. Cats	0	0	76	0	76
6. Guinea Pigs	0	19	50	6	75
7. Hamsters	0	0	0	0	0
8. Rabbits	0	107	68	2	177
9. Non-human Primates	929	865	1917	10	2792
10. Sheep	0	5	43	0	48
11. Pigs	0	0	430	0	430
12. Other Farm Animals	0	0	0	0	0
13. Other Animals	0	1101	37	0	1138
Grand Total	929	2113	2739	18	4870

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during and following actual research, teaching, testing, surgery or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional Official)
I certify that the above is true, correct, and complete (7 U.S.C. Section 2143).

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL	DATE SIGNED
		11/26/03

APHIS FORM 7023
(AUG 91)

Annual Report to USDA
Facility Locations

Peavine Creek Kennels, Emory University
O. Wayne Rollins Research Center, Emory University
Woodruff Memorial Research Building, Emory University
Wesley Woods, Emory University
Dental Building, Emory University
South Clinics (Winship Cancer Center and Eye Center), Emory University
Briarcliff Campus Building, Emory University
Cardiothoracic Research Labs at Crawford Long Hospital, Atlanta, GA
Yerkes Regional Primate Research Center, Emory University
Yerkes Field Station, Lawrenceville, GA
Whitehead Memorial Research Building, Emory University

Summary of Studies (Animal) Listed in Column E

Title: Behavioral Pharmacology of Narcotic Antagonists

- 10 squirrel monkeys

Squirrel monkeys are used in drug discrimination studies for studies of (b)(4) (b)(4) in the brain. In these studies, opioid drugs with differing or unknown profiles of receptor interactions are evaluated. The objective is to identify and study those components of drug action that underlie potential for abuse. It should be noted that an alternative species, rats, is used for most of these studies and squirrel monkeys are involved to a lesser extent.

Squirrel monkeys are trained to (b)(4) (b)(4) Monkeys are loosely seated in a primate chair during these studies. During the training phase and as an aversive stimulus to respond during discrimination trials, a 0.5-1.0 second mild electrical stimulus may be delivered to the monkey's tail after 5 seconds from the beginning of the trial. The monkeys can terminate the trial and prevent the electrical shock by pushing on one of two levers (corresponding to the reference drug or the placebo). The monkeys quickly learn to avoid the stimulus by responding during the five seconds after the start of the trial. After the initial training session, the monkeys rarely, if ever, receive an electrical stimulus. Shocks are never given indiscriminately or without providing the monkey the opportunity, through lever manipulation, to prevent the shock.

Pain-relieving drugs are not used in these studies because any pain experienced will be transient (one second or less) and the animal can take action to avoid all pain (by pushing a lever within 5 seconds of a clear cue). Additionally, pain-relieving drugs, such as narcotics, will confound the pharmacological effects of the opioid compounds studied.

Title: Oxidative Hypothesis – Paradoxes and Pitfalls

- 2 rabbits

Rabbits are (b)(4) subcutaneous injection using a refined procedure that minimizes or eliminates clinically apparent distress by limiting the quantity of (b)(4) given and using small volumes per injections site. However, analgesic agents were not given because of concern that the immune response necessary to elicit antibody production might be impaired.

Title: Animal Model of Newly Emerging Genital HSV-1 Infection

- 6 guinea pigs

Vaginal HSV-1 infection in guinea pigs is used as a model to study the pathophysiology of recurrent clinical herpetic infection. Acute and recurrent infection episodes may cause mild vaginitis and, in small numbers of animals, self-limiting urinary retention and/or transient hind limb paresis. As herpes simplex virus is a neurotropic virus causing persistent, often latent, infection of nerve ganglia, pharmacologic agents with neurologic effects, such as analgesics, cannot be used without potentially altering neuronal function and confounding the results of the study.

Exceptions to Regulations and Standards

Exemptions from Social Enrichment for Nonhuman Primates: Short-term Social Isolation:
There are a variety of human diseases (Parkinson's Disease, Huntington's Disease, progressive supranuclear palsy, narcolepsy, and periodic leg movements during sleep) that are associated with uncontrolled movements in sleep that cause injury. Studies described here are on monkeys with Parkinsonism induced by (b)(4) Monkeys given (b)(4) are kept in social isolation for periods of three days after drug administration while (b)(4) and its toxic metabolites are excreted. On a scheduled basis afterwards, these animals are placed in a cage specially designed for behavioral testing and telemetric recording in a room separated from the other monkeys. These monkeys may be maintained in the observation and recording room for a maximum of 7 days and are then returned to their home cage in a colony with other monkeys of the same species. Isolation from other monkeys is necessary in order to permit sleep undisturbed by commotion caused by other monkeys or human traffic in and out of the room. Monkeys under study are instrumented with (b)(4) which telemeter (b)(4) This telemetric approach allows studying sleep behavior in monkeys that are unrestrained.

- Title: State dependent motor control in neurologic disease: 4 rhesus monkeys

Physical Restraint
Monkeys in these studies are trained to do simple motor tasks such as reaching, depressing a lever, touching a target on a video screen, depressing a key to make a video target appear, or controlling a joystick to move a cursor to a target on a video screen. The monkeys are loosely restrained in a chair and typically spend 1-6 hours per daily session in the laboratory.

- Title: Muscle reassembly in MI skill acquisition: 2 capuchin monkeys
- Title: Behavioral Pharmacology of Narcotic Antagonists: 10 squirrel monkeys

Rabbits in ophthalmologic studies are loosely restrained for 15-30 minutes to permit non-invasive ocular examinations using a slit lamp.

- Title: Inhibition of tissue factor mediated angiogenesis: 10 rabbits.

Physical Restraint and Exemptions from Social Enrichment for Nonhuman Primates: Single-housing In Sight and Sound of Conspecifics:

Included in this section are primates that were housed in any condition other than group or pair housing for any significant period of time. For example, study subjects discussed below include those that were housed continuously in protected-contact housing, and those housed in protected-contact and/or group or pair housing for a significant portion, but not the entirety, of the period covered in this report.

A. Some animals used under these conditions are in studies of normal control of movement or motion disorders induced by (b)(4) Monkeys given (b)(4) may be kept in social isolation for periods of three days after drug administration and while (b)(4) and its toxic metabolites are excreted. Before and after (b)(4) administration, monkeys in these studies are trained to do simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. During these periods, monkeys with head appliances

may also undergo short-term fixed head restraint to access the appliances for neurophysiologic recording and microdialysis. Additionally, the administration of the neurotoxin (b)(4) to induce Parkinson's Disease (PD) in macaques causes physical impairments that put such animals at risk of plummeting in the social order and wounding and fight injury from a cage mate. Consequently, animals given (b)(4) are generally housed singly, but in colony rooms within sight, sound and close physical proximity of other animals of the same species. Likewise, to prevent damage to expensive and sensitive surgically-implanted devices by a conspecific, monkeys may be housed singly, but otherwise within sight and sound of conspecifics.

- Title: Therapeutic role of subthalamic nucleus activation: 2 rhesus monkeys
- Glutamate in Parkinson's disease: 8 rhesus macaques
  - Study involves administration of (b)(4)
- A novel model of Parkinson's disease: 1 rhesus macaque

B. Experiments to test whether (b)(4)

During a period of 4-8 months, subjects will have indwelling venous catheters; protected contact housing is required during this period to avoid removal of catheters by cagemates.

- Growth regulation of the neurobiology of puberty: 75 rhesus monkeys

C. Some of the studies described here involve the development of a SIV/HIV vaccine, investigation of the role of host immune response in protecting against or contributing to the appearance of immune system damage following AIDS infection, evaluation of the function of the thymus during infection with SIV, evaluation of the development and pathogenicity of mutant viruses that develop over time in chronically infected animals, the effect of opiate dependency on the progression of AIDS, and the testing of the immunogenicity and efficacy of different AIDS vaccines. Single housing is required after exposure to the virus to prevent transmission of virus from animal to animal. In addition, the animals need to be accessed frequently for blood draws. The experimental design requires that the efficacy of vaccines will be assessed after a single exposure and without the possible confound of exposure to mutant viruses. Infected animals in an experimental group will be housed together after approximately one month. In some experiments, animals are singly housed one month prior to inoculation to allow sufficient time for acclimatization to the new housing arrangement so that the stress of separation doesn't influence susceptibility to or course of infection.

Another study is being done to establish a pregnant rhesus monkey animal model for human Listeria infection and to develop methodology for determining dose information to be used in a risk assessment for Listeria monocytogenes. Single caging is required during the time between infection and one month post-delivery primarily to prevent transmission of the *Listeria* organism from experimentally infected animals to non-infected animals, as well as to permit the collection of fecal samples from the experimentally infected animal to check for fecal shedding of *Listeria* organisms. If infants are liveborn, they are returned to their mothers following testing.

A study testing the effects of T cell depleting antibodies in SIV-infected mangabeys requires frequent antibody infusions and blood draws during the first 3 weeks of the treatment (animals are assessed up to 4 times per week), followed by weekly blood draws for the remainder of the study, which lasts 2 months. Because these animals will be frequently handled for testing, animals are housed in protected contact housing.

Malaria studies are being done to develop a vaccine and to provide antigens for serologic and molecular studies, genomic libraries, antibody production, and gametocytes for infection of mosquitoes. Other related studies are looking at immunological and molecular biological mechanisms the malaria parasite uses to express and switch expression of the variant antigen at the surface of the infected red blood cell and the relationship of malaria to anemia in pregnant women. Chimpanzees infected with malaria are housed individually in metabolism cages. This is usually required for a period of 1-2 months. It is also necessary to house the animals indoors to prevent contact with the local mosquito population. Following blood collections and treatment of the malaria infection, the animals are returned to their normal housing environment. Protected-contact housing is utilized in other malaria vaccine studies in monkeys due to the requirement of daily heel or ear sticks (as well as blood collection and immunization), as well to avoid frequent reunions following stressful procedures. During the period of treatment in a hepatitis C suppression study, it is necessary to maintain the animals in metabolism cages. This is due to the twice daily drug administration and frequent blood collections.

- Core A: Preclinical trials and pathology (Part of NCVDG Grant: DNA and protein immunogens for SIV/HIV vaccines): 102 Rhesus macaques
- New live viral vectors in candidate AIDS vaccines: animal trials core: 39 rhesus macaques
- Cellular immune responses and AIDS pathogenesis: 14 rhesus macaques and 18 mangabeys
- Core A: Nonhuman primates (Part of program project grant entitled: DNA/MVA immunogens, cross-clade immune responses): 48 rhesus macaques
- Induction of P vivax, P ovale, P malariae and other plasmodium infections in chimpanzees to obtain large volumes of parasites for malaria vaccine studies: 14 chimpanzees
- Molecular evolution of multiply deleted SIV in vitro: 38 rhesus macaques
- Core C: Primate Studies: 59 rhesus macaques
- Fetal immunoprophylaxis against a primate lentivirus: 51 rhesus macaques
- Development of a risk assessment dose-response model for foodborne listeria: 33 rhesus macaques
- Mechanism of oral SIV transmission: 11 rhesus macaques
- Analysis of thymic function during SIV infection: 6 mangabey, 1 rhesus macaque
- Modified nucleosides for HCV: 2 chimpanzees
- T cell turnover in normal and SIV infected sooty mangabeys: 17 mangabeys, 2 rhesus
- SHIV macaque model of oral immunization against sexually transmitted HIV: 12 rhesus macaques and 8 pigtail macaques
- Replication defective HIV vaccine: 7 rhesus macaques
- Impact of anti-CD8 antibody treatment on viral dynamics in SIV-infected sooty mangabeys: 15 mangabeys
- CNS as a viral reservoir in SIV infected macaques: 1 rhesus macaque
- Oral transmission of SIV in neonatal and adult macaques: 12 rhesus macaques
- Role of virus specific immunity in primate AIDS: 3 mangabeys, 2 macaques
- Molecular analysis of antigenic variation in malaria: 19 rhesus macaques
- Malaria, pregnancy and immunophysiopathology: 6 rhesus macaques
- In vivo evaluation of candidate drugs: 12 rhesus macaques

- AIDS & opiates: a monkey model: 29 rhesus macaques
- Determinants of HIV/SIV mucosal transmission: 9 rhesus macaques
- Combination DNA and attenuated virus vaccine for SIV : 18 rhesus macaques
- Immune modulation of neurotropin in SIV infection: 28 rhesus macaques
- IL-16 Mediated Immune Reconstitution during SIV Infection: 10 rhesus macaques
- Experimental Inoculations of Macaques with Rotavirus: 9 rhesus macaques, 15 pigtail macaques
- Face Processing in Chimps Using PET: 4 Chimpanzees
- Environmental Enrichment of Yerkes Primate Center Animal Colony: 236 rhesus macaques
- Colony Management Support: 193 rhesus macaques (Recently received animals in quarantine)
- Molecular Analysis of Antigenic Variation Malaria: 20 rhesus macaques
- Emory-Navy Malaria Vaccine Trials: 20 rhesus macaques

D. Lumbar spine fusion is commonly performed in humans, but the failure to achieve a solid bone union is reported 10-40% of the time. The required doses of bone growth factors, which have enhanced bone formation in lower vertebrates, are much higher in humans. If these bone growth factors were successful in humans, it could improve the frequency of healing success, decrease healing time and decrease pain in patients. Therefore, studies of dose and delivery vehicle in non-human primates have become a critical step to prepare for human clinical trials. Spine fusion surgery will be performed on animals followed by administration of different bone growth factors. Animals receiving adenovirus will be housed singly for 3 days after surgery to insure that viral shedding does not adversely affect other animals or humans. Then animals will be in protected contact housing to prevent possible trauma to the surgical wound.

- Use of osteoinductive factors to enhance spine fusion: 33 rhesus macaques

E. The integration of functional MRI (fMRI) technology with proven utility will significantly advance research efforts in biomedical and behavioral sciences. One research application involves biochemical mechanisms underlying the effectiveness of olanzapine in treating human schizophrenic patients. Another is directed towards brain activation studies during cocaine use. This may help to determine the brain structures and neural circuits that underlie the addictive properties of cocaine. In studies on cocaine and drug abuse, animals will be used for pharmacological and neurochemistry experiments involving the placement of an indwelling venous catheter for drug delivery during daily sessions lasting 1-2 hours. Some animals also have an indwelling guide cannulae. The catheters and guide cannulae must be protected from contact by other animals. If contact is allowed, the preparations can be compromised with the risk of physical injury and infection. Protected contact housing reduces the risk since both animals can control proximity to others. The animals may require single housing if they persistently place themselves at risk to damage their indwelling venous catheters or guide cannulae or that demonstrate a proclivity to damage another animal's catheter.

Determining the relationship between prefrontal cortical circuitry and components of dopaminergic neurotransmission is the focus of one research study that will enhance understanding of the cognitive processes subserved by the prefrontal cortex. This will hopefully shed light on human disease states, notably schizophrenia. In order to identify

particular neural connections in the prefrontal cortex of macaques, axonal tracers will be injected intracerebrally. Following stereotaxic surgery, craniotomies will be made over the prefrontal cortex. Subjects must be in protected contact housing to protect craniotomy sites and sutures.

- Development of functional magnetic resonance imaging (MRI) for behavioral studies in nonhuman primates: 8 Rhesus Macaques
- Cocaine use and pharmacotherapy effectiveness in monkeys: 6 Rhesus macaques
- PET neuroimaging and cocaine neuropharmacology in monkeys: 24 Rhesus macaques
- Cocaine use and monoamine function in nonhuman primates: 56 squirrel monkeys
- Cortical circuitry related to neurotransmission proteins: 6 rhesus macaques

F. Visual, vestibular and oculomotor systems must work together for normal visual function. Various disease processes or injuries can compromise the normal interaction of these systems. Research in this area will provide a basic science foundation for understanding eye movement control in humans. Primates are used since they exhibit the same set of eye movements as humans. To facilitate the research, scleral search-coils are implanted to precisely measure eye movement. In addition, head movements need to be restricted during visual testing to allow accurate tracking of visual targets. Therefore, a stainless-steel receptacle is implanted. It is sometimes necessary to house animals in protected housing when they have surgical implants. This is to protect the animal from any injury due to aggressive behavior of other animals. Animals also sometimes wear goggles which may be removed during paired housing.

- Neural control of visual vestibular behavior: 17 rhesus macaques
- Visual Processing and Smooth Eye Movement: 5 rhesus macaques

G. Studies of pancreas, kidney, and bone marrow transplants as well as arterial grafts are investigating the ability of costimulation blockade to protect the organs from rejection. For experiments involving bone marrow transplantation, single housing is required for the first 75-100 days following the transplant due to the potential complications including immunosuppression, anemia, leukopenia and thrombocytopenia. After that time, the animals may be paired with same sex and age animals. In the pancreatic islet cell transplant model, daily monitoring of urine and stool output are necessary to diagnose steatorrhea, polyuria and ketoacidosis. In addition, pancreatic enzyme replacement and (b)(4) are administered orally in a treat and it is essential that the amount consumed by each animal is recorded. Following renal transplantation, animals will require protected housing so that an accurate assessment of daily food/water intake and urine/feces production be accounted. Prior to surgery, animals may be pair-housed. With immunosuppressive therapy, healing can be delayed. Therefore, animals receiving an arterial graft are housed singly for 21 days after abdominal surgery to allow daily postoperative monitoring.

- Hematopoietic chimerism and transplant tolerance: 14 rhesus macaques
- Non-human primate pancreatic islet cell transplantation: 57 rhesus macaques
- The effect of dosing strategy for LEA29Y on renal allograft survival in rhesus macaques: 23 rhesus macaques
- Activation, apathy, anergy, and apoptosis in transplantation: 58 rhesus
- CD45RB and kidney transplantation: 9 rhesus macaques
- Dose effect of busulfan in the primate model: 11 rhesus macaques

- Transplant Tolerance in Non-Human Primates: Costimulation, chimerism and tolerance in transplantation (Project 3): 49 rhesus macaques

H. Cardiovascular disease remains the leading cause of mortality in Western societies. Blood flow to critical vascular beds become stopped or reduced, leading to heart attacks and strokes. Surgical replacement of diseases arteries with artificial substitutes has worked moderately well for larger vessels, but has been problematic for replacing smaller diameter vessels (less than 6mm i.d.) Specific and effective molecular level therapies may represent a promising strategy. In this study, subjects will have carotid artery graft implants , aorto-iliac graft implants, and aortic interposition grafts. Protected contact housing is required for 7-10 days to protect surgical sites. The remaining time, animals will be group housed. Another study will be looking at probes that interfere with thrombogenesis (activation of blood coagulation, inhibition of platelet activation and inhibition of platelet attachment to injured blood vessel walls). Animals are singly housed to permit repeated access for blood sampling and noninvasive imaging procedures and to protect the surgical access site.

- Evaluation of small vessel prostheses: 71 baboons
- In vivo platelet interactions with adhesive glycoproteins: 28 baboons
- Evaluation of activated Protein C: 18 baboons

Physical Restraint, Exemptions from Social Housing, and Food or Water Restriction of Nonhuman Primates

Nonhuman primates used under these conditions are in motion disorder studies or studies of brain function. Most of the animals are used to research the cause and treatment of Parkinson's Disease (PD) because of the great similarity of brain function and that Parkinson's-like disease can be induced in them by giving the neurotoxic chemical (b)(4) . Monkeys in these studies usually are given (b)(4) by intracarotid injection, so that only one side of the brain is affected. These monkeys have only slight deficits in precise control of movements on one side of the body and have no substantial movement problems. In general, isolation housing is only done for a 3 day period immediately after administration of (b)(4) during the time of excretion of the neurotoxin in the feces and urine. Otherwise, monkeys in these studies are housed within sight and sound of other animals of the species and permitting physical contact with a compatible conspecific.

Monkeys in studies requiring food or water restriction are provided *ad libitum* food and water on weekends according to standard husbandry practices. During weekdays, food or water is restricted overnight and in the morning (12-15 hours total) and then food or water is provided to satiety during morning or afternoon test sessions as an inducement to perform video-based tasks. Single housing is necessary to facilitate food or water restriction – otherwise a conspecific would be subjected to unnecessary restriction or food sharing might occur. Monkeys are trained using food or water as an inducement to perform simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. These monkeys, except as indicated, are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. During these periods, the monkeys with head appliances may also undergo short-term fixed head restraint to access the appliances for neurophysiologic recording and microdialysis. Water or food is provided during and immediately after the testing session to meet the daily ration. The

total intake of the restricted material, food or water, is recorded daily and the animal's body weight is checked and recorded at least twice weekly to ensure that are being well maintained.

In eye movement studies, animals must be awake, alert and comfortably seated. The tasks involve following a smoothly moving or jumping target spot that is rear-projected on a tangent screen. First the animals are fitted with a collar that it will always wear. It is made of a soft nylon material. Animals are then adapted to pole handling and using a primate chair. It takes most animals 4 weeks to reach proficiency. Animals are trained 5 days per week for time periods of 15 minutes to 3 hours.

In cocaine abuse studies, cocaine is scheduled as the consequent event and is sufficiently reinforcing that food and water restrictions are not necessary. However, for self-administration experiments, subjects are trained to sit quietly in standard primate chairs over a 2-4 week period. The pole-and-collar system for handling and training nonhuman primates will facilitate immobilization. Initially, subjects will be immobilized for approximately 20-30 minutes per training session, but over the course of several weeks, the amount of time will increase to from 1 to 4 hours per session. Each subject will be immobilized at least twice per week for 6 weeks. In a related study, changes in sensitivity to the CNS effects of cocaine are assessed after the monoamine neurotransmitter is manipulated pharmacologically. The animals are trained to be seated in a loosely fitting chair during daily (Mon. – Fri.) sessions. The chair is designed to provide minimal skin contact with the animal, and is limited primarily to the waist and buttocks. Typically, experiments are conducted so as to require no more than one hour per day in the apparatus. This minimal restraint provides protection of indwelling catheters used for drug administration and contact with a localized area of the tail for electrical stimulation.

In a study looking (b)(4) changes in neurochemistry, monkeys will be seated in a standard primate restraint chair. Probes will be inserted bilaterally into the guide cannulae and connected to infusion equipment. The experimental perfusion lasts 5 hours. Animals will typically spend time in the chair 2-3 days per week.

For the evaluation of small vessel prostheses, animals will be immobilized for a short duration with (b)(4) administered IM. This is augmented by oxygen + isoflurane if needed.

Startle reflex testing is done in one study after each monkey is habituated to chair restraint. The sessions are 2-3 times per week for 60 minutes each session. The tests continue for 2 weeks. These tests may be repeated every 3-4 months to monitor potential developmental changes in emotionality.

Some of the animals used under these conditions are in oculomotor, visual disorders, and visual cortex studies. Monkeys are used because they are capable of the same range of eye movements as humans. Infant monkeys are swaddled in a blanket. Older animals have a chair adjusted for comfort. The chair includes a standard design that allows the animal to sit in a natural position. The animal is allowed to sit in the chair for 5-15 minutes on the first occasion, during which time treats (apple slices, applesauce, etc) are offered to make the chair session a positive experience. Head movements in the animals during visual testing are restricted by an implanted stainless steel receptacle (SSR) on the head. In other studies, head movement is restricted with a custom-fit helmet. In one study, monkeys under 6 months of age have their heads immobilized with Velcro straps. After 6 months, a small, light-weight aluminum halo, of the type used in patients with neck injuries, to fix the head to the chair. Between 6 and 12 months of age, the halos will be removed every 2 weeks for at least 1 week. The duration of the testing sessions is gradually

increased from 10-15 minutes to an hour over the course of the first two weeks and up to 3 hours over the course of 3 months. Behavioral training occurs up to five times per week. At any sign of distress (e.g., wiggling in the chair or vocalization) the session is terminated.

Monkeys in these studies have transiently-induced movement disorders and are trained to do simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory.

To motivate the animals to work effectively, the first feeding of the day may be reduced or delayed. However, water or food is provided during and immediately after the testing session to meet the daily ration. The total intake of the restricted material, food or water, is recorded daily and the animal's body weight is checked and recorded at least twice weekly to ensure that are being well maintained.

1. Food and/or water restricted, but provided during and after laboratory testing sessions:
   - Title: Basal ganglia discharge patterns in Parkinsonism: 2 rhesus monkeys
   - Title: The substantia nigra in movement and movement disorders: 8 rhesus monkeys
   - Title: Influence of subthalamic nucleus on striatal dopamine: 2 rhesus monkeys
   - Title: Pathophysiology of the basal ganglia in Parkinsonism: 4 rhesus monkeys
   - Title: Deep brain stimulation in the Parkinsonian monkey: 4 rhesus monkeys
   - Development of gaze-holding abilities: 10 rhesus macaques
   - A novel model of Parkinson's disease: 1 rhesus macaque
   - Face Processing in Chimps Using PET: 4 Chimpanzees
   - Characterization of Corticotropin Releasing Factors: 1 rhesus monkey

2. Short-term physical restraint only:

   - Glutamate in Parkinson's disease: 8 rhesus macaques
   - PET neuroimaging and cocaine neuropharmacology in monkeys: 24 rhesus macaques
   - Development of functional magnetic resonance imaging (MRI) for behavioral studies in nonhuman primates: 8 Rhesus Macaques
   - Cocaine use and pharmacotherapy effectiveness in monkeys: 6 Rhesus macaques
   - Effects of (b)(4) on extracellular monoamines in rhesus monkeys: 8 rhesus macaques
   - Cocaine use and monoamine function in nonhuman primates: 56 squirrel monkeys
   - Gene profiling in drug addiction in nonhuman primates: 4 rhesus macaques
   - The error signal for postnatal eye growth in the primate: 16 rhesus macaques
   - Prefrontal Control of Social Behavior in Primates: 6 rhesus macaques and 1 pigtail macaque
   - Emotional and Endocrine Covariates of Macaca mulatta: 34 rhesus macaques

Food or Water Restriction of Dogs

Following gastric by-pass surgery, dogs are not fed for four days to permit uneventful healing of the stomach. Intravenous fluids are given to maintain hydration. Dietary transition is then done to a soft diet and subsequently to feeding conventional canine diets. Providing fluid needs are met, well-nourished animals easily tolerate several days without food. Current veterinary standards dictate that postoperative fasted animals not be subjected to the risk associated with parenteral administration of nutrients (JAVMA 201: 699-73, 2000).

- Helicobacter pylori infection of the excluded stomach after gastric bypass: 5 dogs

Exemptions from Exercise for Dogs

Dogs with an inherited motoneuron disease may be restricted from exercise for 3-4 days while acutely recovering from surgery.

- Title: Functional studies in motoneuron disease: 14 dogs.

Food or Water Restriction of Swine

Swine to undergo survival bowel surgery are restricted from solid food and given an all-liquid diet for 2-3 days prior to surgery in order to fully cleanse the gastrointestinal tract including the lengthy spiral colon.

- Title: Laparoscopic ureteral replacement with reconfigured colon: 3 pigs.

DEC 04 2002

This report is required by law (7 U.S.C. 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150

See reverse side for additional information

Interagency Report Control No. 0180-DOA-AM

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. CERTIFICATE NUMBER: 57-R-0003
CUSTOMER NUMBER: 896

FORM APPROVED OMB NO. 0579-0036

2. Headquarter Research Facility *(Name and address, as registered with USDA.)*
Emory University
1440 Clifton Road, NE
Atlanta, GA 30322

Telephone: (404) 727-7428

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS (*Sites*)

See Attached	

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (*Attach additional sheets if necessary or use APHIS FORM 7023a).*

A. 2002 Animals Covered By the Animal Welfare Regulations	B. 2002 Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research or surgery but not yet used for such purposes.	C. 2002 Number of animals upon which teaching, research, experiments or tests were conducted involving no pain, distress or use of pain-relieving drugs.	D. 2002 Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic or tranquilizing drugs were used.	E. 2002 Number of animals upon which teaching, experiments, research, surger or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report).*	F. 2002 TOTAL NO. OF ANIMALS (Cols. C + D + E)
4. Dogs	0	52	138	0	190
5. Cats	0	0	84		84
6. Guinea Pigs	0	30	70		100
7. Hamsters	0	0	0		0
8. Rabbits	0	181	111	4	296
9. Non-human Primates	1261	341	2322	17	2680
10. Sheep	0	7	19		26
11. Pigs	0	0	292		292
12. Other Farm Animals					0
					0
13. Other Animals	0	638	51		689

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during and following actual research, teaching, testing, surgery or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, th summary includes a brief explanation of the exceptions as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequecy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional Official)
I certify that the above is true, correct, and complete (7 U.S.C. Section 2143).

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL	DATE SIGNED

APHIS FORM 7023
(AUG 91)

KCC

Annual Report to USDA
Facility Locations

Peavine Creek Kennels, Emory University
O. Wayne Rollins Research Center, Emory University
Woodruff Memorial Research Building, Emory University
Wesley Woods, Emory University
Dental Building, Emory University
South Clinics (Winship Cancer Center and Eye Center), Emory University
Cell Biology Building, Emory University
Physiology Building, Emory University
Grady Memorial Hospital, Woodruff Extension, Atlanta, GA
Briarcliff Campus Building, Emory University
Cardiothoracic Research Labs at Crawford Long Hospital, Atlanta, GA
Yerkes Regional Primate Research Center, Emory University
Yerkes Field Station, Lawrenceville, GA
Whitehead Memorial Research Building, Emory University

Summary of Studies (Animal) Listed in Column E

Title: Behavioral Pharmacology of Narcotic Antagonists

- 17 squirrel monkeys

Squirrel monkeys are used in drug discrimination studies for studies of in the brain. In these studies, opioid drugs with differing or unknown profiles of receptor interactions are evaluated. The objective is to identify and study those components of drug action that underlie potential for abuse. It should be noted that an alternative species, rats, is used for most of these studies and squirrel monkeys are involved to a lesser extent.

Squirrel monkeys are trained to discriminate between a reference drug, such as Monkeys are loosely seated in a primate chair during these studies. During the training phase and as an aversive stimulus to respond during discrimination trials, a 0.5-1.0 second mild electrical stimulus may be delivered to the monkey's tail after 5 seconds from the beginning of the trial. The monkeys can terminate the trial and prevent the electrical shock by pushing on one of two levers (corresponding to the reference drug or the placebo). The monkeys quickly learn to avoid the stimulus by responding during the five seconds after the start of the trial. After the initial training session, the monkeys rarely, if ever, receive an electrical stimulus. Shocks are never given indiscriminately or without providing the monkey the opportunity, through lever manipulation, to prevent the shock.

Pain-relieving drugs are not used in these studies because any pain experienced will be transient (one second or less) and the animal can take action to avoid all pain (by pushing a lever within 5 seconds of a clear cue). Additionally, pain-relieving drugs, such as narcotics, will confound the pharmacological effects of the opioid compounds studied.

Title: Oxidative Hypothesis – Paradoxes and Pitfalls

- 4 rabbits

Rabbits are by subcutaneous injection using a refined procedure that minimizes or eliminates clinically apparent distress by limiting the quantity of given and using small volumes per injections site. However, analgesic agents are not given because of concern that the immune response necessary to elicit antibody production may be impaired.

Exceptions to Regulations and Standards

Exemptions from Social Enrichment for Nonhuman Primates: Short-term Social Isolation

There are a variety of human diseases (Parkinson's Disease, Huntington's Disease, progressive supranuclear palsy, narcolepsy, and periodic leg movements during sleep) that are associated with uncontrolled movements in sleep that cause injury. Studies described here are on monkeys with Parkinsonism induced by Monkeys are placed in a cage specially designed for behavioral testing and telemetric recording in a room separated from the other monkeys. These monkeys may be maintained in the observation and recording room for a maximum of 7 days and are then returned to their home cage in a colony with other monkeys of the same species. Isolation from other monkeys is necessary in order to permit sleep undisturbed by commotion caused by other monkeys or human traffic in and out of the room. Monkeys under study are instrumented with which telemeter This telemetric approach allows studying sleep behavior in monkeys that are unrestrained.

In another movement disorder study, monkeys are housed in a specially arranged isolation room for 72 hours after each administration of Although this is a transient, post-operative care housing situation, the animals will be repeatedly isolation-housed. Whenever possible, an already -lesioned monkey will be housed with the recently injected monkey in order to provide visual, auditory and olfactory contact with a conspecific. It is understood that the stress of short-term room changes on a monkey may be a greater than the stress of isolation housing would be for the recently -injected subject, so housing will be evaluated on a case-by-case basis. In the extremely low-dose protocol, with dosing occurring every 2-3 days, the need to house the subject away from other monkeys will be constant. Therefore, the short-term stress of room changes is unlikely to outweigh the benefits to the subject undergoing MPTP dosing.

- State dependent motor control in neurologic disease: 4 rhesus monkeys
- Glutamate in Parkinson's disease: 7 rhesus macaques
    - Study involves administration of

Exemptions from Social Enrichment for Nonhuman Primates: Single-housing in Sight and Sound of Conspecifics

Included in this section are primates that were housed in any condition other than group or pair housing for any significant period of time. For example, study subjects discussed below include those that were housed continuously in protected-contact housing, and those housed in protected-contact and/or group or pair housing for a significant portion, but not the entirety, of the period covered in this report.

A. Experiments to test whether i

During a period of 4-8 months, subjects will have indwelling venous catheters; protected contact housing is required during this period to avoid removal of catheters by cagemates.

- Growth regulation of the neurobiology of puberty: 85 rhesus monkeys

B. Some of the studies described here involve the development of a SIV/HIV vaccine, investigation of the role of host immune response in protecting against or contributing to the appearance of immune system damage following AIDS infection, evaluation of the function of the thymus during infection with SIV, evaluation of the development and pathogenicity of mutant viruses that develop over time in chronically infected animals, the effect of opiate dependency on the progression of AIDS, and the testing of the immunogenicity and efficacy of different AIDS vaccines. Single housing is required after exposure to the virus to prevent transmission of virus from animal to animal. In addition, the animals need to be accessed frequently for blood draws. The experimental design requires that the efficacy of vaccines will be assessed after a single exposure and without the possible confound of exposure to mutant viruses. Infected animals in an experimental group will be housed together after approximately one month. In some experiments, animals are singly housed one month prior to inoculation to allow sufficient time for acclimatization to the new housing arrangement so that the stress of separation doesn't influence susceptibility to or course of infection.

Another study is being done to establish a pregnant rhesus monkey animal model for human Listeria infection and to develop methodology for determining dose information to be used in a risk assessment for Listeria monocytogenes. Single caging is required during the time between infection and one month post-delivery primarily to prevent transmission of the *Listeria* organism from experimentally infected animals to non-infected animals, as well as to permit the collection of fecal samples from the experimentally infected animal to check for fecal shedding of *Listeria* organisms. If infants are liveborn, they are returned to their mothers following testing.

A study testing the effects of requires frequent antibody infusions and blood draws during the first 3 weeks of the treatment (animals are assessed up to 4 times per week), followed by weekly blood draws for the remainder of the study, which lasts 2 months. Because these animals will be frequently handled for testing, animals are housed in protected contact housing.

are being done to develop a vaccine and to provide antigens for serologic and molecular studies, genomic libraries, antibody production, and gametocytes for infection of mosquitoes. Other related studies are looking at uses to express and switch expression of the variant antigen at the surface of the infected red blood cell and the relationship of malaria to anemia in pregnant women. Chimpanzees infected with malaria are housed individually in metabolism cages. This is usually required for a period of 1-2 months. It is also necessary to house the animals indoors to prevent contact with the local mosquito population. Following blood collections and treatment of the malaria infection, the animals are returned to their normal housing environment. Protected-contact housing is utilized in other malaria vaccine studies in monkeys due to the requirement of daily heel or ear sticks (as well as blood collection and immunization), as well to avoid frequent reunions following stressful procedures. During the period of treatment in a hepatitis C suppression study, it is necessary to maintain the animals in metabolism cages. This is due to the twice daily drug administration and frequent blood collections.

- Core A: Preclinical trials and pathology (Part of NCVDG Grant: DNA and protein immunogens for SIV/HIV vaccines): 63 Rhesus macaques
- New live viral vectors in candidate AIDS vaccines: animal trials core: 2 chimpanzees, 16 rhesus macaques
- Cellular immune responses and AIDS pathogenesis: 7 rhesus macaques and 7 mangabeys
- Core A: Nonhuman primates (Part of program project grant entitled: DNA/MVA immunogens, cross-clade immune responses): 42 rhesus macaques
- Induction of P vivax, P ovale, P malariae and other plasmodium infections in chimpanzees to obtain large volumes of parasites for malaria vaccine studies: 6 chimpanzees
- Generation and recovery of plasmodium falciparum liver stage parasites in chimpanzees: 2 chimpanzees
- Molecular evolution of multiply deleted SIV in vitro: 34 rhesus macaques
- Core C: Primate Studies: 22 rhesus macaques
- Fetal immunoprophylaxis against a primate lentivirus: 22 rhesus macaques
- Development of a risk assessment dose-response model for foodborne listeria: 22 rhesus macaques
- Mechanism of oral SIV transmission: 11 rhesus macaques
- Analysis of thymic function during SIV infection: 6 mangabey, 1 rhesus macaque
- Modified nucleosides for HCV: 2 chimpanzees
- T cell turnover in normal and SIV infected sooty mangabeys: 8 mangabeys, 1 rhesus
- SHIV macaque model of oral immunization against sexually transmitted HIV: 8 rhesus/pigtail macaques
- Replication defective HIV vaccine: 7 rhesus macaques
- Impact of anti-CD8 antibody treatment on viral dynamics in SIV-infected sooty mangabeys: 12 mangabeys
- CNS as a viral reservoir in SIV infected macaques: 1 rhesus macaque
- Oral transmission of SIV in neonatal and adult macaques: 12 rhesus macaques
- Role of virus specific immunity in primate AIDS: 3 mangabeys, 7 macaques
- Molecular analysis of antigenic variation in malaria: 19 rhesus macaques
- Malaria, pregnancy and immunophysiopathology: 4 rhesus macaques
- In vivo evaluation of candidate drugs: 12 rhesus macaques
- AIDS & opiates: a monkey model: 29 rhesus macaques
- Determinants of HIV/SIV mucosal transmission: 9 rhesus macaques
- Combination DNA and attenuated virus vaccine for SIV : 14 pigtail macaques
- Immune modulation of neurotropin in SIV infection: 14 rhesus macaques

C. Lumbar spine fusion is commonly performed in humans, but the failure to achieve a solid bone union is reported 10-40% of the time. The required doses of bone growth factors, which have enhanced bone formation in lower vertebrates, are much higher in humans. If these bone growth factors were successful in humans, it could improve the frequency of healing success, decrease healing time and decrease pain in patients. Therefore, studies of dose and delivery vehicle in non-human primates have become a critical step to prepare for

human clinical trials. Spine fusion surgery will be performed on animals followed by administration of different bone growth factors. Animals receiving adenovirus will be housed singly for 3 days after surgery to insure that viral shedding does not adversely affect other animals or humans. Then animals will be in protected contact housing to prevent possible trauma to the surgical wound.

- Use of osteoinductive factors to enhance spine fusion: 30 rhesus macaques

D. The integration of functional MRI (fMRI) technology with proven utility will significantly advance research efforts in biomedical and behavioral sciences. One research application involves biochemical mechanisms underlying the effectiveness of olanzapine in treating human schizophrenic patients. Another is directed towards brain activation studies during cocaine use. This may help to determine the brain structures and neural circuits that underlie the addictive properties of cocaine. In studies on cocaine and drug abuse, animals will be used for pharmacological and neurochemistry experiments involving the placement of an indwelling venous catheter for drug delivery during daily sessions lasting 1-2 hours. Some animals also have an indwelling guide cannulae. The catheters and guide cannulae must be protected from contact by other animals. If contact is allowed, the preparations can be compromised with the risk of physical injury and infection. Protected contact housing reduces the risk since both animals can control proximity to others. The animals may require single housing if they persistently place themselves at risk to damage their indwelling venous catheters or guide cannulae or that demonstrate a proclivity to damage another animal's catheter.

Determining the relationship between prefrontal cortical circuitry and components of dopaminergic neurotransmission is the focus of one research study that will enhance understanding of the cognitive processes subserved by the prefrontal cortex. This will hopefully shed light on human disease states, notably schizophrenia. In order to identify particular neural connections in the prefrontal cortex of macaques, axonal tracers will be injected intracerebrally. Following stereotaxic surgery, craniotomies will be made over the prefrontal cortex. Subjects must be in protected contact housing to protect craniotomy sites and sutures.

- Development of functional magnetic resonance imaging (MRI) for behavioral studies in nonhuman primates: 8 Rhesus Macaques
- Medications for drug abusers: 17 Squirrel monkeys
- Cocaine use and pharmacotherapy effectiveness in monkeys: 6 Rhesus macaques
- PET neuroimaging and cocaine neuropharmacology in monkeys: 20 Rhesus macaques
- Cocaine use and monoamine function in nonhuman primates: 39 squirrel monkeys
- Effects of Olanzapine on extracellular monoamines in rhesus monkeys: 8 rhesus macaques
- Cortical circuitry related to neurotransmission proteins: 3 rhesus macaques

E. Visual, vestibular and oculomotor systems must work together for normal visual function. Various disease processes or injuries can compromise the normal interaction of these systems. Research in this area will provide a basic science foundation for understanding eye movement control in humans. Primates are used since they exhibit the same set of eye

movements as humans. To facilitate the research, scleral search-coils are implanted to precisely measure eye movement. In addition, head movements need to be restricted during visual testing to allow accurate tracking of visual targets. Therefore, a stainless-steel receptacle is implanted. It is sometimes necessary to house animals in protected housing when they have surgical implants. This is to protect the animal from any injury due to aggressive behavior of other animals. Animals also sometimes wear goggles which may be removed during paired housing.

- Neural control of visual vestibular behavior: 18 rhesus macaques

F. Studies of pancreas, kidney, and bone marrow transplants as well as arterial grafts are investigating the ability of costimulation blockade to protect the organs from rejection. For experiments involving bone marrow transplantation, single housing is required for the first 75-100 days following the transplant due to the potential complications including immunosuppression, anemia, leukopenia and thrombocytopenia. After that time, the animals may be paired with same sex and age animals. In the pancreatic islet cell transplant model, daily monitoring of urine and stool output are necessary to diagnose steatorrhea, polyuria and ketoacidosis. In addition, pancreatic enzyme replacement and (b)(4) are administered orally in a treat and it is essential that the amount consumed by each animal is recorded. Following renal transplantation, animals will require protected housing so that an accurate assessment of daily food/water intake and urine/feces production be accounted. Prior to surgery, animals may be pair-housed. With immunosuppressive therapy, healing can be delayed. Therefore, animals receiving an arterial graft are housed singly for 21 days after abdominal surgery to allow daily postoperative monitoring.
   - Hematopoietic chimerism and transplant tolerance: 11 rhesus macaques
   - Non-human primate pancreatic islet cell transplantation: 12 rhesus macaques
   - The effect of dosing strategy for LEA29Y on renal allograft survival in rhesus macaques: 2 rhesus macaques
   - Activation, apathy, anergy, and apoptosis in transplantation: 41 rhesus
   - CD45RB and kidney transplantation: 9 rhesus macaques
   - Dose effect of busulfan in the primate model: 2 rhesus macaques
   - Transplant Tolerance in Non-Human Primates: Costimulation, chimerism and tolerance in transplantation (Project 3): 11 rhesus macaques
   - Transplant tolerance: costimulation, cytokines and chimerism (Project 3: costimulatory blockade and chimerism tolerance): 26 rhesus macaques

G. Cardiovascular disease remains the leading cause of mortality in Western societies. Blood flow to critical vascular beds become stopped or reduced, leading to heart attacks and strokes. Surgical replacement of diseases arteries with artificial substitutes has worked moderately well for larger vessels, but has been problematic for replacing smaller diameter vessels (less than 6mm i.d.) Specific and effective molecular level therapies may represent a promising strategy. In this study, subjects will have carotid artery graft implants , aorto-iliac graft implants, and aortic interposition grafts. Protected contact housing is required for 7-10 days to protect surgical sites. The remaining time, animals will be group housed. Another study will be looking at probes that interfere with thrombogenesis (activation of blood

coagulation, inhibition of platelet activation and inhibition of platelet attachment to injured blood vessel walls). Animals are singly housed to permit repeated access for blood sampling and noninvasive imaging procedures and to protect the surgical access site.

- Evaluation of small vessel prostheses: 34 baboons
- In vivo platelet interactions with adhesive glycoproteins: 28 baboons

H. Some of the animals used under these conditions are in studies of normal control of movement or motion disorders. Monkeys in these studies are trained to do simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. During these periods, monkeys with head appliances may also undergo short-term fixed head restraint to access the appliances for neurophysiologic recording and microdialysis. Administration of the neurotoxin to induce Parkinson's Disease (PD) in macaques causes physical impairments that put such animals at risk of plummeting in the social order and wounding and fight injury from a cage mate. Consequently, animals given ure generally housed singly, but in colony rooms within sight, sound and close physical proximity of other animals of the same species. Likewise, to prevent damage to expensive and sensitive surgically-implanted devices by a conspecific, monkeys may be housed singly, but otherwise within sight and sound of conspecifics.
   - Dystonia in cebus monkeys: 2 capuchin monkeys
   - Muscle re-assembly in MI during skill acquisition: 2 rhesus macaques
   - Therapeutic role of subthalamic nucleus activation: 5 rhesus monkeys
     - Study involves administration of
   - Glutamate in Parkinson's disease: 7 rhesus macaques
     - Study involves administration of
   - A novel model of Parkinson's disease: 1 rhesus macaque

Physical Restraint, Exemptions from Social Housing, and Food or Water Restriction of Nonhuman Primates

Nonhuman primates used under these conditions are in motion disorder studies or studies of brain function. Most of the animals are used to research the cause and treatment of Parkinson's Disease (PD) because of the great similarity of brain function and that Monkeys in these studies usually are given by intracarotid injection, so that only one side of the brain is affected. These monkeys have only slight deficits in precise control of movements on one side of the body and have no substantial movement problems. In general, single housing is only done for a 3 day period immediately after administration of during the time of excretion of the neurotoxin in the feces and urine. Otherwise, monkeys in these studies are housed within sight and sound of other animals of the species and permitting physical contact with a compatible conspecific.

Monkeys in studies requiring food or water restriction are provided *ad libitum* food and water on weekends according to standard husbandry practices. During weekdays, food or water is restricted overnight and in the morning (12-15 hours total) and then food or water is provided to satiety during morning or afternoon test sessions as an inducement to perform video-based tasks. Single housing is necessary to facilitate food or water restriction – otherwise a conspecific would be subjected to unnecessary restriction or food sharing might occur. Monkeys are trained using food or water as an inducement to perform simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. These monkeys, except as indicated, are loosely restrained in a chair or face-mask cage and typically spend 4-6 hours per daily session in the laboratory. During these periods, the monkeys with head appliances may also undergo short-term fixed head restraint to access the appliances for neurophysiologic recording and microdialysis.

In eye movement studies, animals must be awake, alert and comfortably seated. The tasks involve following a smoothly moving or jumping target spot that is rear-projected on a tangent screen. First the animals are fitted with a collar that it will always wear. It is made of a soft nylon material. Animals are then adapted to pole handling and using a primate chair. It takes most animals 4 weeks to reach proficiency. Animals are trained 5 days per week for time periods of 15 minutes to 3 hours.

In cocaine abuse studies, cocaine is scheduled as the consequent event and is sufficiently reinforcing that food and water restrictions are not necessary. However, for self-administration experiments, subjects are trained to sit quietly in standard primate chairs over a 2-4 week period. The pole-and-collar system for handling and training nonhuman primates will facilitate immobilization. Initially, subjects will be immobilized for approximately 20-30 minutes per training session, but over the course of several weeks, the amount of time will increase to from 1 to 4 hours per session. Each subject will be immobilized at least twice per week for 6 weeks. In a related study, changes in sensitivity to the CNS effects of cocaine are assessed after the monoamine neurotransmitter is manipulated pharmacologically. The animals are trained to be seated in a loosely fitting chair during daily (Mon. – Fri.) sessions. The chair is designed to provide minimal skin contact with the animal, and is limited primarily to the waist and buttocks. Typically, experiments are conducted so as to require no more than one hour per day in the apparatus. This minimal restraint provides protection of indwelling catheters used for drug administration and contact with a localized area of the tail for electrical stimulation.

In a study looking at (b)(4) changes in neurochemistry, monkeys will be seated in a standard primate restraint chair. Probes will be inserted bilaterally into the guide cannulae and connected to infusion equipment. The experimental perfusion lasts 5 hours. Animals will typically spend time in the chair 2-3 days per week.

For the evaluation of small vessel prostheses, animals will be immobilized for a short duration with (b)(4) administered IM. This is augmented by oxygen + isoflurane if needed.

Startle reflex testing is done in one study after each monkey is habituated to chair restraint. The sessions are 2-3 times per week for 60 minutes each session. The tests continue for 2 weeks.

These tests may be repeated every 3-4 months to monitor potential developmental changes in emotionality.

Some of the animals used under these conditions are in oculomotor, visual disorders, and visual cortex studies. Monkeys are used because they are capable of the same range of eye movements as humans. Infant monkeys are swaddled in a blanket. Older animals have a chair adjusted for comfort. The chair includes a standard design that allows the animal to sit in a natural position. The animal is allowed to sit in the chair for 5-15 minutes on the first occasion, during which time treats (apple slices, applesauce, etc) are offered to make the chair session a positive experience. Head movements in the animals during visual testing are restricted by an implanted stainless steel receptacle (SSR) on the head. In other studies, head movement is restricted with a custom-fit helmet. In one study, monkeys under 6 months of age have their heads immobilized with Velcro straps. After 6 months, a small, light-weight aluminum halo, of the type used in patients with neck injuries, to fix the head to the chair. Between 6 and 12 months of age, the halos will be removed every 2 weeks for at least 1 week. The duration of the testing sessions is gradually increased from 10-15 minutes to an hour over the course of the first two weeks and up to 3 hours over the course of 3 months. Behavioral training occurs up to five times per week. At any sign of distress (e.g., wiggling in the chair or vocalization) the session is terminated.

Monkeys in these studies have transiently-induced movement disorders and are trained to do simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. During these tasks, these monkeys are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory.

To motivate the animals to work effectively, the first feeding of the day may be reduced or delayed. However, water or food is provided during and immediately after the testing session to meet the daily ration. The total intake of the restricted material, food or water, is recorded daily and the animal's body weight is checked and recorded at least twice weekly to ensure that are being well maintained.

1. Food and/or restricted, but provided during and after laboratory testing sessions, and with short-term periods of restraint:

    - The substantia nigra in movement and movement disorders: 9 rhesus monkeys
    - Influence of subthalamic nucleus on striatal dopamine: 3 rhesus monkeys
    - Pathophysiology of the basal ganglia in Parkinsonism: 4 rhesus monkeys
    - Cortical mechanisms of motor processing: 3 rhesus monkeys
        - Study does not involve MPTP
    - Development of gaze-holding abilities: 8 rhesus macaques
    - Neural control of visual vestibular behavior: 18 rhesus macaques
    - A novel model of Parkinson's disease: 1 rhesus macaque
    - The error signal for postnatal eye growth in the primate: 7 rhesus macaques

2. Short-term physical restraint only:
    - Basal ganglia pathophysiology in dystonia monkeys: A pilot study: 1 capuchin monkey

- Glutamate in Parkinson's disease: 7 rhesus macaques
- PET neuroimaging and cocaine neuropharmacology in monkeys: 20 rhesus macaques
- Development of functional magnetic resonance imaging (MRI) for behavioral studies in nonhuman primates: 8 Rhesus Macaques
- Cocaine use and pharmacotherapy effectiveness in monkeys: 6 Rhesus macaques
- Effects of (b)(4) on extracellular monoamines in rhesus monkeys: 8 rhesus macaques
- In vivo platelet interactions with adhesive glycoproteins: 28 baboons
- Cocaine use and monoamine function in nonhuman primates: 39 squirrel monkeys
- Does brain oxytocin mediate social interactions between juvenile male Macaca mulatta: 31 rhesus macaques
- Evaluation of small vessel prostheses: 34 baboons
- Gene profiling in drug addiction in nonhuman primates: 4 rhesus macaques
- Medications for drug abusers: 17 squirrel monkeys

Food or Water Restriction of Dogs

Following gastric by-pass surgery, dogs are not fed for four days to permit uneventful healing of the stomach. Intravenous fluids are given to maintain hydration. Dietary transition is then done to a soft diet and subsequently to feeding conventional canine diets. Providing fluid needs are met, well-nourished animals easily tolerate several days without food. Current veterinary standards dictate that postoperative fasted animals not be subjected to the risk associated with parenteral administration of nutrients (JAVMA 201: 699-73, 2000).

- Helicobacter pylori infection of the excluded stomach after gastric bypass: 5 dogs

Exemptions from Exercise for Dogs – none

his report is required by law (7 U.S.C. 2143). Failure to report according to the regulations an result in an order to cease and desist and to be subject to penalties as provided for in Section 2150

See reverse side for additional information

Interagency Report Control No 0180-0OA-AM

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

12-03-2001 RCVD

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. CERTIFICATE NUMBER: 57-R-0003
CUSTOMER NUMBER: 896

FORM APPROVI
OMB NO. 0579
0036

2. Headquarter Research Facility *(Name and address, as registered with USDA.)*
Emory University
1440 Clifton Road, NE
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Telephone: (404) 727-7428

REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets necessary.)

FACILITY LOCATIONS (*Sites*)

See Attached

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (*Attach additional sheets if necessary or use APHIS FORM 7023a).*

Animals Covered By the Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments or tests were conducted involving no pain, distress or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surger or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery or tests. (*An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report).*	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
Dogs	25	20	330	0	350
Cats	0	0	99		99
Guinea Pigs	0	49	27		76
Hamsters					0
Rabbits	0	322	399		721
Non-human Primates	153	220	3012	11	3243
Sheep	0	0	13		13
Pigs	0	0	236		236
Other Farm Animals					0
					0
Other Animals	0	1330	160		1490

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during and following actual research, teaching, testing, surgery or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). A summary of all such exceptions is attached to this annual report. In addition to identifying the IACUC-approved exceptions summary includes a brief explanation of the exceptions as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional Official)
I certify that the above is true, correct, and complete (7 U.S.C. Section 2143).

NATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL	DATE SIGNED
		11/29/01

HIS FORM 7023
(G 91)

KCC

Annual Report to USDA
Facility Locations

Peavine Creek Kennels, Emory University
O. Wayne Rollins Research Center, Emory University
Woodruff Memorial Research Building, Emory University
Wesley Woods, Emory University
Dental Building, Emory University
South Clinics (Winship Cancer Center and Eye Center), Emory University
Cell Biology Building, Emory University
Physiology Building, Emory University
Grady Memorial Hospital, Woodruff Extension, Atlanta, GA
West Campus Building, Emory University
Cardiothoracic Research Labs at Crawford Long Hospital, Atlanta, GA
Yerkes Regional Primate Research Center, Emory University
Yerkes Field Station, Lawrenceville, GA

Summary of Studies Listed in Column E

Title: Behavioral Pharmacology of Narcotic Antagonists

- 11 Squirrel Monkeys

Squirrel monkeys are used in drug discrimination studies for studies of in the brain. In these studies, opioid drugs with differing or unknown profiles of receptor interactions are evaluated. The objective is to identify and study those components of drug action that underlie potential for abuse. It should be noted that an alternative species, rats, is used for most of these studies and squirrel monkeys are involved to a lesser extent.

Squirrel monkeys are trained to Monkeys are loosely seated in a primate chair during these studies. During the training phase and as an aversive stimulus to respond during discrimination trials, a 0.5-1.0 second mild electrical stimulus may be delivered to the monkey's tail after 5 seconds from the start of each trial. The monkeys can terminate the trial and prevent the electrical shock by pushing on one of two levers (corresponding to the reference drug or placebo). The monkeys quickly learn to avoid the stimulus by responding during the 5 second period after the start of the trial. After the initial training session, the monkeys rarely, if ever, receive an electrical stimulus. Shocks are never given indiscriminately or without providing the monkey the opportunity, through lever manipulation, to prevent the shock.

Pain-relieving drugs are not used in these studies because any pain experienced will be transient (one second or less) and the animal can take action to avoid all pain (by pushing a lever within 5 seconds of a clear cue). Additionally, pain-relieving drugs, such as narcotics, will confound the pharmacological effects of the opioid compounds studied.

All redactions on this page are pursuant to (b)(4).

Facility 57-R-0003

Exceptions to Regulations and Standards

The following protocols have received IACUC approval for exceptions to standard practices.

Exemptions from Social Enrichment for Nonhuman Primates: Short-term Social Isolation

There are a variety of human diseases (Parkinson's Disease, Huntington's Disease, progressive supranuclear palsy, narcolepsy, and periodic leg movements during sleep) that are associated with uncontrolled movements in sleep that cause injury. Studies described here are on monkeys with Parkinsonism induced by Monkeys are placed in a cage specially designed for behavioral testing and telemetric recording in a room separated from the other monkeys. These monkeys may be maintained in the observation and recording room for a maximum of 7 days and are then returned to their home cage in a colony with other monkeys of the same species. Isolation from other monkeys is necessary in order to permit sleep undisturbed by commotion caused by other monkeys or human traffic in and out of the room. Monkeys under study are instrumented with which telemeter This telemetric approach allows studying sleep behavior in monkeys that are unrestrained.

- State dependent motor control in neurologic disease: 4 Rhesus monkeys

Exemptions from Social Enrichment for Nonhuman Primates: Single-housing in Sight and Sound of Conspecifics

Administration of the neurotoxin to induce Parkinson's Disease (PD) in macaques causes physical impairments that put such animals at risk of plummeting in the social order and wounding and fight injury from a cage mate. Consequently, animals given are generally housed singly, but in colony rooms within sight, sound and close proximity of other animals of the same species. Protocols and numbers of animals listed immediately below may be redundant with other categories o this attachment (i.e., monkeys given in the course of experimentation, may be housed singly, may be food- or water-restricted, and may be subjected to periods of restraint).

- Effects of intrastriatal and intranigral transplantation of fetal mesencephalic tissue in Parkinson monkeys: 20 Rhesus monkeys
- Influence of subthalamic nucleus on striatal dopamine: 2 Rhesus monkeys
- Pathophysiological mechanisms of movement disorders: 1 Rhesus monkey
- Pathophysiology of the basal ganglia in parkinsonism: 3 Rhesus monkeys
- Primate basal ganglia: Functional circuitry: 8 Rhesus monkeys
- The substantia nigra in motion and movement disorders: 7 Rhesus monkeys
- Therapeutic role of subthalamic nucleus inactivation: 2 Rhesus monkeys
- CNS grafting for parkinsonism: 5 Rhesus monkeys
- Sensorimotor transformation in cortical motor areas: 3 Rhesus monkeys

Exemptions from Exercise for Dogs – none.

Food or Water Restriction and/or Restraint of Nonhuman Primates

Some animals used under these conditions are in motion disorder studies or studies of brain function. Most of the monkeys are used to research the cause and treatment of Parkinson's

Disease (PD) because of the great similarity of brain function and that
Monkeys in these studies usually are given MPTP by intracarotid injection, so that only one side of the brain is affected. These monkeys have only slight deficits in precise control of movements on one side of the body and have no substantial movement problems.

Another group of the animals used under these conditions are in oculomotor, visual disorders, and visual cortex studies. Monkeys are used because they are capable of the same range of eye movements as humans. Infant monkeys are swaddled in a blanket and held by a researcher during assessments of ocular/visual development and function. A mild sedative may be administered to reduce head and neck movements. Adult animals are chaired. Ophthalmic examinations under anesthesia are done every 6 months on some of the animals.

Other animals used under these conditions are in cardiovascular disease and vascular thrombosis studies. Pharmacological restraints are used for short duration immobilization for blood draws. Others are trained to wear a jumpsuit that protects the vascular access site, a collar and to accept sitting in the restraining chair for 1-6 hours. Duration of training is 2 weeks minimum, with each daily training session lasting 1-2 hours. If the animals accept the suit during the day (when they can be observed) the suit is left on, initially for 24 hours, then up to 1 week. The animals are checked every other day (short duration immobilization) for appropriate fit of the suit. The animals also will be chaired for 1-3 hours for femoral arteriovenous shunt studies. These studies are performed on animals that have chronic surgically implanted femoral arteriovenous shunts. Each study can last up to 8 hours but usually (99.9%) of all studies last 1-2 hours.
Monkeys in studies requiring food or water restriction are provided *ad libitum* food and water on weekends according to standard husbandry practices. During weekdays, food or water is restricted overnight and in the morning (12-15 hours total) and then food or water is provided to satiety during morning or afternoon test sessions as an inducement to perform video games. Monkeys are trained to perform simple motor tasks such as reaching, touching a target on a video screen, depressing a key to make a video target appear, and controlling a joystick to move a cursor to a target on a video screen. These monkeys, except as indicated, are loosely restrained in a chair and typically spend 4-6 hours per daily session in the laboratory. During these periods, the monkeys with head appliances may also undergo short-term head restraint to access the appliances for neurophysiologic recording and microdialysis. Water or food is provided during and immediately after the testing session to meet the daily ration. Daily baseline weights are obtained from each monkey for five days to determine an averaged baseline weight. The total intake of the restricted material, food or water, is recorded daily and the animal's body weight is checked and recorded at least twice weekly to ensure that they are being well maintained. Studies listed in this category may be redundant with those listed above in social enrichment exemption categories, but are as follows:

1. Food restricted, but provided during and after laboratory testing sessions, and with short-term periods of restraint:
   A. Movement Disorder Studies
      - Cortical mechanisms of motor processing: 6 Rhesus monkeys
        - Study does not involve
      - Pathophysiology of the basal ganglia in parkinsonism: 3 Rhesus monkeys
      - The substantia nigra in motion and movement disorders: 7 Rhesus monkeys
      - Therapeutic role of subthalamic nucleus inactivation: 2 Rhesus monkeys

B. Visual Disorders
- Monkey model for infantile aphakia-amblyopia: 29 Rhesus monkeys
- Observation of visual behavior and ophthalmological examination in normal monkeys: 60 Rhesus monkeys
- A monkey model of late-onset myopia: 4 Rhesus monkeys
- The error signal for postnatal eye growth in the primate: 54 Rhesus monkeys
- Studies of visual processing and smooth eye movements: 85 Rhesus monkeys
- Thalamo-cortical pathways in blindsight: 8 Rhesus monkeys

C. Cardiovascular/Vascular Thrombosis Studies
- Genetically enhanced angioaccess vascular grafts: 60 Baboons
- In vivo platelet interactions with adhesive glycoproteins: 180 Baboons
- Evaluation of small vessel prostheses – 72 Baboons

2. Water restricted, but provided during and after laboratory testing sessions, and with short-term periods of restraint:
   - CNS grafting for parkinsonism: 5 Rhesus monkeys
   - Primate basal ganglia: Functional circuitry: 8 Rhesus monkeys
   - Sensorimotor transformation in cortical motor areas: 3 Rhesus monkeys

3. Food restricted, but provided during and after laboratory testing sessions (no restraint):
   - Effects of intrastriatal and intranigral transplantation of fetal mesencephalic tissue in Parkinson monkeys: 20 Rhesus monkeys

4. Short-term physical restraint only:
   - Basal ganglia pathophysiology in dystonic monkeys: A pilot study: 2 capuchin monkeys
     - Study does not involve (b)(4)
   - Influence of subthalamic nucleus on striatal dopamine: 2 Rhesus monkeys
     - Study does not involve (b)(4)
   - Pathophysiological mechanisms of movement disorders: 1 Rhesus monkey